OSE Immunotherapeutics

Limited Company (*Société anonyme*) with a Board of Directors with a capital of €3,780,220.20

Registered office: 22 Boulevard Benoni Goullin 44200 Nantes

479 457 715 Nantes Trade and Companies Register

2022 UNIVERSAL REGISTRATION DOCUMENT INCLUDING THE ANNUAL FINANCIAL REPORT

This Universal Registration Document has been filed on April 28, 2023, with the AMF, as the competent authority and without its prior approval, in accordance with Article 9 of (EU) Regulation 2017/1129. The Universal Registration Document may be used for the purposes of a public offer of securities or the admission of securities to trading on a regulated market if it is supplemented by a securities note and, where applicable, a summary and its supplement (s). The whole is approved by the AMF in accordance with EU Regulation 2017/1129.

Pursuant to Article 19 of Regulation (EU) No 2017/1129 of the European Parliament and of the Council, the following information is incorporated by reference in this registration document:

- The consolidated financial statements and the corresponding audit reports appearing on pages 190 - 265 of the universal registration document for fiscal year 2021 filed with the AMF on April 15, 22 under No. D22-0298 (https://www.ose-immuno/financial-statements)
- The consolidated financial statements and the corresponding audit reports appearing on pages 173 - 235 of the universal registration document for fiscal year 2020 filed with the AMF on April 15, 2021, under No. D21-0310 (https://www.ose-immuno/financial-statements)

Parts not included in such document(s) are either irrelevant to the investor or covered elsewhere in the registration document or universal registration document.

Copies of this Universal Registration Document are available, on request and free of charge, during normal business hours, at the registered office of OSE Immunotherapeutics, 22 Boulevard Benoni Goullin, 44200 Nantes, and on the Company's website www.ose-immuno.com), as well as on the AMF website (www.amf-france.org).

The information incorporated by reference should be read in accordance with the cross-reference table at the end of this universal registration document. Any information not indicated in this cross-reference table but forming part of the documents incorporated by reference is provided for information purposes only.

WARNING

This Universal Registration Document and the documents incorporated herein by reference, contain information about the Company's objectives and development areas. This information is sometimes identified by the use of the future or conditional tense and by forward-looking terms such as "consider", "envisage", "think", "aim", "expect", "intend", "should", "aspire", "estimate", "believe", "wish", "may", or, where applicable, the negative form of these same terms, or any other variant or similar terminology.

The reader's attention is drawn to the fact that these objectives and development areas depend on circumstances or events whose occurrence or outcome is uncertain.

These objectives and development areas are not historical data and should not be interpreted as guarantees that the facts and data referenced will occur, that assumptions will be correct or that objectives will be achieved. By their very nature, these objectives may not be achieved and the statements or information appearing in this Universal Registration Document may prove to be erroneous, without the Company in any way being obliged to update them, subject to applicable regulations and, in particular, the French Financial Markets Authority's General Regulation.

Investors are advised to give careful consideration to the risk factors described in section 3 of this Universal Registration Document, "Risk factors", before making any investment decisions. The occurrence of some, or all, of these risks is likely to have a negative impact on the Company's business, financial position, net financial income or its objectives. In addition, other risks that the Company has not yet identified or considers immaterial may have the same negative impact and investors may lose all, or part, of their investment.

This Universal Registration Document also contains information about the Company's business as well as the market and industry in which it operates. This information is primarily taken from studies carried out by internal and external sources (analysts' reports, expert studies, industry publications and any other information published by market research companies, public corporations and bodies). The Company believes that this information gives a true and fair picture of the market and the industry in which it operates and faithfully reflects its competitive position. Although this information is considered to be reliable, it has not been independently verified by the Company and the Company cannot guarantee that a third party using different methods to gather, analyze or calculate this market data would obtain the same results. The Company, the Company's direct or indirect shareholders and investment services providers cannot give any assurances or guarantees as to the accuracy of this information.

The global epidemic of the COVID-19 coronavirus continues to evolve rapidly. The extent to which the COVID-19 coronavirus is likely to affect the Company's business and clinical trials will depend on future developments, which cannot be predicted with certainty, such as the ultimate geographic distribution of the disease, its duration, travel restrictions and social distancing measures in the European Union, the United States and other countries, business closures or disruptions and the effectiveness of measures taken in these countries to contain and treat the disease. In addition, the extent of the adverse impact of this epidemic on the financial markets and on the Company's share price is unknown at this time. As of the date of the Universal Registration Document, the global economy is impacted by the epidemic.

* * *

Summary

OSE IMMUNOTHERAPEUTICS IN BRIEF

A strategy based on the development of a clinical portfolio of first-in-class assets in immuno-oncology and immuno-inflammation, and on two innovative preclinical platforms

On October 7, 2022, OSE Immunotherapeutics announced the appointment of Nicolas Poirier as Chief Executive Officer. Throughout his career, Dr. Nicolas Poirier has demonstrated both his expertise as an international scientific leader, pioneering the discovery and development of innovative immunotherapies, and in-depth knowledge of the biotech sector through various strategic leadership roles. He has been instrumental in the development of OSE Immunotherapeutics, notably as the initiator of 5 programs in the Company's portfolio that are now in clinical stage. He also played a major role in the signature of 4 strategic pharmaceutical partnerships for OSE Immunotherapeutics.

OSE Immunotherapeutics is a clinical-stage biotechnology company specializing in therapeutic innovations in immuno-oncology and immuno-inflammation. Its Research and Development platforms are based on its recognized expertise in T lymphocyte cell immunity and myeloid cell immunity. A wealth of experience established in these two fields has enabled the development of leading "First in class" products that the Company develops directly or through partnerships with the pharmaceutical industry actively seeking new therapies.

Clinical stage portfolio

Tedopi®, a T-specific immunotherapy based on highly selected neoepitopes, is being developed in a Phase 3 clinical trial. The product activates T lymphocytes capable of killing tumor cells that they have learned to recognize. This product has obtained significant results versus chemotherapy in "Non-Small Cell Lung Cancer" in patients with secondary resistance after failure of checkpoint inhibitors [Anti PD-(L) 1] where therapeutic need is very important.

Based on positive recommendations from the US Food and Drug Administration (FDA) "Type C" meeting following the European Medicines Agency (EMA) scientific advice, OSE Immunotherapeutics is preparing a new pivotal Phase 3 clinical study to support the regulatory registration of Tedopi® in second line. This confirmatory trial will evaluate Tedopi® versus the standard treatment in second line in HLA-A2 positive patients with advanced non-small cell lung cancer.

Patients can benefit from Tedopi® through compassionate use programs in third or further lines of treatment (post chemotherapy and immunotherapy) currently approved in France, Italy and Spain, confirming thereby the significant medical need for new therapeutic alternatives.

Other Phase 2 clinical trials of Tedopi® in combination are ongoing with international clinical research groups. The Company will capitalize on the clinical results to discuss with the regulatory authorities and to actively prepare the continuation of this development.

OSE-279 is an anti-PD1 antibody that blocks a T lymphocyte brake enabling activation of non-specific T cells in oncology. It is currently in Phase 1/2 clinical trial in advanced solid tumors and lymphomas. It is also the "backbone" component of a platform called BiCKI® for new original bispecific or bifunctional therapies.

OSE-127/S95011, an interleukin-7 receptor antagonist monoclonal antibody involved in the survival of pathogenic T lymphocytes, is being developed in partnership with Servier. Two Phase 2 clinical trials are underway in autoimmune diseases where T lymphocytes are involved, ulcerative colitis (OSE as sponsor) and Sjögren's Syndrome (Servier as sponsor). The completion of patient enrollment in the Phase 2a in primary Sjögren syndrome was announced in November 2022 and the results are expected in 2023.

In addition, preclinical results in certain leukemias, such as acute lymphoblastic leukemias (ALL) were published in December 2021 at the annual meeting of the ASH (American Society of Hematology).

FR 104 (VEL-101), a "First in Class" anti-CD28 monoclonal antibody capable of blocking T lymphocytes, this time pathogenic in transplant and autoimmune diseases. A Phase 1/2 clinical trial is underway in renal transplant (sponsored by the *Centre Hospitalier Universitaire de Nantes*). A license agreement in transplantation with Veloxis Pharmaceuticals, Inc., makes it possible to study a

new subcutaneous formulation in Phase 1 in the United States and to prepare for further development in transplantation with this pharmaceutical player specializing in this field.

BI 765063 (OSE-172), an anti-SIRPα monoclonal antibody, a target expressed on myeloid cells on the SIRPα/CD-47 axis, is developed in partnership with Boehringer Ingelheim in advanced solid tumors. The positive results of the Phase 1 dose escalation clinical trial as a single agent and then in combination with ezabenlimab (Boehringer's PD1 antagonist) have enabled the initiation of two ongoing Phase 1 cohort expansion trials.

Two preclinical platforms

The BiCKI® platform in immuno-oncology, is an anti-PD1 platform merged with innovative immunotherapy targets. Preclinical efficacy studies with BiCKI®-IL-7 were presented at international congresses. This first bifunctional therapy targets PD1 and simultaneously delivers the cytokine IL-7. This product is able to restore the function of exhausted T lymphocytic cells, a frequent cause of clinical escape of anti-PD1. It increases T stem cells capable of reconstituting memory and effector T cells to increase antitumor efficacy.

The Myeloïd platform aims at optimizing the therapeutic potential of myeloid cells in immuno-oncology and immuno-inflammation. In resolving inflammation, OSE-230 is a first agonist antibody to the ChemR23 target, expressed on myeloid cells, and has been developed with the ability to resolve chronic inflammation by driving affected tissues to complete the inflammation program and restore tissue integrity. These results, published preclinically for several chronic inflammatory pathologies, make it a first clinical candidate for a new therapeutic class.

The Company's registered office is based in Nantes, the Company has been listed on Euronext Paris since 2015 and has continued its development mainly through its industrial agreements. The future activities and financing of the Company depend on a combination of factors, OSE Immunotherapeutics should be able to continue to be financed, in particular through existing or future industrial agreements or other financing, if the work in progress proves positive, also taking into account the development of competitive therapies and the regulatory approval of innovations developed at different stages of development.

1 Responsible persons, third-party information, experts' reports and approval from the competent authority

1.1 Person responsible for the Universal Registration Document

Nicolas Poirier

Chief Executive Officer

OSE Immunotherapeutics Registered office: 22 Boulevard Benoni Goullin, 44200 Nantes, France

Telephone: +33 (0)2 28 29 10 10

Email: nicolas.poirier@ose-immuno.com

1.2 Statement by the Person Responsible for the Universal Registration Document

"After having taken all reasonable measures to ensure that this is the case, I hereby certify that the information contained in this Universal Registration Document is, as far as I am aware, accurate and does not omit any material facts.

I hereby certify that, as far as I am aware, the financial statements have been prepared in accordance with applicable accounting standards and give a true and fair picture of the assets and liabilities, financial position and net income of the Company and of all the companies included in its scope of consolidation, and that the management report appearing on page 318 faithfully reflects the business developments, net income and financial position of the Company and of all the companies included in its scope of consolidation and that it describes the main risks and uncertainties faced.

Nantes, April 27, 2023

Nicolas Poirier
Chief Executive Officer

1.3 Statement by a person acting as an expert in respect of this document

None

1.4 Third-party information

On the date of this document, the Company does not have any information sourced from third parties, nor has it received, or been notified of, any expert statements or declarations of interest.

1.5 Approval of the Universal Registration Document

As the Company has had a Registration Document approved by the AMF for at least two consecutive fiscal years and subsequently filed such documents on an annual basis, this Universal Registration Document has been filed without prior approval from the AMF, in accordance with Article 9.3 of EU Regulation 2017/1129 of the European Parliament and of the Council of June 14, 2017. It may, however, be reviewed at a later date by the French Financial Markets Authority, the competent authority, where the latter deems this necessary.

2 Auditors

2.1 Statutory Auditors

Joint Statutory Auditor

Ernst & Young and Others

Represented by Mr. Cédric Garcia

Tour First - 1-2 place des Saisons

92037 Paris La Défense Cedex, France

Start date of first term: appointed by decision of the sole shareholder on April 27, 2012

Duration of current term: six fiscal years from the date of appointment (decision taken by the Combined General Shareholders' Meeting of June 13, 2018)

End date of current term: at the end of the General Shareholders' Meeting called to approve the financial statements for the fiscal year ending on December 31, 2023

Joint Statutory Auditor

SA RBB business advisors

Represented by Mr. Marc Baijot

133 bis rue de l'Université, 75007 Paris, France

Start date of first term: appointed by the General Shareholders' Meeting of September 17, 2014

Duration of current term of office: six fiscal years from the date of appointment (General Shareholders' Meeting of June 16, 2020)

End date of current term of office: at the end of the General Shareholders' Meeting called to approve the financial statements for the fiscal year ended on December 31, 2025

2.2 Information on auditors that have resigned, been removed or not been reappointed

None

3 RISK FACTORS

The Company operates in a constantly changing environment, which involves many risks, some of which are beyond its control.

Investors are advised to consider all the information contained in this Universal Registration Document, including the risk factors described in this chapter, before deciding to acquire or subscribe for shares of the Company.

The risk factors set out in this Universal Registration Document are limited to only those risks that the Company considers, at the date of this document, to be specific to it and/or its securities and that are important for making an informed investment decision, as corroborated by the content of this Universal Registration Document and as may be corroborated by those indicated in a future securities note.

In preparing this document, the Company has assessed the importance of risk factors based on the likelihood of their occurrence and the estimated magnitude of their adverse impact. It has thus categorized the various risks according to its scientific and economic model, namely:

- Risks related to capital requirements: research programs are very capital intensive and without new money, the Company would not be able to pursue all of its programs and projects. Although the Company was able to take advantage of the resources generated by the licensing agreements, it also chose to seize market opportunities by raising €18.6 million from institutional investors at the end of 2020. End of April 2023, the Company also decided to set up a PACEO program with a player recognized on the market as being concerned about the quality of its market operations. This need for additional capital and potential financing on the markets could lead to a further dilution of shareholders.

- Risks related to the development of its drug candidates: the Company is working on drug candidates at the pre-clinical and clinical stages, which implies certain specific risks related to experimental and theoretical research, or to the early phases of verification of the properties of a potential future drug;

- Risks linked to the partnership strategy: the Company currently has three products in partnership (with Boehringer Ingelheim, Servier and Veloxis), which implies various risks inherent in the relationships with its partners and the development phases to be carried out;

- Risks related to marketing drugs: the Company is working towards the future marketing of drug candidates, either within the framework of its partnerships or for products that it could market itself in certain geographic areas; in all cases, this implies obtaining the regulatory approvals necessary for such marketing;

- Risks linked to intellectual property rights: being in a research field, the Company is highly exposed to risks related to the protection of its intellectual property, mainly patents but also other intellectual property;

Risks described in the Universal Registration Document are those identified by the Company as likely to significantly affect its business, its prospects, its financial position, its results or its ability to achieve its objectives.

The Audit Committee thus reviewed the risk mapping prepared by the Company's Management. This chapter, prepared in line with this mapping, was submitted to the Audit Committee at its meeting of April 25, 2023.

The Company highlights the fact that in accordance with article 16 of the Prospectus Regulation n°2017/1129, only the most important risks are listed and the list below is not exhaustive and others risks, currently unknown or, at the date of this Universal Registration Document, considered as unlikely to have a significant negative impact on the Company, its activity, its prospects, its financial position, its results and its development, could exist or might happen.

The table below summarizes the main risks organized according to the five categories described above. Within each category, the residual risks remaining after the implementation of management measures are classified according to the level of criticality (combination of probability of occurrence and estimated impact) assessed during risk mapping. Only risks assessed with a "significant" level of criticality are detailed in this chapter.

Assessment of this « significance » level can be modified at any time, notably in case of new events.

Important Note

As of the date of this Universal Registration Document, the Company considers that it is exposed to a limited risk on its operations due to the Russian-Ukrainian conflict.

However, it does not exclude that a maintenance or an increase in the sanctions put in place against Russia, or a broader extension of the conflict involving other countries may affect the smooth running of its outsourced activities, in particular the conduct of clinical trials and manufacturing operations. Furthermore, the effect of these events on the global financial markets could have an impact in the short term on its ability to obtain financing on the capital markets and, as a result, the conduct of its activities. The Company has thus identified four risks likely to be aggravated by this context: they are indicated by an asterisk (*) in the matrix and the table below, and the circumstances of aggravation are detailed in the corresponding section.

3.1	**Risks linked to the development of our drug candidates**	**Probability of occurrence**	**Estimated impact**
3.1.1	Risks linked to product development	High	High*
3.1.2	Risks linked to the completion of the clinical and preclinical phases of its products in development	High	High*
3.1.3	Risks of sub-contractor default (in particular those linked to clinical study outsourcing and product manufacturing)	High	High
3.1.4	Risk of dependency or operational delay in relation to programs under development	High	Moderate
3.1.5	Risks linked to the immuno-therapeutic approaches selected by the Company	Moderate	High
3.2	**Risks linked to the partnership strategy**		
3.2.1	Risks linked to research and dependency on current and future partnerships	High	High*
3.2.2	Risks linked to potential conflicts could affect the Company's relationship with its licensees	Weak	Moderate
3.3	**Risks linked to marketing**		
3.3.1	Risks linked to obtaining a Marketing Authorization (MA)	High	Moderate
3.3.2	Risks linked to the lack of commercial success of the products	High	Moderate
3.3.3	Risks linked to changes in drug reimbursement policies	High	Moderate
3.4	**Risks linked to intellectual property rights**		
3.4.1	Risks linked to uncertain protection of patents and other intellectual property rights	Moderate	High
3.4.2	Risks linked to legal liability, in particular product liability risks	Moderate	High
3.4.3	Risks linked to patents and intellectual property rights held by third parties	Weak	High
3.5	**Risks linked to capital requirements**		
3.5.1	Risks linked to the financing requirement of the business	High	Critical*
3.5.2	Risks linked to the availability of public grants and research tax credits	Moderate	Moderate
3.5.3	Valuation of intangible assets and impairment tests	Moderate	Moderate

However, the situation described is subject to ongoing changes and may change, even significantly, at any time.

In particular, the situation of global economic instability generated by the Russian-Ukrainian conflict or the loss of confidence in the financial markets could make access to capital more difficult for the Company.

3.1 Risks linked to the development of our drug candidates

OSE Immunotherapeutics is active in the biotechnology sector and in particular in the field of immunotherapy. The Company develops neoepitopes that specifically stimulate T lymphocytes (small peptides of interest derived from tumor antigens - Tedopi®) and biotherapies that are agonists or antagonists of immunological targets that block or activate immune responses. It thus combines research and development expertise in the fields of immunoregulation and immune activation, with complementary teams developing projects at the start-up and later clinical stages.

3.1.1 Risks linked to product development

The Company's ability to make judicious strategic and scientific choices, such as the choice of an indication for a given drug, the choice of a partner or the choice of a drug at various stages of development, is essential to ensure the Company's continued operations. The organization of the various management bodies, as well as the use of external expertise, is designed to limit risk and thus optimize decision-making.

The Company has preclinical and clinical programs leading to the eventual marketing of therapeutic options in immuno-oncology and immuno-inflammation. Product development is a long and costly process that takes place in several phases with uncertain outcomes. The objective is to demonstrate the therapeutic benefit provided by the product with good tolerance for one or more given indications, compared to existing products or products in development.

Each clinical trial in human is subject to prior approval and/or post-approval and all development data is evaluated by the competent regulatory authorities, according to its development plan (in particular the EMA - European Medicines Agency, and the FDA - Food & Drug Administration).

These regulatory authorities could prevent the Company from undertaking clinical trials or pursuing clinical development if it is found that the data submitted have not been produced in compliance with applicable regulations or if they consider that the relationship between the expected benefits of the product and its potential risks is insufficient to justify the trial.

In addition, the Company may elect, or the regulatory authorities may require the Company, to suspend or terminate clinical trials if patients are exposed to unexpected and serious risks. Deaths and other adverse events, whether or not related to the treatment under trial, could occur and require the Company to delay or stop the trial and thus prevent the Company from continuing the development of its product in the targeted indication or in other indications.

In addition, the conduct of clinical trials and the ability to recruit patients into these trials depend on many factors such as:

- The nature of the targeted indication;
- The number of patients affected by the targeted pathology and eligible for treatment;
- The evolution of the pathology of the patients included in the trial;
- The existence of other clinical trials involving the same population;
- The ability to convince clinical investigators to recruit patients into a trial;
- The ability to recruit and treat patients at a given clinical investigation center;
- Availability of sufficient quantities of the product under study.
- The number of patients who can and want to participate in a clinical trial is limited and recruitment can be difficult and slow, leading to excessive delays in conducting clinical trials. In order to overcome this difficulty, the Company may have to increase the number of clinical centers or service providers, which increases the complexity of the follow-up and the cost of the trial.

In addition, the COVID-19 strain of coronavirus, which is spreading in many countries, including France, or an equivalent crisis, could lead to extend the duration of ongoing clinical trials or, more generally, disruptions that could have a material adverse effect on the Company's business and its clinical trials, in particular:

- Delays or difficulties in recruiting patients for its clinical trials;
- Delays or difficulties in launching clinical sites, including difficulties in recruiting investigators and clinical site staff;
- Diversion of healthcare resources from the conduct of clinical trials, including the diversion of hospitals used as sites for the Company's clinical trials and of hospital personnel supporting the conduct of such clinical trials;

- The interruption of key clinical trial-related activities, such as the monitoring of clinical trial sites, due to travel restrictions imposed or recommended by federal or state authorities, employers or others;
- Limitations of human resources that would normally be focused on conducting the Company's clinical trials, in particular due to disease amongst employees or members of their families or the desire of employees to avoid all contact with significant groups of persons.

In addition to the risks listed above, and in the context of clinical trials conducted by the Company in countries that are experiencing an increased impact from the COVID-19 coronavirus, the Company could also experience the following adverse impacts:

- Delays in obtaining authorizations from the administrative authorities necessary to launch the clinical trials planned by the Company;
- Delays in the receipt by clinical sites of supplies and equipment required to conduct the Company's clinical trials;
- The interruption of global maritime trade that could impact the transportation of clinical trial materials, such as investigational drugs and drugs used as the basis for comparison in the Company's clinical trials;
- Changes in local regulations as a result of the COVID-19 coronavirus outbreak, which could require the Company to modify the terms of its clinical trials, which could result in unforeseen costs or even the interruption of such trials;
- Delays in necessary interactions with local authorities, ethics committees or other key agencies and third-party contractors due to human resource limitations or forced leaves of absence of government employees;
- The refusal of regulatory authorities to accept data from clinical trials conducted in these affected geographic areas.

These same disruptions could materialize in the event of an outbreak of another contagious disease or another strain of a virus.

For trials for which all or part of the execution is entrusted to service providers, the Company depends on their ability to perform their services under the agreed conditions and within the agreed deadlines. The remoteness or geographical distribution of clinical investigation centers may raise operational and logistical difficulties, which could result in costs and delays. The disruptions related to the COVID-19 health crisis described above or an equivalent crisis could similarly affect the Company's service providers (see also 3.1.3 below).

Clinical trials are expensive. If the results of these tests are not satisfactory or conclusive, the Company may have to choose between abandoning the program, resulting in the loss of the financial investment and the corresponding time, or continuing it, with no guarantee that the additional expenses incurred will be successful.

Many pharmaceutical companies have experienced significant setbacks in clinical trials, including at an advanced stage or during the regulatory approval process, even after promising results.

The Company's inability to conduct and successfully complete clinical trials could have a material adverse effect on its business, outlook, financial position, income and development. Although these risks are common to all players in the pharmaceutical industry, they are all the more significant for the Company given its limited financial and human resources capacities.

In addition, the communication of erroneous interim or final results of clinical studies could have a significant impact on the Company's reputation with key audiences such as the scientific and medical world, pharmaceutical companies or financial markets. The definition and implementation of a communication plan that includes a process for reviewing outgoing data limits this risk.

This risk is particularly sensitive to geopolitical risks, in particular with regard to access to raw materials at reasonable costs, or the increase in the cost of energy. A worsening of the health crisis situation in 2022 as well as a maintenance or an increase in the economic sanctions put in place against Russia in the context of the Russian-Ukrainian conflict, or a wider extension of the conflict involving other countries could amplify this risk significantly. The Company considers that it is currently indirectly exposed for its trial 127. These external factors could have a significant short-term impact on the Company's ability to complete its clinical trials and, therefore, on the conduct of its business.

3.1.2 Risks linked to the completion of the clinical and preclinical phases of its products in development

The risks encountered are linked to the risks of research and development of innovative products – neoepitopes (small selective peptides), agonist or antagonist monoclonal or bispecific antibodies, in immuno-oncology and in immuno-inflammatory diseases.

The development risks for these biotechnology products are linked to the development stages to be completed: humanization of the antibody and bioproduction - pharmaceutical development stages - pharmaco-toxicology stages - various clinical stages in order to complete a registration dossier in a specific clinical indication.

IN CLINICAL PHASE

PROPRIETARY PRODUCTS

- **TEDOPI®** (immunotherapy activating tumor specific T-cells, off-the-shelf, neoepitope-based): this therapeutic vaccine is the Company's most advanced product. Tedopi® has shown positive Phase 3 results (Atalante-1) in non-small cell lung cancer (NSCLC) in patients with secondary resistance after failure to immune checkpoint inhibitors. Authorizations for compassionate use* of Tedopi® in NSCLC have been granted by Health Agencies in Europe - in France, Italy and Spain - in third line post-chemotherapy and immunotherapy.

  Regulatory Agencies in the US and in Europe gave positive outcomes for a confirmatory Phase 3 clinical trial in NSCLC in second line treatment, in secondary resistance to checkpoint inhibitors.

  The French National Authority for Health issued a negative decision on the cohort early access program in third line treatment. Patient inclusion in the previous phase 3 (Atalante-1) was suspended due to the COVID crisis, and the consecutive primary analysis has been conducted based on stratification criteria and on a biological rationale in a population of interest with secondary resistance. Moreover, patients can benefit from Tedopi® through compassionate use programs in third or further lines of treatment (post chemotherapy and immunotherapy) currently approved in France, Italy and Spain.

  Other clinical trials, sponsored by oncoly clinical group, are conducted to evaluate Tedopi® in combination in solid tumors (non-small cell lung cancer, pancreatic cancer, ovarian cancer).

The main risk associated with Tedopi® is related to the continuation of its clinical development towards a registration, based on the results from the Phase 3 trial stopped due to the COVID-19 pandemic showing a significantly improved global survival versus chemotherapy, with a benefit/risk ratio in favour of Tedopi® observed in a particular population identified, in third line treatment and in secondary resistance to checkpoint inhibitors. A confirmatory Phase 3 trial is planned to be conducted in a population of metastatic lung cancer patients in second line treatment, in secondary resistance after failure of a first line of chemotherapy combined with a checkpoint inhibitor and in escape from this latter treatment.

- **OSE-279** is a humanized anti-PD1 monoclonal antibody blocking both PD-L1 and PD-L2, the ligands of PD1 overexpressed by tumor cells and tumor microenvironment.

  Since December 2022, OSE-279 is under a Phase 1/2 clinical trial in patients with advanced solid tumors or lymphomas.

The risks associated with OSE-279 are linked to the results of its clinical development.

PRODUCTS DEVELOPPED IN PARTNERSHIP

- **OSE-127/S95011**, a humanized monoclonal antibody IL-7 receptor antagonist, is developed in partnership with Servier. A Phase 2 clinical trial is ongoing in ulcerative colitis (sponsorship OSE Immunotherapeutics). An independent Phase 2 is conducted in parallel in the primary Sjögren Syndrome (sponsorship Servier): completion of enrollment was announced in November 2022 and the results are expected in 2023.

  Preclinical studies are ongoing in acute lymphoblastic leukemia.

The risks associated with OSE-127/S95011 are linked to the results of its clinical development and its continued development within the framework of a partnership.

- **FR104** is an immunomodulator consisting of an optimized monoclonal antibody fragment targeting the CD28 receptor, a key element in transplantation. FR104 is developed in partnership with Veloxis Pharmaceuticals, Inc., in transplantation who is sponsor of a Phase 1 clinical trial is conducted in the United States.

In parallel, a Phase 1/2 clinical trial is carried out at the "Centre Hospitalier Universitaire de Nantes" in renal transplantation.

The risks on FR104 are related to the results of its clinical development in renal transplantation. The risks on FR104 in transplantation are transferred to Veloxis under the licensing agreement, with OSE providing the necessary first doses (for compensation) and benefiting from potential milestones according to the different phases of the development, registration and marketing of the product.

- **BI 765063 (OSE-172)** is a monoclonal anti-SIRPα antibody on the axis SIRPα/CD47 axis developed in partnership with Boehringer Ingelheim in advanced solid tumors. The escalation dose Phase 1 in monotherapy and in combination (step 1), in particular with the anti-PD1 antibody ezabenlimab, has shown positive results in advanced solid tumors. The expansion Phase 2 (step 2) is ongoing in patients with microsatellite stable colorectal or endometrium advanced cancer. In parallel, an international Phase 1b trial of BI 765063 in combination with ezabenlimab or with other drugs is ongoing (under the sponsorship of Boehringer Ingelheim) in metastatic or in relapse head and neck cancer and in hepatocellular carcinoma.

The risks associated with BI 765063 are linked to the results of its clinical development and its continued development within the framework of a partnership.

IN PRECLINICAL PHASE

MYELOID PLATFORM: this platform aims at optimizing the therapeutic potential of myeloid cells in immuno-oncology and immuno-inflammation (I&I).

- **OSE-230** (agonist antibody against ChemR23) is the most advanced candidate generated by the platform, with the potential to resolve chronic inflammation by driving affected tissues to tissue integrity.

- **CLEC-1** ((among CLR receptors-C-type lectin receptors) is a myeloid checkpoint and a new therapeutic target of interest in immuno-oncology.

BICKI® PLATFORM, focused on immuno-oncology (IO) is a bispecific fusion protein platform built on the key backbone component of anti-PD1 combined with a new immunotherapy target to increase anti-tumor efficacy. **BICKI®-IL-7** is the most advanced BiCKI® candidate targeting anti-PD1xIL-7.

There is a risk that evaluation of these products in preclinical development will not allow their clinical development to be continued.

RESEARCH & DEVELOPMENT

In R&D, the Company is developing other agonist or antagonist monoclonal or bifunctional antibodies targeting new receptors of interest in immuno-oncology, autoimmune and inflammatory diseases.

The risks associated with these products are the usual risks of research and development.

To identify and validate new therapeutic targets, the Company works in close collaboration with academic and university research centers.

The risks associated with this academic collaboration are the usual risks associated with research.

3.1.3 Risks of sub-contractor default (in particular those linked to clinical study outsourcing and product manufacturing)

The Company uses subcontracting as part of its activities and in particular to conduct ongoing clinical trials covering the different activities involved (trial monitoring, patient recruitment, data base follow-up, statistical analysis, pharmacovigilance, translational data analysis, etc.) and in particular: in the Phase 3 trial with Tedopi® in NSCLC, whose Step-1 and Step-2 were positive in secondary resistance, in the trials sponsored by clinical investigator groups: the Phase 2 with Tedopi® in therapeutic combination in lung

cancer (sponsor FoRT) , the Phase 2 trial with Tedopi® in pancreatic cancer (sponsor GERCOR), the Phase 2 trial with Tedopi® in combination in ovarian cancer (sponsor ARCAGY-GINECO), the Phase 1 and expansion Phase 1 trial of BI 765063 (OSE-172) for advanced solid tumors, the Phase 2 trial of OSE-127/S95011 for ulcerative colitis. The Company also outsources to specialized companies the production of clinical batches of these products in clinical development stage.

The Company utilizes subcontractors to perform certain tasks including the management of these clinical trials or the manufacturing of clinical slots and development of complex procedures that must be highly monitored. If these subcontractors fail to carry out their tasks, deliver inadequate performance, or are slower than required or usual, the Company will not be able to successfully produce, develop, or market its products.

The main subcontractors in charge of managing the clinical trials or in charge of the manufacturing of clinical batches are experts in their area and their selection is based on calls for proposal.

In addition, dependency on respect to third-party manufacturers presents additional risks that the Company would not face if it manufactured its own products, i.e.:

- Non-compliance of these third parties with regulatory standards and quality control;
- Breach of agreements by these third parties;
- Termination or non-renewal of these agreements for reasons beyond its control;
- Bankruptcy of subcontractors, resulting in suspension of services, not allowing the Company the time to find an alternative solution.

If the products manufactured by third-party suppliers are non-compliant with regulatory standards, sanctions could be imposed on the Company. These sanctions could include fines, injunctions, civil penalties, refusal by regulatory organizations to grant Marketing Authorization for its products, delays, suspension or withdrawal of authorizations, license revocations, seizures or product recalls, operating restrictions and legal proceedings, all of which could have a considerable adverse impact on the Company's business.

Moreover, the agreements entered into with subcontractors usually contain clauses that limit their liability, which means that the Company could possibly not obtain full compensation for any damages that it could suffer as a result of the violation of these commitments by the subcontractors in question.

In the event that the Company changes manufacturers for its products, it would be required to undergo re-approval of the new manufacturer's processes and procedures in accordance with applicable Good Manufacturing Practices ("GMP") standards. This re-approval could be costly, time-consuming and require the attention of its most qualified staff. If re-approval is not successful, the Company could be forced to look for another supplier, which could delay the production, development, and marketing of its products and increase their manufacturing costs.

Such events could have a material adverse impact on the Company's business, prospects, financial position, results, and development. In order to limit these risks, the Company pays the greatest attention to the importance of its relationships and communications with its subcontractors. Sub-contractors are evaluated and must undergo strict audits by regulatory agencies and by the Company.

In addition, the Company depends on third parties to supply it with certain biological products (including peptides/adjuvants) needed to manufacture its drugs.

Even if the Company's policy is to build long-term contractual relationships with its strategic suppliers, and rely on large suppliers in the pharmaceutical industry, its provisioning of certain biological products could be limited, interrupted, or restricted. In addition, in such a case, the Company might not be able to find acceptable quality laboratory products from other suppliers, in the necessary volumes or at an acceptable cost. If its key suppliers or manufacturers are unreliable or its supply of products or materials is reduced or interrupted, it might be unable to develop, produce, and then market its products in a timely and competitive manner.

If the Company encounters difficulties in the provisioning of its biological products or is unable to maintain its subcontracting agreements, sign new agreements, or obtain the biological products necessary for the development and manufacturing of its products in the future, its business, prospects, financial position, results, and development could be materially impacted.

Finally, the current COVID-19 health crisis, a war such as the one between Ukraine and Russia, the appearance of another contagious disease or another strain of a virus could also create disruptions among the Company's subcontractors that could have a material adverse impact on the Company's business and its clinical trials, in particular:

- Delays or difficulties in provisioning, manufacturing, or transport of biological products, supplies, or materials necessary to conduct the Company's clinical trials;

- Diversion of resources to produce complex procedures;
- Changes in regulatory and quality-control standards applicable to subcontractors, making their services more time-consuming, costly or even impossible; and
- Limitations of human resources that would normally be the Company's responsibility, in particular due to diseased employees or members of their families or the desire of employees to avoid all contact with significant groups of persons.

It is difficult to predict the evolution of the epidemic and how restrictions on individuals or additional government measures might impact future patient recruitment at sites participating in ongoing studies.

For patients who are already participating in the various clinical trials, there is a risk that some participants may not be able to attend the follow-up visits prescribed by the study protocol due to government or local restrictions. The Company seeks to mitigate this risk by using teleconferences and videoconferences as part of the monitoring of clinical studies with, in particular, clinical investigators. In addition, the pandemic could cause delays in preclinical studies.

3.1.4 Risk of dependency or operational delay in relation to programs under development

OSE Immunotherapeutics is a biotechnology company focused on developing innovative immunotherapies acting on activator or suppressor cells to stimulate or inhibit the immune response for immuno-oncology and immuno-inflammation. It develops next generation products optimized to better target the key receptors of the immune response's activation or regulation, allowing the therapeutic effect to be sustained over time. The Company aims to become a leading international player in the field of immunotherapy with an innovative technology base and expertise in the selection and optimization of receptor targeting that will lead to significant therapeutic advances.

It masters the technologies of immunoregulation and immunoactivation of the immune system with complementary international teams and expertise involved in the research and optimization of drug candidates, pharmaceutical development, clinical development and registration.

The Company has a diversified portfolio of advanced immunotherapy products ranging from Phase 3 to Phase 1 clinical and preclinical development. These next generation products have independent development risks and could be attractive to different players in the pharmaceutical industry. They may be subject to early or late licensing for specific regions and/or with pharmaceutical partners interested in one of the clinical areas targeted by the Company (immuno-oncology and immuno-inflammation).

Research and development programs aimed at identifying new candidate products require significant technical, financial and human resources. While research programs may initially show promise in identifying potential candidate products, there can be no assurance that such programs will be successful in generating products suitable for clinical development that could attract the interest of potential partners, in particular because of the following factors:

The research method used may not identify potential candidate products;

Or the candidate products could, as a result of new studies or clinical trials, be difficult to produce, ineffective, unstable, have dangerous side effects, undifferentiated properties, or other characteristics suggesting their likely ineffectiveness or potential harm.

If the Company were unable to develop these innovative products for the various immunological targets identified in its research and development programs, it would encounter difficulties in finding new partners, and its business, financial position, result, development and medium- and long-term outlook would be significantly impacted.

The development of a drug requires the involvement of highly qualified personnel. The departure of research and development experts could present a risk to the Company with a possible delay in development before the recruitment of key complementary skills.

The future success of the Company and its ability to generate long-term revenues will depend on the successful development as well as the commercial success of its activating or regulatory immunotherapy products developed in immuno-oncology and immuno-inflammation, and in particular on the occurrence of numerous factors, such as:

IN IMMUNO-ONCOLOGY

- **Tedopi®**: from the positive final results of Phase 3 in lung cancer after failure of a checkpoint inhibitor (published at the ESMO - European Society for Medical Oncology - in September 2021 and at the ASCO – American Society of Clinical Oncology – in 2022), OSE Immunotherapeutics is preparing a Phase 3 pivotal confirmatory clinical trial to support the regulatory registration of Tedopi® as a new standard of care for the treatment of advanced or metastatic NSCLC in secondary resistance after failure to an immune checkpoint inhibitor treatment. As part of a 'Type C' meeting, the US Food and Drug Administration (FDA) has issued positive recommendations following the European Medicines Agency (EMA) scientific advice for the confirmatory trial in second line treatment.

  The 3 following trials are investigator group sponsored and the Company provides a financial and/or technical support without being the sponsor: the successful completion of the ongoing Phase 2 clinical trial of Tedopi® in combination with FOLFIRI chemotherapy in pancreatic cancer versus FOLFIRI chemotherapy (trial conducted under the sponsorship of GERCOR); the successful completion of the Phase 2 clinical trial of Tedopi® as maintenance treatment alone or in combination with the anti-PD1 drug Keytruda® (pembrolizumab) versus the reference treatment in patients with platinum-sensitive recurrent ovarian cancer whose disease is controlled after platinum-based chemotherapy (trial conducted under the sponsorship of ARCAGY-GINECO); the successful completion of the Phase 2 clinical trial evaluating Tedopi® in combination with Opdivo® (nivolumab) in non-small cell lung cancer (trial sponsored by the FoRT Foundation).

- **OSE-279**: a Phase 1/2 clinical trial started in December 2022 to evaluate OSE-279, a high affinity anti-PD1 blocking monoclonal antibody, in patients with advanced solid tumors or lymphomas. This first-in-human open label Phase 1/2 dose escalation and expansion study aims to determine the Maximum Tolerated Dose and/or the recommended Phase 2 dose of OSE-279 as a monotherapy in advanced solid tumors or lymphomas.

- **BI 765063 (OSE-172)**: this program, developed under an exclusive worldwide collaboration and licensing agreement with Boehringer Ingelheim Internal GmbH, will have to successfully complete its ongoing Phase 1 clinical trial in advanced solid tumors and the subsequent steps of its clinical development in immuno-oncology; The data presented in 2021 at the ASCO (American Society of Clinical Oncology) and ESMO (European Society for Medical Oncology) conferences, resulting from the dose escalation (step 1) of the trial, showed initial signs of clinical efficacy of BI 765063 in combination with anti-PD1 BI 754091 in patients with stable microsatellite tumors (MSS). Anti-PD1 monotherapy treatments have shown limited activity in these MSS patients, whose medical need is very high. The trial is currently recruiting MSS advanced colorectal and advanced endometrium cancer patients in the expansion of Phase 1 trial (Step 2).

- **CLEC-1, BiCKI®**: the continuation or not of the development of these products will depend on the results of their preclinical development steps to lead them to a clinical program in immuno-oncology.

IN IMMUNO-INFLAMMATION

- **FR104**: in the field of transplantation, a Phase 1 clinical trial, sponsored and conducted by Veloxis Pharmaceuticals, Inc., started in May 2022 in the United States in the prophylaxis of acute rejection in solid organ transplant recipients. In parallel, a Phase 1/2 clinical trial, sponsored by the Nantes Hospital Center with the support of the Company, is conducted in renal transplant. OSE Immunotherapeutics has retained all rights to develop FR104 in autoimmune diseases, based on positive Phase 1 clinical results in healthy volunteers.

- **OSE-127/S95011**: this program, developed under the 2-step licensing option with Servier, after successfully completing its Phase 1 clinical trial to evaluate its potential in autoimmune inflammatory diseases, will have to successfully complete the Phase 2 clinical trial step, with priority in Sjögren's Syndrome (Phase 2a led by Servier), or in ulcerative colitis (Phase 2 led by OSE Immunotherapeutics), before this program can be supported by Servier.

- **OSE-230:** the continuation or not of the development will depend on the results of the preclinical development steps to lead OSE-230 towards a clinical program in the resolution of the inflammation.

- For research and development programs on other products developed by the Company, the establishment of partnerships and/or licensing agreements;

- Marketing Authorization ("MA") granted or not by the regulatory authorities;
- Production on an industrial scale and in sufficient quantities of pharmaceutical batches of constant and reproducible quality;
- The acceptance or non-acceptance of the Company's products by the medical community, healthcare prescribers and third-party payers (such as social security systems), and their effective commercial success.

Thus, the most common risks encountered are the following:

- In general, as with any new drug development, there is a significant risk if the lack of efficacy of the product is proven, or if serious adverse events occur, which would have a negative impact on the outcome of the study. Similarly, the project may not succeed if the number of patients admitted to the clinical studies is insufficient to conclude efficacy. In addition, unforeseen risks of intolerance, or changes in applicable regulatory requirements could affect the timing and nature of clinical development activities, the relative costs and the timing of payments contingent upon completion of the various phases and the reimbursement of expenses.
- If the Company's products were to prove ineffective or have unacceptable side effects, it would be impossible to market them, which could have a material adverse effect on the Company's business or outlook, financial position, income and development.
- The risk linked to the failure to develop its products is highly related to the stage of maturity of the drug and is necessarily inherent to the Company's business. For the development of the drug in Phase 3 in lung cancer, the Company believes that there is a lower risk in Phase 3 (compared to Phase 2 projects) of not reaching the marketing authorization stage.
- For Tedopi®, regulatory authorizations may not be obtained, may be delayed pending new clinical trials, or may only be obtained under more restrictive conditions.
- The current COVID-19 health crisis, the appearance of another contagious disease or another strain of a virus leading to quarantine, the total or partial paralysis of the economy and/or the hospital system in any form whatsoever, particularly in the countries in which the Company is conducting or planning to conduct clinical trials, could lead to a suspension or even a complete halt in recruitment, which could jeopardize the initial development strategy of the product; or delay the conduct of clinical trials as such or a delay in the regulatory review by the competent authorities.
- Existing signed pharmaceutical partners may decide not to complete the development and marketing of candidate drugs due to internal priorities or may not have adequate resources to complete them.
- The exclusive property rights of third parties could prevent the Company and its partners from marketing the candidate drugs.
- Authorized products may not find their place on the market and/or be limited in their selling price.
- In such a case, the estimates made on the business outlook offered by the market could turn out to be too optimistic.
- In the absence of successful development, marketing authorization or commercialization of its drugs, the Company would be unable to generate significant revenue. If development programs are delayed, the Company may be required to raise additional capital or to reduce or discontinue, in whole or in part, its operations, research projects or development programs.

3.1.5 Risks linked to the immuno-therapeutic approaches selected by the Company

The Company develops agonist or antagonist immunotherapy products used to activate or regulate the immune system. They are intended to fight against cancer and immune diseases linked to immuno-inflammatory diseases and transplantation.

IN IMMUNO-ONCOLOGY

As of the date of this Universal Registration Document, there are several registered anti-cancer immunotherapy products on the market.

The first immunotherapy products against cancer are checkpoint inhibitors (anti-CTLA4 or anti-PD-(L)1) activating T cells while releasing the brakes (Yervoy® BMS, Opdivo® BMS, Keytruda® Merck, Tecentriq® Roche, Imfinzi® AstraZeneca, Bavencio® Merck Serono, Jemperli® GSK, Libtayo® Regeneron and others of that type registered or being registered).

A therapeutic vaccine is also registered in prostate cancer, Provenge®.

The first T specific immune activation product, Provenge®, has been registered on the market as a cell therapy product against prostate cancer. It was authorized in the United States in 2010 (Provenge® or sipuleucel-T, developed by the US company, Dendreon, subsequently acquired by the pharmaceutical company, Valeant).

Recently, a personalized therapeutic vaccine (Moderna) showed convincing results in a Phase 2b trial in combination with an anti-PD1 checkpoint inhibitor (KEYNOTE-942/mRNA-4157-P201 - trial number NCT03897881) in adjuvant treatment in patients with melanoma at high risk of recurrence, after complete resection; this trial has allowed the designation of "breakthrough therapy" by the FDA, a first key step for an accelerated registration of this product with an additional phase 3 planned. In this melanoma trial, the messenger RNA-based cancer vaccine (mRNA-4157/V940 encoding up to 34 neoantigens) was combined with pembrolizumab (Keytruda®). This combination showed clinically significant improvement of the trial's primary endpoint, recurrence-free survival (RFS) compared to pembrolizumab administered alone. The therapeutic vaccine 'mRNA-4157/V940' combined with pembrolizumab significantly reduced the risk of recurrence or death by 44% compared to monotherapy with pembrolizumab alone (HR, 0.56; 95% confidence interval, 0 .31-1.08; p=0.0266).

Checkpoint inhibitors acting on T lymphocytes

A new class of products called checkpoint inhibitors (non-specifically removing the blocking of cytotoxic T cells) has also entered the market. Checkpoint inhibitors were first registered for melanoma since 2011, then for lung cancer from 2014 to 2018 and for other indications.

Yervoy® (ipilimumab, BMS and ONO): this first entry is a monoclonal antibody (preventing the immunosuppressive inhibition of T lymphocytes called CTLA4). It has been registered worldwide for metastatic melanoma since 2011. A combination of Yervoy® and Opdivo® was authorized for a special type of melanoma (compared with BRAF); these two products were already registered for this indication. In 2018, the product was registered in combination with nivolumab (Opdivo®) in metastatic colorectal cancer and in first-line treatment of renal cancer.

Opdivo® (nivolumab, BMS and ONO): a monoclonal antibody/checkpoint inhibitor acting on as a brake on other T lymphocytes called PD1. First marketing authorization: December 2014 (metastatic melanoma). Since then, Opdivo® has been registered in metastatic non-small cell lung cancer (NSCLC) (in second-line treatment in 2015, in first-line treatment in 2020, in neoadjuvant treatment in 2022), (2015), renal cancer (2015), Hodgkin's lymphoma (2016), head and neck cancer (2016), bladder cancer or urothelial carcinoma (2017), metastatic colorectal cancer (MSH-H or dMMR) (2017), hepatocellular carcinoma (2017). In 2018, the product was registered in combination with ipilimumab (Yervoy®) in metastatic colorectal cancer and in first-line therapy in renal cancer. In 2022, two Opdivo®-based regimens were approved as first-line treatments for unresectable advanced or metastatic esophageal squamous cell carcinoma.

Keytruda® (pembrolizumab, Merck & Co.): second monoclonal antibody targeting the same PD1 inhibitor. First marketing authorization: in 2014 in metastatic melanoma. Since then, Keytruda® has been registered in non-small cell lung cancer (NSCLC)) (in second-line treatment in 2015, in first-line treatment in 2019), head and neck cancer (2016), Hodgkin's lymphoma (2017), bladder cancer or urothelial carcinoma (2017), gastric cancer or gastro esophageal junction cancer (2017), cervical cancer (2018), diffuse large B cell lymphoma (June 2018), hepatocellular carcinoma (2018), Merkel cell carcinoma (an aggressive skin tumor) (2018), renal cancer (2019), esophageal cancer (2019) and endometrial cancer (2019).

After registration in 2015 as a second-line therapy for patients suffering from metastatic non-small cell lung cancer (NSCLC) with a PD1 biomarker expression, in October 2016, Keytruda® was registered in first-line therapy in NSCLC for patients expressing the PD1 marker (PD-L1 expression over 50% at tumor level). In May 2017, Keytruda® obtained its conditional registration in first-line therapy (in combination with pemetrexed and carboplatin) in NSCLC, whatever the PD-L1 expression. In August 2018, Keytruda® was registered in first-line therapy (in combination with pemetrexed and platinum-based chemotherapy) in metastatic non-epithelial NSCLC without tumor-genomic aberration of the EGFR or ALK gene. In October of the same year, it was registered in first-line therapy (in combination with carboplatin and paclitaxel) in NSCLC, whatever the PD-L1 expression. In April 2019, the product was registered in first-line monotherapy for stage III NSCLC (PD-L1 proportion expressed at over 1% at the tumor level). In January 2023, the Food & Drug Administration approved Keytruda® as adjuvant treatment following surgical resection and platinum-based chemotherapy for patients with stage IB (T2a ≥4 centimeters), II, or IIIA Non-Small Cell Lung Cancer (NSCLC).

Tecentriq® (atezolizumab, Genentech - Roche): designed to target the PD-L1 protein (a PD1 ligand acting on the same pathway as T lymphocyte inhibitors), was approved in the United States for bladder cancer in May 2016, with a companion test to identify PD-L1 positive patients (Ventana PD-L1-SP 142 assay). In October 2016, this product was registered for the treatment of lung cancer as a second-line therapy for patients suffering from metastatic non-small cell lung cancer (NSCLC) whose disease has progressed

during or after platinum-based chemotherapy, and during an appropriate targeted treatment in the presence of a tumor with EGFR or ALK gene mutation. In December 2018, Tecentriq® obtained its registration as a first-line therapy for metastatic non-epithelial NSCLC in combination with Avastin® and chemotherapy. In March 2019, the product was registered in metastatic triple negative breast cancer and in first-line therapy of small cell lung cancer. In 2020, it was registered in combination with Avastin® for hepatocellular carcinoma. In October 2021, Tecentriq® received registration as an adjuvant therapy after surgery and platinum-based chemotherapy in NSCLC in stage II-IIIA patients with tumor expression of PD-L1 ≥ 1%. In December 2022, Tecentriq® was approved in the treatment of adult and pediatric patients two years of age and older with rare unresectable or metastatic alveolar soft part sarcoma (ASPS).

Bavencio® (avelumab, Merck Darmstadt or EMD Serono in collaboration with Pfizer - Javelin program) is a monoclonal antibody targeting the anti-PD-L1 target. This antibody is an IgG1, a cytotoxic antibody. Bavencio® was registered in March 2017 for Merkel cell carcinoma (an aggressive skin tumor), and in May 2017 for bladder cancer or urothelial carcinoma.

Imfinzi® (durvalumab, AstraZeneca) is a humanized monoclonal antibody targeting the PD-L1 ligand. It was registered for bladder cancer (May 2017) and for unresectable non-small cell lung cancer (February 2018) in patients whose cancer has not progressed after chemo and radiotherapy. In 2022, Imfinzi® was approved with Imjudo with chemotherapy in the US for patients with metastatic NSCLC. The same year and in the US, it was approved plus chemotherapy as the first immunotherapy regimen for patients with advanced biliary tract.

Tremelimumab, an anti-CTLA-4 drug (Astra), was developed in combination with durvalumab, from the same company, for various indications.

Many monoclonal antibodies targeting PD1 or its PD-L1 ligand are being developed in the United States, Europe and especially in China.

Third-line treatments for advanced lung cancer are offered but are essentially palliative. To date there is no approved treatment available for patients who are unresponsive to checkpoint inhibitors.

The products developed by the Company are immunotherapies for which preclinical and clinical data on their safety and efficacy are still limited. Many uncertainties therefore weigh on the prospects for the development and profitability of products resulting from these technologies as long as their safety, efficacy, and acceptance by patients, medical doctors and healthcare payers have not been established.

The Company has observed a long survival significantly correlated with the immune response in its Phase 2 of Tedopi® conducted in patients with advanced and metastatic non-small cell lung cancer in escape from previous chemotherapy treatments. Then the Company conducted a first Phase 3 trial (called Atalante-1) and obtained final positive results in 2021-2022. The patients had advanced and metastatic lung cancer. The trial was randomized (2/1 balancing the groups evaluated with 2 patients receiving Tedopi® versus 1 patient receiving standard chemotherapy based on docetaxel or pemetrexed). Upon recommendation of the trial's independent committees, enrollment in this Phase 3 trial was prematurely suspended in 2020, due to the COVID-19 pandemic having a strong impact on mortality in lung cancer (363 patients were initially planned - 219 patients were finally recruited and followed). The primary endpoint was survival. These patients entered the trial mainly in third line treatment, i.e. after a first line of platinum-based chemotherapy followed by failure of a second line line checkpoint inhibitor treatment (anti-PD-(L)1) as last treatment - N= 183 patients). In this third line population representing 84% of the total trial population, the median survival was significantly improved with 9.23 months in the group receiving Tedopi® versus 7.56 months in the docetaxel group (HR: 0.695 p=0.038) . The treatment line was a predefined stratification factor in the trial protocol (stratification enables to have treatment arms comparable for major prognostic criteria). Due to the trial's suspension, the statistical plan was revised and presented to the American health agency (FDA) before the database closing to propose, as main trial's analysis, a population of interest integrating the major stratification factor (third line) and a strong biological rationale, patients with secondary resistance to checkpoint inhibitors (i.e. a treatment of at least 12 weeks) being considered as sensitive to immunotherapy.

The main statistical analysis showed that in these patients with secondary resistance after failure to checkpoint inhibitors (N = 118 patients –– 54% of the population), the significant effect of the product Tedopi ® was increased compared to chemotherapy with 11.1 months of median survival versus 7.5 months in the chemotherapy group (HR: 0.59 p=0.017). The 12-month survival rate was 44% in the Tedopi® group versus 27.5% in the chemotherapy group. The tolerance and quality of life of these patients were also significantly better with Tedopi®.

In terms of possible risk factors, these results may not be confirmed by the subsequent Phase 3 planned in a larger number of patients. However, the new confirmatory trial is planned in patients in second line treatment, they will be in secondary resistance to checkpoint inhibitors, i.e. having escaped an initial first line treatment combining both chemotherapy and immunotherapy, then

escaping maintenance immunotherapy treatment given at least for 12 weeks, immunological conditions of escape very close to those of the first Phase 3 trial.

Today, given the positive outcomes from the Food & Drug Administration (FDA) **"**Type C" meeting following the European Medicines Agency (EMA) scientific advice, the Company is preparing a new Phase 3 clinical trial to support the registration of Tedopi®. This confirmatory trial will evaluate Tedopi® versus the standard treatment, in second line in HLA-A2 positive advanced NSCLC patients.

OSE Immunotherapeutics is committed to provide Tedopi® through cohort early access and nominative compassionate use programs across European countries in third line treatment to address patients' needs alongside physicians' engagement.

Patients can benefit from Tedopi® through compassionate use programs in third or further lines of treatment (post chemotherapy and immunotherapy) currently approved in France, Italy and Spain, confirming thereby the significant medical need for new therapeutic alternatives.

The French National Authority for Health issued a negative decision on the cohort early access program in third line treatment related to the COVID crisis which led to the suspension of patient inclusion in the previous Phase 3 Atalante-1 and the consecutive primary or main analysis on a population of interest with secondary resistance.

Moreover, the Company is developing, in partnership with Boehringer Ingelheim International, a new generation checkpoint inhibitor, BI 765063 (OSE-172), that acts on suppressor myeloid cells and macrophages. The Company received authorization from French and Belgian health authorities in March 2019 for Phase 1 clinical trials of the product for different types of solid cancers and has published its first results in 2021. The dose escalation (Step 1) Phase 1 data were presented at the ASCO annual meeting (June 2021) and at the ESMO annual meeting (September 2021) in monotherapy and in combination with anti-PD1 BI 745091 (ezabenlimab). These data have shown a good tolerance and a promising clinical activity of BI 765063, including a partial response in monotherapy and three partial responses in combination in patients with advanced solid tumors and heavily pretreated. In September 2021, the first treatments were initiated in the expansion Phase 1 clinical trial evaluating BI 765063 in combination with anti-PD1 BI 745091 (ezabenlimab) in patients with advanced MSS (Microsatellite Stable) endometrium or colorectal cancer.

The data from clinical trials could be afterwards strongly impacted by the COVID-19 pandemic, still present (the Worldwide Health Organization confirms that COVID-19 remains a global urgency, but the pandemic could come to an end in 2023) and by the increased risk for patients with advanced lung cancer, as COVID-19 can cause serious pulmonary complications and deaths in this immunocompromised patient population.

Moreover, as more and more frequently in oncology, the Company's products may be administered in combination with other therapies. Many uncertainties therefore weigh on the prospects for the development and profitability of products resulting from these technologies as long as their safety, efficacy, and acceptance by patients, medical doctors and healthcare payers have not been established.

IN IMMUNO-INFLAMMATORY DISEASES

The immunological treatment of immuno-inflammatory diseases is based on three approaches:

Eliminate pathogenic autoantibodies modulates activation of lymphocytes and synthesis of cytokines (immunosuppressors such as corticosteroids, cyclosporin A, the molecules interfering with purine metabolism such as azathioprine (Imurel®) or mycophenolate mofetil (Cellcept®) and, in a more targeted fashion, modify the immune response to make it non-pathogenic (immunomodulation, for example, by inhibiting the cytotoxic action of TNFα by anti-TNFα antibodies by blocking B lymphocytes by anti-CD20s).

The key players in the autoimmune disease market are pharmaceutical groups Johnson & Johnson (J&J), AbbVie, Amgen, Genentech/Roche, Astellas, UCB, Eli Lilly, Sanofi, AstraZeneca, Novartis and Biogen.

The Company's products are developed for new targets:

- **FR104** finalized the Phase 1 trial with positive results; however, the first results may not be confirmed by the subsequent clinical phases. FR104 is being evaluated in transplantation in a phase 1/2 trial conducted in University Hospital of Nantes and in immunosuppression of renal transplant in a phase 1 trial conducted by Veloxis Pharmaceuticals, Inc.
- **OSE-127/S95011** showed positive Phase 1 results (evaluated in healthy volunteers) with a good safety and tolerability profile and a dosing and administration schedule defined for the Phase 2 clinical trial. The ongoing clinical trials will have to demonstrate product efficacy in patients with primary Sjögren's Syndrome or in ulcerative colitis; no certainty currently exists

that appropriate clinical results will be obtained for the rest of their development with competitive advantages that remain to be clinically demonstrated.

In such cases, product development might not be continued, which would have a significant impact on the business, results, financial position, and development of the Company.

3.2 Risks linked to the partnership strategy

3.2.1 Risks linked to research and dependency on current and future partnerships

3.2.1.1 Licensing and license option agreements

To develop and market products, the Company seeks to enter into agreements for collaboration and licensing with pharmaceutical companies that can assist it in drug development and financing. As of the date of this Universal Registration Document, the Company has five license and license option agreements.

A first licensing and distribution agreement for **Tedopi® in Israel** was signed in May 2015 with **Rafa Laboratories**, a pharmaceutical company specializing in oncology and rare lung diseases, long established on this market promoting innovation. This exclusive long-term agreement includes the license, distribution and sales of Tedopi® in Israel. Under the terms of this agreement, commercialization and distribution will be carried out in the territory over the long term. Rafa Laboratories made a cash upfront payment of €100,000 upon signing. Milestone payments are expected as the product is developed, steps that have not been completed to date. RAFA will share equally with OSE Immunotherapeutics profits from Tedopi® sales in Israel.

According to the initial agreement signed in December 2016, OSE Immunotherapeutics granted **Servier** a two-step license option to acquire the exclusive world rights for development and marketing of **OSE-127/S95011** until the finalization of a Phase 2 study planned for ulcerative colitis, an autoimmune bowel disease. This agreement, in a total amount that could reach €272 million including an upfront payment of €10.25 million (received in early 2017) and a payment of €30 million upon exercise of a two-step license option (including €10 million on Option 1 - exercised in February 2019 and paid in March 2019 and €20 million upon exercise of Option 2). An amendment of March 2020 modified the terms of the potential exercise of step 2 of the license option into two parts which are associated two payments:

- A first milestone payment of €5 million, paid in the third quarter of 2021, upon inclusion of the first patient in the ongoing Phase 2a clinical study (sponsored by Servier) in primary Sjögren's Syndrome, a systemic autoimmune disease characterized by an exocrine gland condition affecting the tear and salivary glands.
- A second potential payment of €15 million upon exercise of the option, at the end of the two planned Phase 2 trials. Servier, sponsor of the Sjögren's study, is primarily interested in the results of this study in Sjögren's Syndrome. Nevertheless, all options remain open depending on the results of the two studies on Servier's decision. The second payment of €15 million is indivisible.

Subsequent payments will be linked to clinical development milestones, registration in multiple indications, then sales-related milestones with double-digit royalties.

An exclusive worldwide collaboration and licensing agreement was entered into in April 2018 with **Boehringer Ingelheim** International for the joint development of **BI 765063** (OSE-172) for the treatment of advanced solid tumors. Boehringer Ingelheim acquired worldwide rights for the development, registration, and marketing of BI 765063. Under the terms of the agreement, OSE Immunotherapeutics received from Boehringer Ingelheim an amount of €15 million upon signature of the contract, a total of €15 million in milestone payments following regulatory approval for the launch of Phase 1 in March 2019 and the inclusion of the first patient in this study, and €8 million upon the treatment of the first patient in the Phase 1 expansion (Q4 2021) and a €10 million in milestone upon initiation of the expansion Phase 1 conducted by Boehringer Ingelheim in cellular hepatocarcinoma and head & neck cancer.

Overall, the agreement provides for a potential amount of more than €1.1 billion according to predefined development steps, marketing authorization, and sales, plus royalties on net worldwide sales of the product.

A licensing and distribution agreement for Tedopi® in Korea was signed in November 2019 with Chong Kun Dang Pharmaceutical Corporation (CKD), a pharmaceutical company long established in this market promoting innovation.

Under the terms of the agreement, OSE Immunotherapeutics will receive milestone payments totaling €4.3 million, including €1.2 million upon signature (€700,000) and upon the positive outcome of Atalante-1 step 1 (€500,000 already paid following the positive results of step 1 of Atalante-1). The milestone payments for an additional €3.1 million are related to Tedopi® registration and marketing milestones. The agreement also provides for royalties on sales of the product and a margin as part of the transfer price at a level slightly below thirty percent. The deal applies specifically to development and licensing of Tedopi® in the Korean market which accounts for approximately 1% of the total global oncology market.

In April 2021, OSE Immunotherapeutics entered into a worldwide licensing agreement for **Veloxis Pharmaceuticals** for the development, manufacturing and marketing of **FR104**, a CD28 antagonist, in graft and organ transplantation market. At the same time, OSE Immunotherapeutics retains all rights to develop FR104 in autoimmune diseases. Through this agreement, Veloxis plans to develop FR104 to provide a new therapeutic option for the prophylaxis of organ rejection in solid organ transplant patients. Veloxis will assume all production, development and marketing costs of FR104 in transplantation indications. Under this agreement, OSE Immunotherapeutics will be able to receive up to €315 million in potential milestone payments, including a payment of €7 million paid at signature and royalties on sales. In early 2022, the acceptance of the IND application prepared by Veloxis Pharmaceuticals, Inc. in the United States triggered a milestone payment of €5 million.

The Company, however, cannot guarantee that these agreements will lead to the registration of these products currently in clinical development phases.

Moreover, in the current COVID-19 health crisis, the appearance of another contagious disease or another strain of a virus leading to an equivalent situation (quarantine, total or partial paralysis of the economy and/or the hospital system in any form whatsoever) the Company cannot guarantee that the projections of key clinical steps will be effective, and consequently that the milestone payments will be paid according to the schedule planned by the Company. Likewise, such events could seriously disrupt the activity of current and future partners, and prevent them from using all or a major part of their essential infrastructures, jeopardize their desire to continue their agreements with the Company, suspend developments or co-developments, redirect or limit the resources assigned to conducting the clinical trials to other research programs or delay the progress of clinical trials that they must provide in order for the Company to receive the milestone payments and royalties.

Such events could seriously disrupt the activity of the Company and have a material adverse impact on its business including its ongoing clinical trials, its schedule for obtaining marketing authorizations, its financial position, and its prospects.

When the Company conducts research products and markets its product as part of collaboration agreements, some key tasks or functions are under the responsibility of its partners. Consequently, the Company runs the risk that they will not perform as expected. In addition, the decisions may be under the control of its partners, or subject to their approval. The Company and its partners may also have diverging views on certain matters. Failures in the development process or disagreements in terms of priority could arise and harm the activities conducted under these collaboration agreements. The Company could also encounter conflicts or possible difficulties with its partners during the term of the agreements or when they are renewed or renegotiated. The relationships with its partners could also experience ups and downs.

In addition, if a current or future partner encounters difficulty obtaining its own laboratory products necessary to develop and manufacture its own products or difficulty obtaining the licenses required to this effect (for example for the BI 754091 checkpoint inhibitor from Boehringer Ingelheim for the myeloid checkpoint inhibitor), there could be a delay, suspension, or re-orientation of the partnership that could significantly impact the business, prospects, the financial position, the results and the growth of OSE Immunotherapeutics.

All these events could impact the development, the launch and/or the marketing of some of its products or its candidate products and could cause a decline in its revenue and adversely impact its operating income.

In addition, the Company faces standard commercial risks inherent in the biopharmaceutical industry, including, without limitation:

- Competition resulting from existing therapies and/or new drugs;
- Size of the market of the indications of the leading product;
- Pricing of the products and reimbursement policies;
- Interests of partners and potential investors;
- Development time for new clinical trials;
- Protection afforded by patents and the capacity to prevent counterfeits.

More broadly, the Company could fail to adequately estimate the scientific and medical results of the development operations at the time it enters into a partnership agreement, and therefore the compensation linked to these partnerships, or not have the resources or access to all the necessary information to fully assess them, in particular concerning the potential of research and development portfolios, the difficulties linked to production, questions of compliance, and monitoring the outcome of ongoing disputes.

3.2.1.2 Consortium agreements

In order to obtain financial support and public-private scientific collaboration to develop its research programs, the Company seeks to take part in collaborative programs in consortium agreements. As of the date of this Universal Registration Document, several programs have been developed as part of French consortium agreements.

- **OSE-127/S95011 in the EFFIMab consortium**, a preclinical and clinical program of €20 million aiming to establish the clinical proof of concept of the product in ulcerative colitis, an autoimmune disease of the colon. EFFIMab is financed in part by the public investment bank Bpifrance in the Industrial-Strategic-Innovation (ISI) program. The consortium is composed of several private and public partners. The failure of one of the partners without possible alternative in spite of the best efforts of the other partners could lead to the failure of the program overall.

  In January 2021, new funding of €1.3 million was triggered by the completion of several key milestones of the OSE-127/S95011 product including the strengthening of preclinical and translational data in the indication ulcerative colitis (UC), the completion of the Phase 1 clinical study, the first regulatory authorization for a Phase 2 clinical study in UC and specific steps in the manufacturing of the product.

- **BI 765063 (OSE-172) in the EFFI-CLIN consortium** (July 2017), a program with funding of €9.2 million, whose aim is to study the tolerability and clinical efficacy of BI 765063 (OSE-172), a new immunotherapy for cancer that will be evaluated as a monotherapy or in combination in various indications where the presence of myeloid cells is a poor prognostic factor. This collaborative project is financed by the French General Investment Commission (CGI) and managed by Bpifrance. The consortium is composed of private and public partners. OSE Immunotherapeutics received €6.9 million of this financing; the €2.3 million being released upon the achievement of certain milestones (inclusion of patients and interim results of the Phase I/II study, validation of the efficacy of Sirpα MCA in the chosen indication) and depending on the nature of the expenses related to these milestones.
- **OSE-703** obtained funding of €386 thousand (December 2017) as part of a call for projects of the **French Single Interministry Fund (FUI)** - Regions, dedicated to financing projects from competitiveness centers, to identify new monoclonal antibodies and new therapeutic targets in a collaborative program to develop an innovative test enabling the exploration and measurement of the cytotoxicity of monoclonal antibodies. This research project, called HybridADCC, with a total cost of €2.4 million, is financed by the FUI at €1.2 million and was labeled by the Atlanpole Biotherapies center. The Company obtained a six-month extension on this project, bringing it to the end of June 2022.
- **CoVepiT**: €5.2 million was granted to the Company in December 2020 as part of the PSPC-COVID call for projects, operated on behalf of the French State by Bpifrance as part of the Future Investments Program (PIA). Funding from the French State, totaling €5.8 million for the entire consortium, planned €5.2 million for OSE Immunotherapeutics, in particular to support the CoVepiT 1 study, the production of a clinical batch according to Good Manufacturing Practices and the clinical Phase 1 intended to assess the safety and immunogenicity of CoVepiT in healthy adult volunteers.

  In addition, on May 18, 2021, the Company obtained public financing of €10.7 million as part of the "Capacity Building" call for expressions of interest, operated on behalf of the French State by Bpifrance in as part of the Future Investments Program (PIA) and the France Relance plan, to support the development program of CoVepiT, its multi-variant vaccine against COVID-19 currently in Phase 1 clinical trial. This additional funding made it possible to expand the clinical development of CoVepiT.

As part of the consortium agreements, the failure of one of the partners without possible alternative in spite of the best efforts of the other partners could lead to the failure of the program overall.

The Company might not be able to find partners or not find good partners to develop its products. If it finds these partners, they could decide to withdraw from the agreements. The Company might also not be successful in entering into new agreements on its other drugs. In addition, its current and future collaboration and licensing agreements might not bear fruit.

If the Company is unable to maintain its existing collaboration and licensing agreements or enter into new agreements, it may need to study alternative development conditions, including the complete abandonment or sale of some programs, which could hinder, even limit its growth.

The Company might not be able to control either the amount or the schedule of the resources that its existing or future partners will dedicate to the development, manufacturing, and marketing of its products. These partners may not meet their obligations as anticipated by the Company. This is why it could face significant delays or not be successful in introducing its products on certain markets.

Moreover, in the case of the COVID-19 health crisis, of the appearance of another contagious disease or another virus strain leading to an equivalent situation (quarantine, total or partial paralysis of the economy and/or hospital system in any form whatsoever), the business activity of the partners could be seriously disrupted, which would prevent them from using all or a large part of their essential infrastructures, jeopardize their desire to continue the agreements reached with the Company, suspend developments or co-developments, redirect or limit the resources allocated to clinical trials to other research programs or delay the progress of clinical trials that they must provide in order for the Company to receive the milestone payments and royalties.

This risk is particularly sensitive to health and geopolitical risks, particularly with regard to clinical trials and manufacturing operations. A worsening of the health crisis situation in 2023 as well as a maintenance or an increase in the economic sanctions put in place against Russia in the context of the Russian-Ukrainian conflict, or a wider extension of the conflict involving other countries could amplify this risk significantly, for the Company directly or through the impact that this risk could have on its partners and subcontractors.

Moreover, even though it seeks to include non-compete clauses in its collaboration and licensing agreements, these restrictions might not be able to offer adequate protection to the Company. Its partners could decide to pursue alternative competing technologies with others.

To successfully complete certain tasks in product development, the Company relies on a network of scientific experts intervening as outside consultants, including researchers attached to academic institutions. To build and maintain such a network in acceptable conditions, the Company faces intense competition. These external advisers can end their commitments at any time. The Company has only limited control over their activities. Most of these scientific advisers, however, are also shareholders of the Company, or benefit from equity incentives in the form of share subscription warrants (BSAs), founders' warrants (BSPCEs) or consulting agreements, thereby enhancing their interest in the success of the Company. On the other hand, the Company considers that its development programs in the cancer immunotherapy segment, its experience in transplantation, autoimmune diseases, its product optimization platforms, its experience, and the professional network of its management are the means of attracting and retaining high quality scientific partners.

The occurrence of one or more of these risks could have a material adverse impact on the business, prospects, financial position, results, and development of the Company. In order to limit the risks linked to current and future partnerships, partnership strategies, strategies for growth and acquisition of new candidates are maintained.

3.2.1.3 Initial partnerships

Risks linked to the off-balance sheet commitments generated by the acquisition of rights with Takeda for Memopi® and the INSERM for FR104 and MD707

As part of the initial transaction for the acquisition of the Tedopi® (Memopi® technology) assets from the pharmaceutical company Takeda, the Company made a commitment to pay an earn-out at the time its product was registered, then no more than single-digit royalties on future sales (see Section 20 – Major agreements).

In addition, OSE Immunotherapeutics researchers are working in close collaboration with INSERM researchers. Sometimes, the result of their work leads to patents jointly owned by Effimune/OSE and INSERM, subject to operating agreements.

Two operating agreements have been established with the INSERM for research conducted in collaboration with patents filed as co-property on behalf of Effimune and the INSERM. These agreements grant worldwide operating rights on the patent licenses for each of the agreements:

In October 2011, an operating agreement was signed with the INSERM for the monoclonal antibody project from the MD707 clone targeting the Interleukin-7 alpha receptor. These joint research projects resulted in the filing of a jointly owned patent. This 2011 patent and the antibodies resulting from the patent were studied in various autoimmune disease models, but in view of the results,

were not retained for final development. This 2011 patent was thus not used as part of the EFFIMab consortium for development of the OSE-127/S95011 product in autoimmune diseases.

In March 2013, an operating agreement was signed with the INSERM for the FR104 antibody including the filing of a jointly owned patent. For the FR104 product, the exercise of the license by Janssen Biotech in July 2016 led to financial settlements with the INSERM. Upon the signature of the contract with Veloxis, new financial settlements have been made and additional payments are planned according to the achievement of key steps.

Depending on the results and advances of different jointly owned products, diverging views and distributions could arise, leading to conflicts or possible difficulties with these entities during the term of its agreements or when they are renewed or renegotiated. The relationships with these entities could also experience ups and downs. More broadly, the Company could fail to adequately estimate the scientific and medical results of the development operations at the time it enters into an operating agreement, and therefore the compensation linked to these agreements, or not have the resources or the access to all the necessary information to fully assess them, in particular concerning the potential of the research and development portfolios, the difficulties linked to production, questions of compliance, and monitoring the outcome of ongoing disputes.

3.2.2 Risks linked to potential conflicts could affect the Company's relationship with its licensees

The Company's strategy for some of its development products, in particular OSE-127/S95011 (2 step license option agreement with Servier), BI 765063 (OSE-172) (collaboration and licensing agreement with Boehringer Ingelheim International) and FR104 (license and collaboration agreement with Veloxis Pharmaceuticals Inc.) is to license these latter to pharmaceutical laboratories. The signing of licensing agreements and their outcomes is thus important for the Company.

Conflicts could arise, moreover, between licensees during execution of agreements binding on the Company, that could affect their continuation and consequently the manufacturing or marketing of the products developed by the Company. These could be conflicts concerning the conditions of the signing of the agreements or their proper execution, by either of the parties, of their obligations pursuant to those agreements. For example, some agreements entered into with licensees typically contain clauses on which a party will pay costs and fees, and such clauses could be subject to interpretation or dispute, thereby endangering the profits that the Company could expect from that partnership. Such conflicts could materially impact the business, the financial position, the results, the development, and the prospects of the Company.

3.3 Risks linked to marketing

3.3.1 Risks linked to obtaining a Marketing Authorization (MA)

To obtain a marketing authorization for one or more of its products, the Company, or its partners, must demonstrate to the regulatory authorities their pharmaceutical quality, their safety of use, and their efficacy for the targeted indications.

The Company's ability to obtain a marketing authorization for its products depends on several factors, in particular:

- The possibility of continuing development of its products (manufacturing of batches and tests), and firstly for the drug Tedopi®, that validated its Phase 3 results despite the trial suspension due to the COVID-19, in a population of interest identified in secondary resistance after failure with a checkpoint inhibitor. The phase 3 is the last clinical study phase before registration but the Company is preparing a confirmatory pivotal Phase 3 clinical trial to support the registration of Tedopi® as a new standard of care in advanced or metastatic NSCLC in secondary resistance after failure with a checkpoint inhibitor.
- The fact that the Company or its partners are able to carry out clinical trials, in the designated time frames with the initially planned human, technical, and financial resources;
- The fact that its products have already been approved or not for another indication that has already received a marketing authorization; and
- The fact that its competitors have not announced clinical results likely to change the evaluation criteria used by the regulatory authorities.

If the Company does not obtain any marketing authorization, it will not be able to market its products. In addition, its products might not obtain marketing authorization for a given geographical region, which could significantly limit the marketing of the product in question.

The occurrence of one or more of these risks could have a material adverse impact on the business, prospects, financial position, results, and development of the Company.

3.3.2 Risks linked to the lack of commercial success of the products

3.3.2.1 Risks linked to market penetration difficulties

If the Company is able to obtain a marketing authorization or find developing commercial partners allowing it to market its products in the future, it would need time to obtain the support of the medical community, healthcare providers, and third-party payers. The degree of market acceptance depends on several factors, in particular:

- Healthcare providers' perception of the product's therapeutic benefit;
- Clinical developments made after the marketing authorization;
- Occurrence of unwanted impacts after obtaining marketing authorization;
- Existence of alternative therapeutic options;
- Ease of the product's use, especially the method of administration;
- Cost of treatment;
- Reimbursement policies of governments and other third parties;
- Effective implementation of a scientific publication strategy; and
- Support of recognized experts;

Poor market penetration, by the Company or by its pharmaceutical partners, resulting from one of these factors could have a material adverse effect on the business, prospects, financial position, results, and development of the Company.

This risk will only be present, however, when the Company's products are registered and marketed or are close to being marketed.

3.3.2.2 Risks linked to the competitive environment and technological changes

The pharmaceutical market is characterized by rapidly evolving technologies, the predominance of products protected by intellectual property rights, and intense competition. Numerous entities, including pharmaceutical laboratories, biotechnology companies, academic institutions and other research organizations, are actively engaged in the discovery, research, development, and marketing of drugs, including immunotherapy and other products to treat cancer and autoimmune diseases (see paragraph 6.2.2, Targeted pathologies and immuno-oncology treatments). Should the Company obtain marketing authorization for one of its immunotherapy products, it would compete against a number of established therapies. This product could also compete with a certain number of innovative therapies being developed or recently introduced on the market, such as targeted therapies, monoclonal antibodies, cell therapy, gene therapy, and checkpoint inhibitors.

Tedopi®, FR104, OSE-127/S95011 and BI 765063 (OSE-172) are first-in-class drugs, that currently do not have an equivalent on the market. Other companies, in particular, large pharmaceutical laboratories, are also developing first-in-class drugs, some of which target the immune system in a similar manner and thus have the potential to compete with the Company in the targeted markets.

Many of the Company's competitors that are actively developing anti-cancer therapies have much greater resources and experience in management, research, patient access in clinical trials, manufacturing, and marketing than those of the Company. In particular, the big pharmaceutical laboratories have significantly more experience than the Company in conducting clinical trials and obtaining regulatory authorizations. Smaller or early-stage companies, especially in immunotherapy, could also be significant competitors. These companies are also likely to compete with the Company to acquire rights to promising products and other complementary technologies.

The Tedopi® product, via neoepitopes selected and optimized from five tumor antigens, targets other cancers expressing the same tumor antigens that can benefit from this T specific immunotherapy product. Tedopi® thus will not necessarily hinder other existing techniques or those in development by other players in the pharmaceutical industry (such as checkpoint inhibitors), but in some cases, could be used in relevant therapeutic combinations in this innovative domain of immunotherapy.

Finally, the Company cannot guarantee that its products will:

- Obtain the necessary licenses or receive marketing authorization more rapidly than its competitors;
- Remain competitive with other products developed by its competitors that could be safer, effective, or less costly;
- Remain competitive faced with the products of its competitors who are more effective in their production and their marketing;
- Be a commercial success; or
- Not be rendered obsolete or unprofitable by technological progress or other therapies developed by competitors.
- Such events could have a material adverse impact on the Company's business, prospects, financial position, results, and development.

The Company believes that the competition risk is relatively high for its business, in particular taking into account the size of some of its potential competitors. The competitive issue is integrated in the Company's development choices, that is why it is closely monitoring the development of competing drugs. The fact for example that oncology treatments can be combined with others (checkpoint inhibitors, combinations of checkpoints inhibitors, chemotherapy, targeted therapies, immunotherapies acting on different targets or different cell types) helps limit the risk of competition because the development of one drug does not necessarily make another drug less interesting.

3.3.3 Risks linked to changes in drug reimbursement policies

Once marketed, market acceptance of the Company's products will depend, in part, on the reimbursement rates offered by the public health insurance funds and private insurance companies. The primary health insurance funds and other third-party payers will seek to limit the cost of care by restricting or refusing to cover reimbursement of costly products and treatment protocols. This risk is actually greater in Europe due to the budget crisis in certain countries and more generally due to weak economic growth.

The Company's ability to successfully market its products will depend in part on obtaining adequate reimbursement rates for its drugs and related therapies from the public authorities, private insurers and other organizations in Europe and the United States. The third-party payers more and more frequently question the prices of therapeutic products and medical services. Cost control measures implemented by healthcare service providers and reimbursement organizations and the effect of any healthcare system reforms could adversely impact the Company's operating income. It might therefore not obtain satisfactory reimbursement rates for its products, which could harm their market acceptance, in which case the Company would be unable to receive an adequate return on its investments.

The occurrence of one or more of these risks could have a material adverse impact on the business, prospects, financial position, results, and development of the Company.

3.4 Risks linked to intellectual property rights

3.4.1 Risks linked to uncertain protection of patents and other intellectual property rights

OSE Immunotherapeutics holds, directly and indirectly through its wholly owned subsidiary OSE Pharma International, the worldwide rights on its anti-cancer T-specific immunotherapy technology.

The Company obtained orphan drug status for Tedopi® in the United States in 2013 for so-called "non-small cell" lung cancer in patients positive for the HLA-A2 marker. This technology directed against five tumor antigens benefits from extended protection under United States orphan drug status that gives seven years of additional protection after the marketing authorization. As the tumor antigens that it covers are present in other cancers, the clinical applications of the Company's technology allow different developments in these types of cancer or according to different combinations with other products.

The Company directly holds intellectual property rights over five patent families concerning FR104, two patent families for OSE-127/S95011, five patent families for BI 765063 (OSE-172), and three patent families for OSE-703. These latter are presented in paragraph 5.5 of this Universal Registration Document.

The ability to protect oneself in a patent lawsuit represents a significant risk, in cases in which the intellectual property is not adequately protected or if the products harm the intellectual property rights of a competitor. The Company will therefore strive to file all patent applications necessary to best protect the products and technologies that it develops. In addition, it will ensure that it maintains very strict confidentiality standards and enforce application of confidentiality agreements among its employees and all collaborating parties to protect the secrets inherent in its business.

It is important for the success of the Company's business, that the Company and its licensees and licensors are able to obtain, maintain and enforce its patents and its intellectual property rights in Europe, United States and other countries. It cannot be ruled out that:

- The patents granted or licensed to its partners or itself could be challenged, or held invalid, or be unenforceable by the Company;
- The extent of any patent protection may be inadequate to protect the Company from its competitors; or
- Third parties could claim rights on patents or other intellectual property rights owned by the Company.

The grant of a patent does not guarantee its validity or enforceability and third parties could challenge these two aspects. The grant and enforceability of a biotechnology patent are highly uncertain and raise complex legal and scientific issues. So far, no uniform worldwide policy has emerged in terms of the content of patents granted in the area of biotechnology and the scope of allowable claims. Litigation may be necessary to enforce the Company's intellectual property rights, protect its trade secrets or determine the validity and scope of its intellectual property rights. Any litigation could result in considerable expenses, reduce its profits and fail to offer it adequate protection. Its competitors could successfully dispute patents granted or licensed to the Company in court or other proceedings, which could ultimately reduce the scope of its patents. In addition, these patents could be successfully counterfeited or infringed due to innovations.

In addition, some countries could try to grant mandatory licenses to third parties on patents protecting the originator products, which would limit the value of the patent protection given to these products.

The occurrence of any of these events concerning one of its patents or intellectual property rights could have a material adverse effect on its business, prospects, financial position, results, and development. These risks are even greater for the Company in view of its limited financing and human resources capacities. In order to mitigate this risk, the process for managing patents and the Company's rights was created and organized.

3.4.2 Risks linked to legal liability, in particular product liability risks

The Company is exposed to potential liability, including product liability, intrinsic to conducting clinical trials, manufacturing and marketing therapeutic products in humans. It could also be held liable in connection with clinical trials, including the preparation of therapeutic products tested and unexpected side effects resulting from the administration of these products. Claims or legal proceedings could be filed or brought against the Company by patients, regulatory agencies, pharmaceutical companies, or other third parties using or selling its products. These legal proceedings could include claims arising from the actions of its partners, licensees, and subcontractors, over whom the Company exercises little or no control. The Company cannot ensure that its current insurance coverage is adequate to protect it against lawsuits that could arise or in response to an exceptional or unexpected situation. If the Company, its partners, licensees, and subcontractors are found liable in a legal proceeding and are unable to obtain and maintain appropriate insurance coverage at an acceptable price, or to protect themselves by whatever means against product liability claims, it could seriously affect the marketing of its products and more generally harm its business, prospects, financial position, results, and development. The Company could also be subject to civil or criminal proceedings and its image would be harmed. To limit this risk, the Company has subscribed to the insurance policies detailed in the section and will obtain additional insurance coverage as necessary as its products are developed.

The Company's activity is subject to a more and more restrictive regulatory framework. This regulatory framework itself could be impacted due to measures taken with respect to the COVID-19 epidemic or any equivalent epidemic, that could require the Company to modify its clinical trial procedures, delay the necessary interactions with the local authorities, ethics committees, or other important agencies and third-party co-contractors or change the criteria used by health authorities to accept the data from clinical trials conducted in these affected geographical regions.

The pharmaceutical industry worldwide faces constant changes in its legal and regulatory environment and increased monitoring by authorities and the public that require ever more guarantees on the safety and efficacy of drugs or the conduct of its business. In addition, incentives for research are reduced.

The health authorities and, in particular, the United States Food and Drug Administration (FDA), have imposed heavier and heavier requirements concerning the amount of data needed to demonstrate product efficacy and safety. These conditions have reduced the number of products authorized. The products marketed, moreover, are subject to regular re-evaluation of the benefit/risk ratio following their authorization. Late discovery of issues not identified at the research stage can lead to restrictions on marketing, product suspension, or withdrawal as well as the risk of legal proceedings.

To the extent that new regulations could lead to additional constraints on the conduct of business and increase the cost of obtaining and maintaining the marketing authorizations of products or limit the economic value of new products for the inventors, the prospects for growth of the pharmaceutical and medical industry and of the Company could be reduced.

In addition, all clinical studies must receive prior approval by the health authorities and ethics committees in the countries in which the studies will be conducted; a negative opinion could hinder or stop the Company's clinical development program. Likewise, in conducting its studies, the Company monitors data and safety, and it could decide to end a study early, definitively or not, and discontinue the development of certain products.

In addition, health authorities could decide to suspend or terminate prematurely an ongoing clinical trial depending on the information that it receives during a study, in particular on the occurrence of serious adverse events.

The occurrence of one or more of these risks could have a material adverse impact on the business, prospects, financial position, results, and development of the Company.

3.4.3 Risks linked to patents and intellectual property rights held by third parties

The expansion of the biotechnology industry and the growing number of patents granted increase the risk that third parties could maintain that their own intellectual property rights are infringed by the Company's products or technologies. In general, patent applications are only published 18 months after the date of priority applications. In the United States, some patent applications are not published prior to the grant of the patent itself. Also, in the United States, patents can be granted on the basis of their invention date, under the "first-to-invent, first-to-file" rule, which does not always result in a patent being granted to the party who first filed the application. Discoveries are sometimes published or patented months or even years later. The Company cannot be sure that third parties were not the first to invent products or file patent applications on inventions also covered by its pending patent applications or those of its partners. In such instances, the Company may need to obtain licenses from those third parties holding the patents (licenses which may not be obtained under reasonable terms, if at all), or cease production and sale of certain products or develop alternative technologies.

Any litigation or claim against the Company, regardless of its outcome, could result in substantial costs and could compromise its reputation. Some of its competitors with greater resources may be better able to bear the costs of complex legal proceedings. Any litigation of this type could severely impact the Company's ability to continue its activities. Specifically, intellectual property litigation could force the Company to:

- Cease selling or using any of its products that are part of the disputed intellectual property, which would reduce its revenue;
- Obtain a license from the holder of the intellectual property rights, which may not be obtainable in reasonable terms, if at all.

Active monitoring of intellectual property matters helps limit this risk.

3.5 Risks linked to capital requirements

3.5.1 Risks linked to uncertain additional funding

The Company has the necessary cash to continue its activities during the next 12 months, based on the publication of the financial results at December 31, 2022 (25,604 K€ at 12/31/2022) and to finance its clinical and preclinical programs (Tedopi®; OSE-279; OSE-230; CLEC-1; FR104; OSE-127/S95011, whose development is partly supported through Phase 2 under the licensing option

agreement with Servier and the EFFIMab consortium; BI 765063 (OSE-172), whose development is supported under the collaboration and licensing agreement with Boehringer Ingelheim (April 2018) and the EFFI-CLIN consortium supporting several stages of development and a clinical program planned through Phase 2).

The financing as well as the repayment schedule for the loans and repayable advances available to the Company are detailed in note 5 to the consolidated financial statements.

On April 27, 2023, the Company signed a financing contract with the Company Vester Finance in the form of an equity financing line (commonly called equity line) for a maximum volume representing up to 14.8% of the Company's capital. This line of financing materializes through the exercise of 2,800,000 BSA. The parity is 1 warrant for 1 share, the exercise of which is carried out by Vester Finance, which has, however, the obligation to exercise a minimum number of 300,000 warrants per quarter, with a maximum discount of 6% on the lowest average daily price weighted by volumes over the period of the two trading sessions preceding each issue.
Based on the current price, this would raise an amount of €3.4 million by December 31, 2023, and an additional €1.7 million until April 30, 2024.
The Company has also received support from the "Pays de la Loire" Region through a line of financing in the form of a Redeployment loan in the amount of €1.5 million, with an interest rate of 2%, with two years of deferred global capital repayment and 4 annual repayments. This loan is subject to final approval by the Commission, scheduled for the end of May. Management considers the finalization of this financing as highly probable.

The Company has also set up financing through a banking pool (CIC, Crédit Mutuel, BNP Paribas): a Resilience "Prêt Garanti par l'Etat", PGE (loan agreement guaranteed by the French State)in the amount of €1.3 million with an interest rate of up to 2%, with a repayment *in fine* at 12 months (subject to completing the formalities related to the PGE Resilience relating to the impact of the Ukrainian conflict on the activity of the company); and a global loan of €1 million, with an interest rate of 4%, with repayment over 36 months. This banking pool agreement is subject to the lifting of several conditions, namely the 70% counter-guarantee from Bpifrance and the loan agreement from the Pays de la Loire Region detailed above.

Beyond its products in preclinical or clinical phase, the Company considers that, in view of its activity, in the future it might need to obtain new sources of funding for its clinical trials and long-term growth, in particular through possible agreements including milestone payments related to its development programs that could be licensed to partners, the signing of industrial and commercial partnerships and any new capital increases.

In 2023, the Company has generated revenue from the selling of Tedopi® further to the compassionate use program obtained at the end of 2023 in France.

The program OSE-127 is conducted by Servier in Phase 2 in the Sjögren syndrome. In parallel, OSE-127 is evaluated by the Company in a Phase 2 clinical trial in ulcerative colitis and in preclinical phase in hemato-oncology in lymphoblastic leukemia, this program could trigger a license exercise up to €15 million.

The Company is also working on a new partnership on an innovative product. As of the date of this Universal Registration Document, none of the Company's products has been marketed under the Marketing Authorization and has therefore not generated commercial revenue. The Company's ability to generate profit will come from its ability to quickly obtain marketing authorizations internationally, in order to successfully market its products, alone or in partnership.

The Company foresees the following revenue sources for the next four years:

- Revenue linked to achieving milestones
- Exercise of options
- Payments made by future partners under certain agreements
- Public grants and reimbursements of research tax credits

The Company cannot guarantee that it will generate revenue from the sale of products enabling it to become profitable in the near future. The interruption of one of these sources of revenue, or a worldwide health or geopolitical crisis, could have a material adverse impact on its business, prospects, financial position, results, and development. This would have a significant impact on the business, results, financial position, and development of the Company.

In order to face this, the Company could sign partnership agreements more upstream according to the development, results, and prospects of its various projects. These partnerships would allow the Company to generate additional revenue to finalize its preclinical and clinical trials or lead to redefining the allocation of its financing needs depending on the potential of the products in clinical development.

OSE Immunotherapeutics could also call on investors and the market according to its development needs and depending on favorable economic circumstances. It could also receive public aid as part of consortia for business innovation, for example the EFFIMab consortium for the OSE-127/S95011 program, the EFFI-CLIN consortium for the BI 765063 (OSE-172) program.

Future capital needs will depend on many factors that are largely beyond the control of the Company, for example:

- Higher costs and slower progress than expected for its research and development programs;
- Higher costs and longer delays than expected in obtaining regulatory approvals, including the time to prepare submissions to regulatory agencies;
- Costs for preparing, filing, defending, and maintaining its patents and other intellectual property rights;
- Costs for responding to technological and market developments, establishing and maintaining collaboration agreements, and ensuring the efficient manufacturing and marketing of its products;
- Additional costs for marketing its own products, should the Company decide to undertake this marketing itself; and
- New opportunities for developing promising new products or opportunities to acquire technologies, products, or companies.

Disruptions to global supply chains, accompanied by tight labor markets, and rising energy prices are also translating into higher inflation, notably in the United States, where a massive budgetary impulse plan strongly stimulated demand. Europe and emerging countries are also facing inflationary pressures, with potentially a lasting impact on inflation, consumer purchasing power and ultimately on economic activity. The Russian-Ukrainian conflict is likely to increase some of these imbalances, particularly in Europe where, for example, gas prices have risen sharply and remain very volatile.

Like most companies, the Company is impacted by rapidly rising inflation, leading to an increase in the price of the products, raw materials and consumables it needs, as well as the cost of services invoiced by its service providers and subcontractors for conducting its R&D activities. This represents a substantial increase in the Company's expenses, not offset by income or by possible re-invoicing on other players, or on the prices of the Company's drugs, since it does not currently market any products.
The Company cannot guarantee that additional funds will be available to it when it will need them and, as the case may be, that the funds will be available in acceptable conditions. To that extent, interest rate global increases may affect the availability of capital in the biotechnology industry. Investors may prefer to deploy their available capital into less risky financial products than investing in the biotechnology industry. The Company's access to capital may be adversely affected.

If the necessary funds are not available, the Company could find it necessary to:

- Delay, reduce, or even eliminate development programs;
- Obtain funding through partnership agreements that might require it to give up rights to technologies or products, that it would have continued holding under different circumstances;
- Acquire licenses or enter into new collaboration agreements that could be less attractive to it than those it would have been able to obtain under different circumstances; or
- Consider selling assets, or even merging with another company.

The Company's ease in securing additional funding depends to great extent on its past, present and future financial position. In this regard, since its founding until 2017, the Company has mostly experienced operating losses.

As of December 31, 2022, the Company had operating losses of €18.4 million, and it anticipates potential operating losses in upcoming years, in connection with its development activities, and in particular due to its ongoing investments in drug development (manufacturing of batches and conducting clinical trials).

In addition, to the extent that the Company could raise capital by issuing new shares or other financial instruments that may ultimately give access to the Company's capital, the shareholders' participation could be diluted.

The Company does not rule out new fundraising from qualified investors or more broadly from the market, depending on market opportunities.

Debt financing, to the extent it is available, could also include restrictive conditions.

For example, on February 15, 2021, the Company signed a financing agreement with the European Investment Bank for a maximum amount of €25 million. The first tranche of €10 million, not subject to conditions and for which OSE Immunotherapeutics will request payment before the end of June 2021, has enabled the expansion of the clinical development of Tedopi® for new cancer indications by evaluating it in combination with a checkpoint inhibitor. The loan agreement also contains an agreement to issue share subscription warrants to EIB for the first two tranches of the financing, in particular the issue of 850,000 share subscription

warrants as part of the first tranche, which occurred on July 8, 2021, has a dilutive effect for shareholders in case of exercise. The agreement also provides for an anti-dilution clause for the BEI allowing it to maintain 4.44% of the capital in the event of a subsequent capital increase (after application of a deductible of 1,500,000 shares and as long as the share price is less than 20 euros).

Following the achievement of milestones defined in the contract with the EIB, the Company has drawn the 2nd tranche of €10 million. The loan agreement is supplemented by an agreement to issue warrants in favor of the EIB of 550,000 warrants (i.e. 2.97% of the share capital on a non-diluted basis). The anti-dilution clause presented above also applies for this 2nd tranche.

Consequently, the above dilution could more important if the Company were to carry out capital increases leading to the need to issue additional warrants, and therefore a right to additional shares, for the EIB.

The occurrence of one or more of these risks could have a material adverse impact on the business, prospects, financial position, results, and development of the Company, as well as the position of shareholders.

The Company includes financing risk in its management issues. The signing of partnerships that includes upfront payments, payments during product development, and royalties on sales, aims to decrease, with time, the financing risk and the need to use capital financing. The Company, however, considers that its exposure to the economic and market environment remains substantial.

On the filing date, taking into account the elements described above, the Company considers that it is able to finance its current operating expenses in the next 12 months.

On the filing date, taking into account the establishment of a line of financing with Vester Finance, the new loans that will be taken out with the Pays de la Loire Region and the banking pool, and a general saving of expenses and the assumption of pre-financing of the 2023 research tax credit for an amount of €4 million, OSE Immunotherapeutics has strengthened its financial visibility until the second quarter of 2024 and considers that its available cash at the date of this Universal Registration Document therefore allows it to finance its current operating expenses in the next 12 months.

In the event that the pre-financing of the 2023 research tax credit is not obtained, the Company estimates that it will need €3.6 million to cover its expenses until April 30, 2024. The Company specifies that it could benefit from a minimum €1.7 million under the equity line contract above (based on the current share price).

Available cash at March 31, 2023 was €15.6 million and does not take into account the 2022 research tax credit of €5.4 million, the equity financing line, and new borrowings obtained at the end of April 2023.

The Company also estimated the impact of the war between Russia and Ukraine on its cash and cash equivalents.

The Company considers that its liquidity risk is sensitive to geopolitical risks, particularly with regard to access to capital and/or debt markets. A resurgence or a worsening of the health crisis situation in 2023 as well as a maintenance or an increase in the economic sanctions put in place against Russia in the context of the Russian-Ukrainian conflict, or a wider extension of the conflict involving other countries could amplify this risk significantly. These external factors could have a significant short-term impact on the Company's ability to complete its clinical trials and, therefore, on the conduct of its business, even though certain milestones could be shifted by several months following the slowing of clinical trials, the expenses should also be delayed.

Thus, the Company believes that its current cash and cash equivalents should enable it to finance both ongoing and future clinical trials, in particular to continue clinical and preclinical development related to Tedopi®, OSE-279, BI 765063 (OSE-172), CLEC-1, OSE-127/S95011, FR104, OSE-230 and ongoing R&D over the 12 months following the date of this Universal Registration Document.

The Company also intends to benefit from existing public aid, in particular the research tax credit.

While the Company has recently made substantial use of the bank loan (EIB funding of €20 million drawn down in July 2021 and in December 2022), it remains attentive to the market for a funding via the issue of any available equity or debt instrument. In this regard, it should be noted that the Company benefited from three loans totaling €7 million in May 2020 under the French Government-Guaranteed loan program.

Under these conditions, as a result of the EIB loan, the Company is exposed to liquidity risks in the event of the occurrence of a usual event of default in such a matter, leading to the early repayment of this bank loan and interest.

To cover the financing that the Company might need in order to accelerate the clinical development of its products or develop new products, the Combined General Shareholders' Meeting of June 23, 2022, delegated powers to the Board of Directors to carry out secondary fundraising transactions.

The Company could call upon various sources of financing, either from investors in a transaction on financial markets, through public aid, or through new industrial agreements on the portfolio products. This additional source of financing would be used to finance the Company's growth, new projects, or new indications for its current products.

3.5.2 Risks linked to the availability of public grants and research tax credits

Since it was founded, the Company has received public funding for research expenses (see Note 5 to the 2022 financial statements), to finance its activities. OSE Pharma, that became OSE Immunotherapeutics, received a research tax credit of €675 thousand for 2015, €2,645 thousand for 2016, €2,940 thousand for 2017, €4,487 thousand for 2018, €3,059 thousand for fiscal year 2019, €5,120 thousand for 2020, €4,344 thousand for fiscal year 2021 and should receive €5,432 thousand for 2022.

The research tax credit is one source of funding. The Company has no assurance that it will have access to this source of funding, or that the funding will be maintained in the future. This source of funding could in fact be threatened by regulatory changes or by an audit by tax authorities that could lead to a reduction in the amount received or to be received even if the Company meets the requirements for documentation and eligibility of expenses. Taking into account the advanced status of the Company's development programs, and the limited portion that this aid represents and will represent, compared with the overall budget of the Company, this risk is limited.

3.5.3 Valuation of intangible assets and impairment tests

The Company OSE Immunotherapeutics, following the merger of OSE Pharma with Effimune, recognized intangible assets in its statement of financial position. In the Company's upcoming accounting statements, adverse changes in its activities, business forecasts, and discounted cash flow assumptions could result in the recognition of impairment losses that could have significant impacts on the results of OSE Immunotherapeutics. These tests will be conducted when events or circumstances indicate that a reduction in value is likely to have occurred and at least once per year.

These tests were performed at the close of the 2022 fiscal year and did not result in any recognition of impairment.

3.6 Risk linked to the control system for foreign investors in France

Any investment (i) by (a) a natural person of foreign nationality, (b) a natural person of French nationality who is not resident in France within the meaning of Article 4 B of the General Tax Code, (c) an entity governed by foreign law, and (d) an entity governed by French law controlled by one or more persons or entities referred to in points (a) to (c), (ii) which would result in (a) acquiring control, within the meaning of Article L. 233-3 of the Commercial Code, of a French company, (b) to acquire all or part of a branch of activity of a French company, or (c) for natural persons who do not have the nationality of a Member State of the European Union or of a State party to the Agreement on the European Economic Area which has concluded a mutual administrative assistance agreement with France and/or who are not domiciled in any of these States, or for legal persons of which at least one of the members of the chain of control is not subject to the law of one of these States or does not have its nationality and/or is not domiciled there, to cross the threshold of 25% of the voting rights of a French company and (iii) whose activities relate, even on an occasional basis, the research and development of so-called critical technologies, such as biotechnologies, and considered essential for the protection of public health, requires the prior authorization of the Minister of the Economy. For any investment in activities covered by the foreign investment control procedure, the investor concerned must obtain prior authorization from the Ministry of the Economy.

In addition, since August 2020, Decree No. 2020-892 of July 22, 2020, as amended by Decree No. 2021-1758 of December 22, 2022 and Decree No. 2022-1622 of December 23, 2022 , has (i) lowered, until December 31, 2023, the scope of application of the foreign investment control regime to the threshold of 10% acquisition of the voting rights of the French companies concerned whose shares are listed on a regulated; and (ii) subject this new threshold to a rapid review procedure (the investor is exempted from the application for authorization usually provided for, provided that the investment project has been the subject of a prior notification to the Minister of the Economy and that the investment operation has been carried out within a period of six months following the

notification; except in the event of an objection from the Minister of the Economy, the operation is deemed to have been authorized in the absence of a response at the end of a period of 10 working days from the notification).

If an investment requiring the prior authorization of the Minister of the Economy has been made without authorization, the Minister of the Economy may cancel the transaction or order the investor concerned (possibly under penalty) (i) to file a request for authorization, (ii) to restore the previous situation at its expense or (iii) to modify the investment. In addition, the Minister may impose covenants and conditions on the investor (including regular reporting commitments). The investor concerned could also be declared criminally liable and expose themselves to penalties, including exclusion from any public contract or a fine, the amount of which cannot exceed the highest of the following sums: (i) double the amount of the investment concerned, (ii) 10% of the amount of the annual turnover excluding tax of the Company and (iii) 5 million euros (for a legal person) or 1 million euros (for a natural person).

The application of these regulations could constitute a potential obstacle to investments made by investors located outside the European Economic Area and therefore risks limiting the Company's access to certain sources of financing.

3.7 Insurance and risk coverage

The Company believes that its internal procedures governing risk prevention and safeguarding, as well as the insurance policies it holds, are adequate to cover the main insurable risks that it has identified.

The Company has implemented a coverage policy for the principal insurable risks with coverage amounts that it considers compatible with its cash flow requirements. The total premiums paid for all insurance policies amounted to €88 thousand during fiscal year 2022.

Taking into account the specificity of its activities - concentrated on development at this stage - and on the innovative character of its approach, the quantification of any risks in the absence of a direct damage rate, or damage indicators in its sector of activity, makes it difficult to determine a coverage amount, in particular for civil liability. The Company, however, believes that the insurance policies mentioned below adequately cover the risks inherent in its activities and its insurance policy is consistent with the practices in its sector of business. The Company does not foresee any particular difficulties in keeping adequate levels of insurance in the future limited by the conditions and capacities of the market. The insurance policies are held with insurance companies that have good financial ratings and were chosen for their ability to contribute to the growth of the Company. OSE Immunotherapeutics deems that its insurance coverage and the limitations of its coverage are reasonable and prudent taking into account its activities and the associated risks.

The Company has subscribed to several insurance policies, including the following:

- A “business and professional civil liability” insurance policy with CNA (€4 thousand paid in 2022);
- A “managers’ liability” policy with AIG that covers the civil liability of the legal and factual executive corporate managers of the Company and its subsidiary, when such liability is incurred in the execution of their duties (€13 thousand paid in 2022);
- A professional multi-risk insurance policy taken out with Generali (€2 thousand paid in 2022) as well as cyber risk insurance (€1 thousand);
- In view of its investments made in laboratory equipment during 2018, the Company now has a specific insurance policy covering this equipment (€5,000 paid in 2022);
- The Company has also subscribed to insurance policies for the Phase 1 trials of OSE-127/S95011 (€44 thousand recognized for 2022) and BI 765063 (OSE-172) (€5 thousand recognized for 2022), €9 thousand for CoVepiT and €1 thousand for OSE-279.

The rates and coverage amounts depend on local regulations applicable to the clinical investigation centers concerned, such as in France, where the Public Health Code specifies an insurance obligation for clinical trial sponsors as well as the conditions of that insurance.

These agreements do not provide coverage against operating losses. The Company deems that the cost/benefit ratio of covering losses from operations in the event of an accident at its stage of development, particularly given the lack of revenue on sales of its products, does not justify subscribing to such coverage. The Company’s liability in clinical trials will be covered by specific agreements, whose rates and coverage amounts depend on local regulations applicable to the clinical investigation centers concerned, such as in France, where the Public Health Code sets out an insurance obligation for clinical trial sponsors as well as the conditions of that insurance. The overall amount of insurance premiums paid, and coverages held for clinical trials depends therefore on the number of trials, their location, and the predicted number of patients included in the trial.

The Company has also subscribed to an insurance policy for the civil liability of its executive corporate managers when such liability is incurred in the exercise of their duties.

The Company cannot guarantee that it will always be able to maintain or obtain similar insurance coverage at an acceptable price, which could lead it to accept more costly insurance policies and assume a higher level of risk. This will be important as the Company's business activity grows. Moreover, the occurrence of one or more major accidents, even if covered by insurance, could seriously impact the Company's business and financial position due to the interruption of its activities, the time for repayment by the insurance companies, should policy coverage limits be exceeded and, finally, due to premium increases resulting from such an accident.

The occurrence of one or more of these risks could have a material adverse impact on the business, prospects, financial position, results, and development of the Company.

Taking into account the Company's prospects and, in particular, as it initiates a greater number of clinical trials, the Company anticipates that its insurance premium expenses will continue to rise while remaining relatively low compared with the costs of its research and development, its annual losses, and the value of its assets.

3.8 Exceptional events and litigation

During the 2022 fiscal year and up to the registration date of this Universal Registration Document, the Company has not been involved in any administrative, criminal, legal, or arbitration procedure that could have a material adverse impact not reflected in the financial statements of the Company, on its activity, financial position, results or development.

4 Information about the issuer

4.1 Company name

The name of the Company is "OSE Immunotherapeutics" and its trade name is "OSE Immunotherapeutics".

4.2 Place of registration and registration number

The Company is listed in the Nantes Trade and Companies Register under ID number 479 457 715.

The Company's activity code is 7211Z. This corresponds to biotechnology research and development.

The Company's LEI is 969500HIUWVGY6NZSM05.

4.3 Date and term of incorporation

Initially formed as a limited liability company ("Société À Responsabilité Limitée") on November 17, 2004, it was converted into a public limited company ("Société Anonyme") with a Board of Directors by decision of the General Shareholders' Meeting of April 27, 2012.

The Company was formed for a period of 99 years from the date of its listing in the Trade and Companies Register, unless the term is extended or the Company is dissolved early.

The reporting date was set at December 31, every year from the Company's date of incorporation.

4.4 Registered office, legal form and legislation

The Company's registered office is at 22 boulevard Benoni Goullin, 44200 Nantes, France.

The Company is a public limited company (société anonyme) with a Board of Directors, governed by French law. It is governed by current and future legislation and regulations, in particular the French Commercial Code and amendments thereto, as well as by its bylaws.

Telephone: +33 (0)2 28 29 10 10

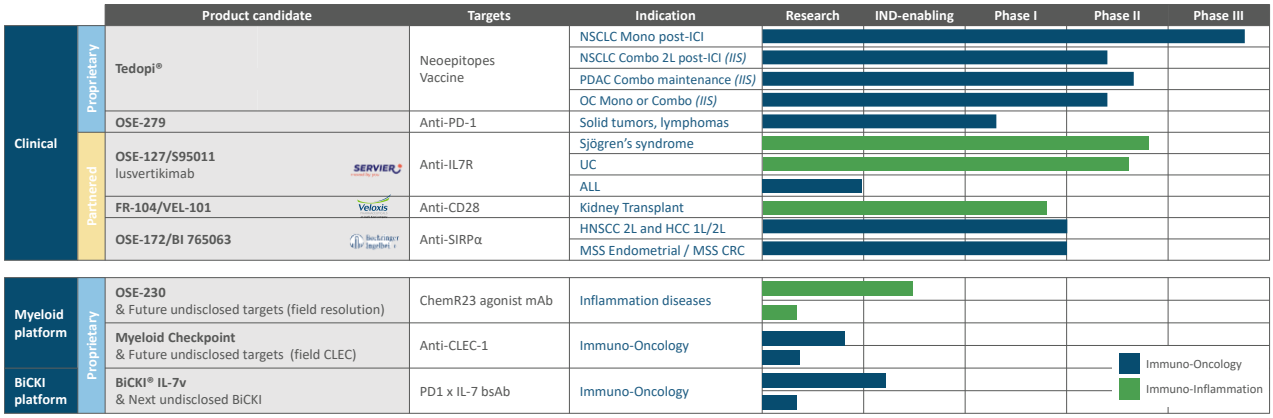
The Company website is: www.ose-immuno.com.

The reader's attention is drawn to the fact that, unless otherwise stated in this Universal Registration Document, the information appearing on this website does not form part of this document.

5 Business overview

OSE Immunotherapeutics is a biotechnology company focused on developing and partnering therapies to control the immune system for Immuno-Oncology and Immuno-Inflammation. The Company's clinical portfolio has a diversified risk profile from research to phase 3 clinical phase with independent risks. Five products are at clinical stage.

5.1 Principal activities



NB: To date, no product in the portfolio has been the subject for a Marketing Authorization application

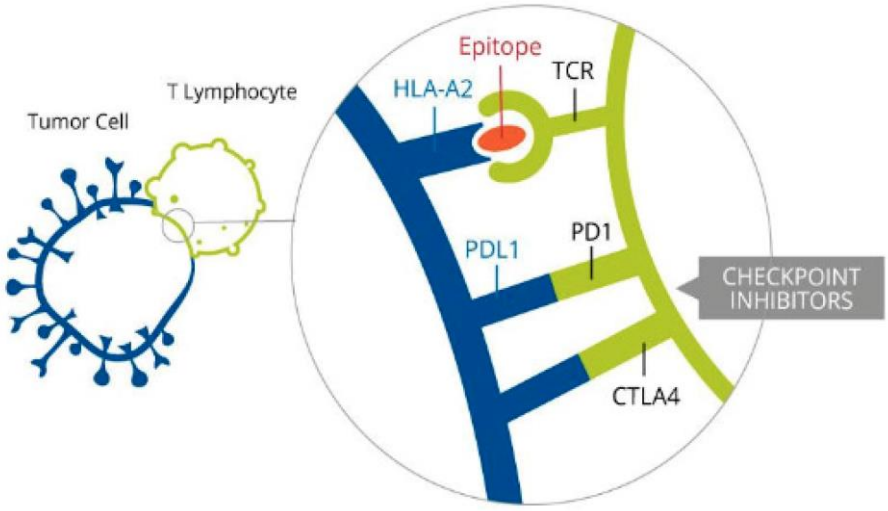
5.1.1 Proprietary products in clinical development

5.1.1.1 TEDOPI®, therapeutic vaccine developed for non-small cell lung cancer

Tedopi® is a combination of 10 neoepitopes (small peptides) selected and optimized from five tumor antigens present in several cancers that generate a specific cytotoxic T cell response directed against tumor cells that express at least one of those tumor antigens and an associated T helper response.

These five tumor antigens (CEA, p53, HER-2/neu, MAGE-2 and MAGE-3) were selected because their presence represents a poor prognostic factor in several types of cancers. Ninety percent of invasive tumors express at least one of these five tumor antigens. The 10 selected epitopes trigger a synergistic increased T lymphocyte response with no immunodominance (i.e. no preferential response to one or two epitopes). These strong cytotoxic T cell-specific responses cause the immune system to destroy tumor cells that express HLA-A2 and one of the targeted tumor antigens.

This product has been granted orphan status in the United States for lung cancer patients who are HLA-A2 positive, representing 45% of that population (under 200,000 people). This special status allows accelerated product development.



Tedopi®: mechanism of action

PHASE 3 CLINICAL TRIAL ATALANTE-1

The patients had advanced and metastatic lung cancer. The trial was randomized (2/1 balancing the groups evaluated with 2 patients receiving Tedopi® versus 1 patient receiving standard chemotherapy based on docetaxel or pemetrexed). Upon recommendation of the trial's independent committees, enrollment in this Phase 3 trial was prematurely suspended in 2020, due to the COVID-19 pandemic having a strong impact on mortality in lung cancer (363 patients were initially planned - 219 patients were finally recruited and followed). The primary endpoint was survival. These patients entered the trial mainly in third line treatment, i.e. after a first line of platinum-based chemotherapy followed by failure of a second line line checkpoint inhibitor treatment (anti-PD-(L)1) as last treatment - N= 183 patients). In this third line population representing 84% of the total trial population, the median survival was significantly improved with 9.23 months in the group receiving Tedopi® versus 7.56 months in the docetaxel group (HR: 0.695 p=0.038). The treatment line was a predefined stratification factor in the trial protocol (stratification enables to have treatment arms comparable for major prognostic criteria). Due to the trial's suspension, the statistical plan was revised and presented to the American health agency (FDA) before the database closing to propose, as main trial's analysis, a population of interest integrating the major stratification factor (third line) and a strong biological rationale. Patients with secondary resistance to checkpoint inhibitors (after a treatment of at least 12 weeks) are patients with an acquired resistance after a clinical benefit and are being considered as sensitive to immunotherapy (primary resistance to checkpoint inhibitors is described by a lack of benefit and a rapid escape in the 12 months of treatment).

The main analysis has shown a significant and clinically relevant effect of Tedopi® versus chemotherapy in patients with secondary resistance after checkpoint inhibitor failure (N=118 patients – 54% of the population). Globally, the tolerance and quality of life of these patients were significantly better with Tedopi®.

PHASE 3 CLINICAL TRIAL DETAILED RESULTS IN NON-SMALL CELL LUNG CANCER: THE MOST ADVANCED CLINICAL APPLICATION

The international Phase 3 clinical trial of Tedopi®, Atalante-1, was designed to evaluate the benefits of the product in HLA-A2 positive patients in second- or third line (84% of the randomized population) therapy versus chemotherapy (docetaxel or pemetrexed) in invasive stage IIIB or metastatic stage IV non-small cell lung cancer after failure of treatment with anti-PD1 and anti-PD-L1 checkpoint inhibitors.

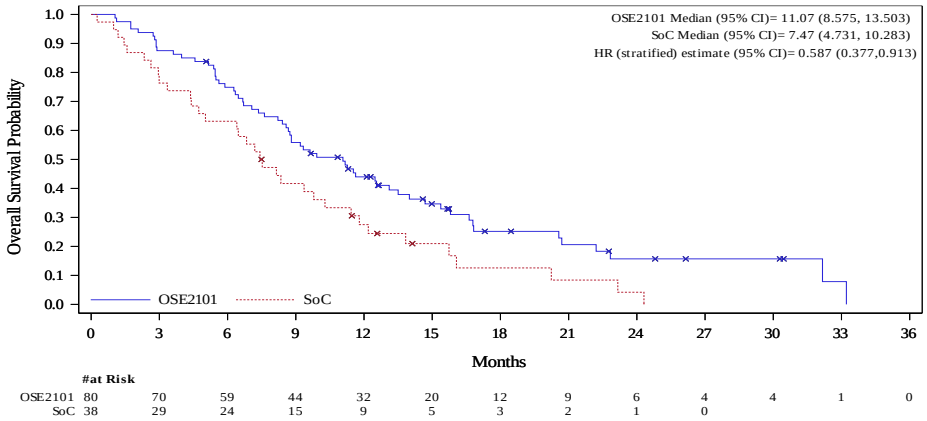
The post checkpoint inhibitor patient population, to which the Atalante-1 study is addressed, is currently growing, since anti-PD1 and anti-PD-(L)1 T checkpoint inhibitors are recognized as standard treatment both at an earlier stage of stage III disease, as first-line therapy for invasive stage IIIB and metastatic stage IV (instead of or in combination with chemotherapy) and as second-line treatment (after failure of first-line platinum-based therapy).

The positive of the Atalante-1 trial were presented at the ESMO 2021 annual meeting: "*Activity of OSE-2101 in HLA-A2 + non-small cell lung cancer (NSCLC) patients after failure to immune checkpoint inhibitors (IO): Final results of Phase 3 Atalante-1 randomized trial"*, completed at the 2022 ASCO and ESMO congresses.

POSITIVE CLINICAL DATA FROM THE INITIAL PHASE 3 CLINICAL TRIAL, ATALANTE-1, IN THIRD LINE TREATMENT

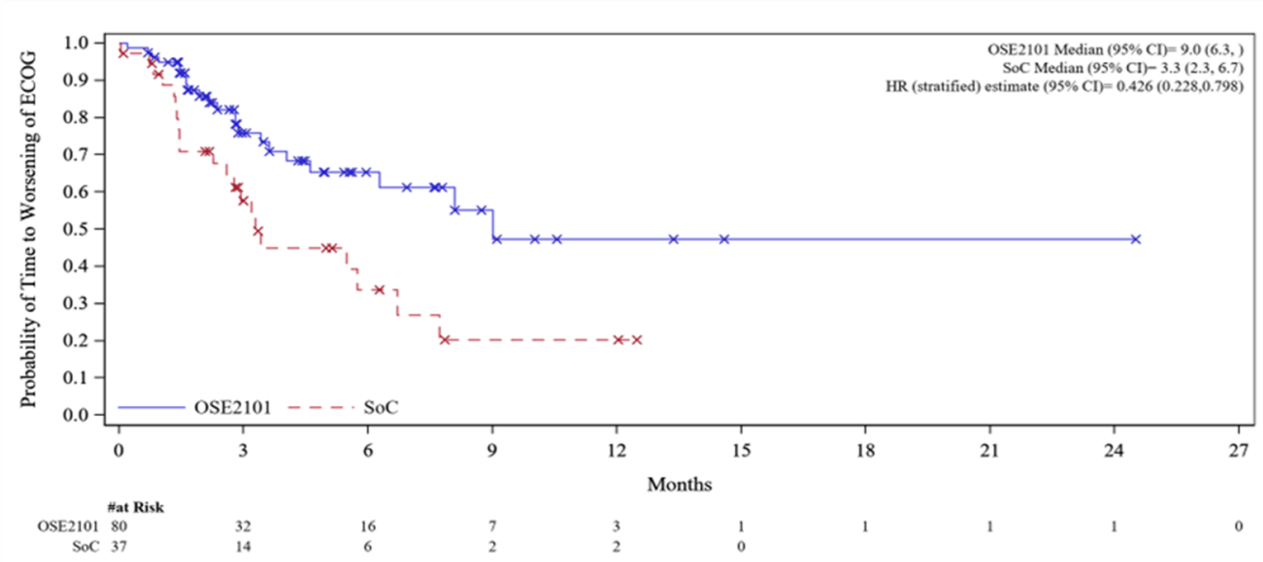
Tedopi® is the first cancer vaccine to show clinically meaningful efficacy results associated with a better safety and quality of life profile in monotherapy versus active comparator (chemotherapy-based standard of care) post-immune checkpoint inhibitors (ICI) failure in advanced or metastatic NSCLC:

- Significant **overall survival** (primary endpoint) (p=0.017, HR=0.59) with 44.4% overall survival (OS) rate at 1 year with Tedopi® versus 27.5% for chemotherapy and a meaningful gain of median OS of 3.6 months (ESMO 2021);



- Improved **post-progression survival** benefit in the Tedopi® arm (7.7 months versus 4.6 months, p=0.004, HR=0.46) (ESMO 2021);
- Significant **delayed median time to worsening ECOG* performance status** with a difference of 5.3 months (p<0.01, HR=0.43) (ASCO 2022);

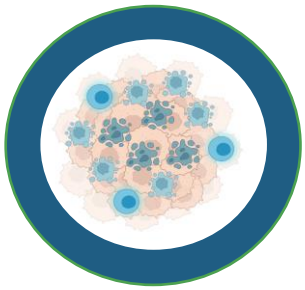
*The *ECOG score is a performance scale used to assess the overall state of health of the patient. It is subdivided into 5 grades from 0 to 5, ranging from fully active (0) to completely disabled and then to death (5).*



- Significant **better safety profile** with less severe (Grade 3-5) adverse events (11% with Tedopi® versus 35% with chemotherapy, p<0.05) (ESMO 2021);

- Significant **better Quality of Life** (Global health status: p=0.045; Role Functioning: p=0.025) (ASCO 2022) and **positive Net Treatment Benefit** (p=0.032) with Tedopi® compared to chemotherapy (ESMO 2022).

These positive clinical results in a clearly defined target population in secondary resistance to checkpoint inhibitors for this first Phase 3 trial are based on a strong biological rationale: increased specific T-cell responses induced by Tedopi®'s innovative mechanism of action correlated to the overall survival in HLA-A2+ non-small cell lung cancer patients. The direct activation of tumor specific T-cells by Tedopi® differs from immune checkpoint inhibitors releasing the break of immune response. In case of escape, T lymphocytes are described as "exhausted" ("exhausted T cells") and lose their effector function.



POSITIVE RECOMMENDATIONS FROM THE US FOOD AND DRUG ADMINISTRATION (FDA) "TYPE C" MEETING FOLLOWING THE EUROPEAN MEDICINES AGENCY (EMA) SCIENTIFIC ADVICE FOR THE CONFIRMATORY PHASE 3 TRIAL IN SECOND LINE TREATMENT

Both Agencies supported the continuation of the clinical development for Tedopi® through a new confirmatory phase 3 clinical trial versus standard of care in second line treatment for HLA-A2+ patients in advanced in non-small cell lung cancer (NSCLC).

OSE Immunotherapeutics working on the protocol development for the next confirmatory Phase 3 pivotal trial to support the regulatory registration of Tedopi® in second line treatment. The Company plans the selection of the different organizations under contract (specialized Clinical Research Organizations) necessary to conduct this research et the HLA-A1 test. This confirmatory Phase 3 is planned for HLA-A2+ patients with secondary resistance to immunotherapy (IO) after a first line of chemo-IO followed by a IO maintenance treatment of at least 12 weeks (defined as the threshold for secondary/acquired resistance by international expert consensus recommendations). The protocol design is developed with the support of the international NSCLC clinician experts' group which were already involved in the previous phase 3 Atalante-1 trial.

ONGOING COMPASSIONATE USE PROGRAMS IN THIRD LINE TREATMENT IN SECONDARY RESISTANCE POST-SEQUENTIAL CHEMOTHERAPY AND IMMUNOTHERAPY

OSE Immunotherapeutics is committed to provide Tedopi® through cohort early access and nominative compassionate use programs across European countries to address patients' needs alongside physicians' engagement.

The French National Authority for Health issued a negative decision on the cohort early access program in third line treatment related to the COVID crisis which led to the suspension of patient inclusion in the previous phase 3 (Atalante-1) and the consecutive main analysis on a population of interest with secondary resistance.

Patients can benefit from Tedopi® through compassionate use programs in third or further lines of treatment (post chemotherapy and immunotherapy) currently approved in France, Italy and Spain, confirming thereby the significant medical need for new therapeutic alternatives.

At the same time, given that the positive Phase 3 results significantly strengthened the value of Tedopi®, the Company is continuing to explore potential partnering opportunities for the product by region.

PHASE 1/2 CLINICAL TRIALS

TWO PHASE 1/2 CLINICAL TRIALS were conducted in the United States in patients with mildly aggressive cancers expressing HLA-A2 positively. The objective was to measure the tolerability of the product administered via repeated subcutaneous injections (5mg/peptide/dose) with six injections spaced three weeks apart. The efficacy criterion for the treatment sought was to

quantify and assess the specific cytotoxic T cell response induced with respect to natural epitopes and chemically modified optimized epitopes.

A positive cytotoxic T immune response was obtained in 93% of the patients in whom it was measured (16 patients who received six injections). Eight out of 15 patients responded to more than five epitopes, and on average, each patient induced a cytotoxic T cell response against four epitopes.

The effector activity of T lymphocytes from treated patients was also measured in their ability to destroy tumor cells presented to them if those tumor cells have the required receptors (ex vivo results). This T lymphocyte effector activity has been significantly established in human tumor cells that express HLA-A2 versus human tumors that do not express HLA-A2. The tumors studied also express one of the tumor antigens targeted by the epitopes (fresh human tumor lines and reference human colon or breast tumor lines).

The results of these Phase 1/2 trials showed that the product was generally well tolerated by patients. In addition, the regimen and doses were validated in these trials. This regimen was subsequently used in the Phase 2 trial with an initial induction period during the first six injections (three weeks apart) followed by a period of consolidation of the response through a subcutaneous injection every two to three months. This mode of administration was also the one used in the Phase 3 trial in non-small cell lung cancer.

PHASE 2 CLINICAL TRIAL

A Phase 2 clinical trial of Tedopi® was conducted in the United States in Stage IIIB invasive or IV metastatic non-small cell lung cancer (NSCLC) in HLA-A2 positive patients after failure of at least one first line of therapy. The purpose of the study was to evaluate the tolerability, efficacy (tumor response and survival), and cytotoxic T immunogenicity of the product.

The results of this study showed the efficacy of the treatment, with an increase in survival associated with good tolerability. The median survival of patients treated with Tedopi® was 17.3 months compared to 12 months for the control group (composed of HLA-A2 negative patients).

135 patients entered this trial; 64 patients were HLA-A2 positive; 72 patients were HLA-A2 negative with information available only on one-year survival for this observation group.

A large majority of patients were metastatic at inclusion (67% of patients). 31% of patients had received at least one prior first line of therapy; 28% received two prior lines, and 37.5% of patients received three or more therapeutic lines (up to six therapeutic lines). 92% had received prior platinum therapy and 34% had received prior targeted therapy (gefitinib or erlotinib).

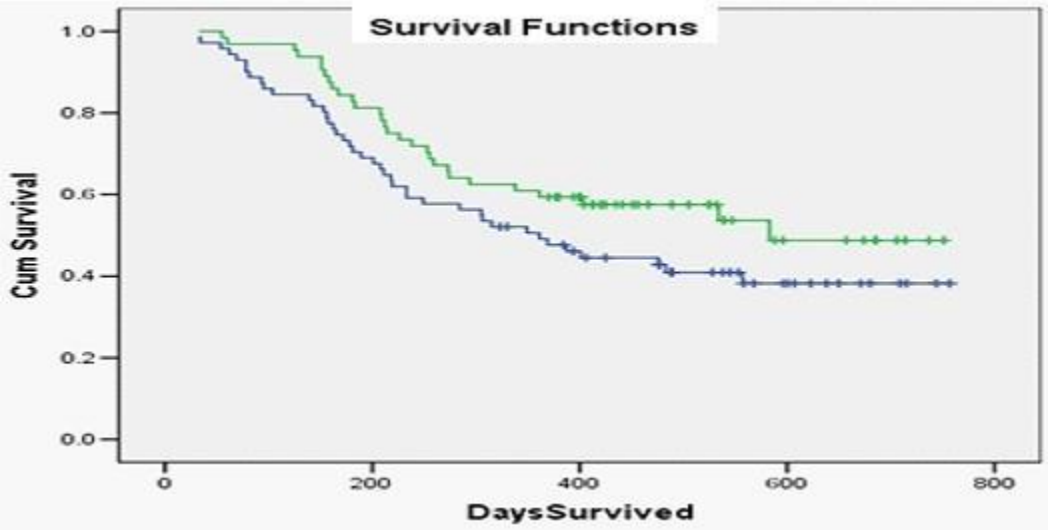
The group of 72 HLA-A2 negative patients was monitored only for one-year survival data, as the trial was designed to assess the one-year survival rate.

SURVIVAL RESULTS

The median survival was 17.3 months in the Tedopi®-treated group and 12 months in the HLA-A2 negative group not treated with immunotherapy (observation group receiving standard therapy). This median survival of 17 months is especially important in this trial population, with 67% of patients metastatic. In addition, this population was previously heavily pre-treated with different therapeutic lines (65% of patients received more than two lines - patients receiving third-line therapy, and 92% received at least one platinum-based chemotherapy).

The one-year survival rate was 59% in the HLA-A2 positive group compared to 49% in the HLA-A2 negative group. This difference in efficacy in favor of the treatment under study, although not significant, is very interesting because the HLA-A2 negative control group has a better prognosis for survival (Nagata et al. 2009, Bulut et al. 2009). The two-year and three-year survival rates for the immunotherapy group were 39% and 27%, respectively. At four years, the long-term survival rate was maintained for 25% of patients (see curve).

Figure 1: Survival curve

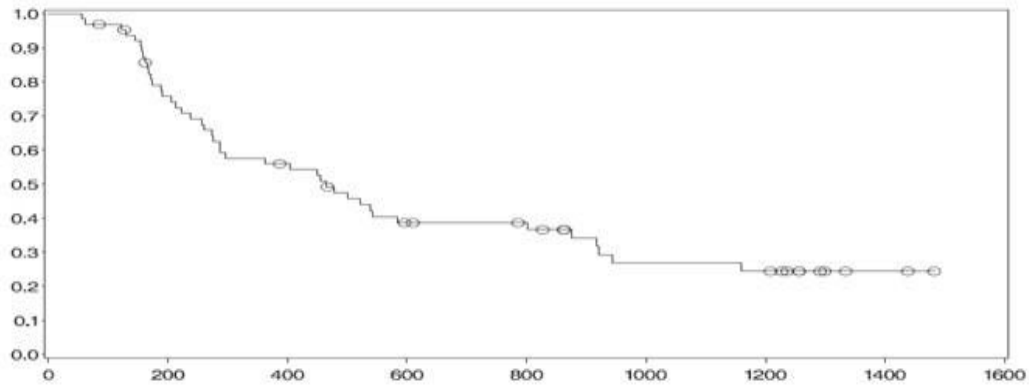


Green = HLA-A2+: Patients treated with Tedopi® (n= 64 - 29 deaths)
Blue = HLA-A2-: Control group (n = 71 - 42 deaths)
1-year survival rate: p = 0.063; 59% survival (HLA-A2+ treated group); 49% survival (HLA-A2- control group)

Median survival (days): p = 0.086: 17.3 months (HLA-A2+ treated group); 12 months (HLA-A2- control group)

Figure 2: Long-term survival curve

Long-term survival curve: 25% of patients present at four years



The long-term survival curve is all the more interesting since the majority of patients included were metastatic and heavily pre-treated previously.

Evaluation of progression-free time: at the same time, the median progression-free time for patients treated with Tedopi® was estimated at 9.4 months, with 47% of patients still progression-free at one year.

Evaluation of tumor response: stabilization of tumor response was observed in 89% of the population.

Cytotoxic T cell immune response correlated with observed survival

With Tedopi® a T cell immune response (measured in Elispot) for at least one epitope is observed in 91% of this population most often at a metastatic stage. The immune response is positive for three epitopes in 64% of the population.

The correlation between survival and the number of epitope responses was established to a significant degree (log Rank test). Longer survival was correlated to a significant degree with the number of positive responses to the various epitopes ($p<0.001$).

From 0 to 1 epitope: 406 ± 58 days of survival

From 2 to 3 epitopes: 778 ± 72 days of survival
From 4 to 5 epitopes: 875 ± 67 days of survival

New exploratory data from a translational analysis were presented in a poster session *entitled: "Survival is improved by antigen-specific cytotoxic T lymphocytes (CTL) responses after treatment with the neoepitope-based vaccine Tedopi® in HLA-A2 positive advanced non-small cell* lung cancer (NSCLC) patients" *, at the Society for Immunotherapy of Cancer (SITC) conference held in National Harbor, Maryland, USA, November 6-10, 2019. This poster session described the results of immunogenicity assays to explore the predictive effect of neoepitopes on overall survival by type and number. The results presented demonstrated that in advanced non-small cell lung cancer (NSCLC) patients, survival was significantly prolonged in patients immunized with the combination of neoepitopes used in Tedopi®.

The long-term survival observed at four years is accompanied by a favorable tolerability profile.

(M. Barve et al. JCO 2008 - J. Clin Oncol 26: 2008 (May 20 suppl; abst 8057) (Janus et al. 2012)

(J. Nemunaitis et al., Denver IASLC 2015).

TEDOPI® IN CLINICAL DEVELOPMENT IN ADVANCED PANCREATIC CANCER SPONSORED BY THE GERCOR COOPERATIVE GROUP IN ONCOLOGY

The Phase 2 clinical trial, TEDOPaM, is a non-comparative, randomized study of Tedopi® alone or in combination with nivolumab or FOLFIRI* after an induction treatment with FOLFIRINOX** as maintenance treatment in patients with advanced or metastatic pancreatic adenocarcinoma.

A poster presented the 2022 ASCO congress has shown the preliminary results of this study.

This presentation featured the first interim results from this Phase 2 clinical trial of Tedopi® in advanced or metastatic pancreatic cancer. The primary endpoint of the trial is the one-year survival rate (Fleming- futility analysis; null hypothesis <25%), and the key secondary endpoint was the Time to maintenance Strategy Failure (TSF= time maintenance + FOLFIRI reintroduction).

The interim results refer to the 29 randomized HLA-2 positive patients with no progression after 8 cycles of FOLFIRINOX: 9 patients included in standard arm A (FOLFIRI) with 44% of 1-year Overall Survival (OS) rate and one partial response (11%); 10 patients in experimental arm B (Tedopi® monotherapy) with 40% of 1-year OS rate and one partial response (10%); 10 patients in arm C (nivolumab + Tedopi®) with 30% of 1-year OS rate and no partial response.

Tedopi® as maintenance monotherapy showed a favorable safety profile and encouraging time to strategy failure warranting further evaluation. Nivolumab + Tedopi® was associated with poorer outcomes leading to the closing of this arm. Following an Independent Data Monitoring Committee (IDMC) recommendation, the study is ongoing with an amended protocol comparing a maintenance treatment Tedopi® in combination with FOLFIRI versus FOLFIRI chemotherapy after treatment with FOLFIRINOX.

Clinicaltrials.gov : NCT03806309
**FOLFIRINOX: a chemotherapy regimen combining folinic acid, fluorouracil, irinotecan and oxaliplatin*
***FOLFIRI: a chemotherapy regimen combining folinic acid, fluorouracil and irinotecan*

TEDOPI® IS CURRENTLY BEING EVALUATED IN PHASE 2 COMBINATION TRIALS IN THREE INDICATIONS:

The development of Tedopi® was expanded with two Phase 2 trials in combination with a PD1 inhibitor sponsored by clinical partners, including a trial in patients with non-small cell lung cancer in secondary resistance to non-small cell lung cancer. checkpoint inhibitors, and the other trial in ovarian cancer.

PHASE 2 CLINICAL TRIAL IN NON-SMALL CELL LUNG CANCER AFTER FIRST-LINE CHEMO-IMMUNOTHERAPY SPONSORED BY THE ITALIAN FOUNDATION FORT

The Phase 2 clinical trial Combi-TED, started in November 2021, evaluates Tedopi® in combination with Opdivo® (nivolumab), a checkpoint inhibitor targeting the PD1 receptor of Bristol Myers Squibb, or with chemotherapy as a second-line treatment in HLA-A2 positive patients with metastatic non-small cell lung cancer after first-line chemo-immunotherapy. Clinical trial sponsored and conducted by the Italian Oncology Foundation FoRT and sponsored by Bristol Myers Squibb and OSE Immunotherapeutics.

Clinicaltrials.gov : NCT04884282

PHASE 2 CLINICAL TRIAL IN OVARIAN SPONSORED BY THE ONCOLOGY GROUP ARCAGY-GINECO

The Phase 2 clinical trial TEDOVA includes three treatment arms and evaluates Tedopi® as a maintenance treatment as monotherapy or in combination with the anti-PD1 Keytruda® (pembrolizumab), a Merck checkpoint inhibitor, versus the reference treatment in patients with platinum-sensitive recurrent ovarian cancer and whose disease is controlled after platinum-based chemotherapy.

It is planned to include 180 patients in the TEDOVA trial, the first of which was randomized on August 26, 2021. The first results of the study are expected in early 2025.

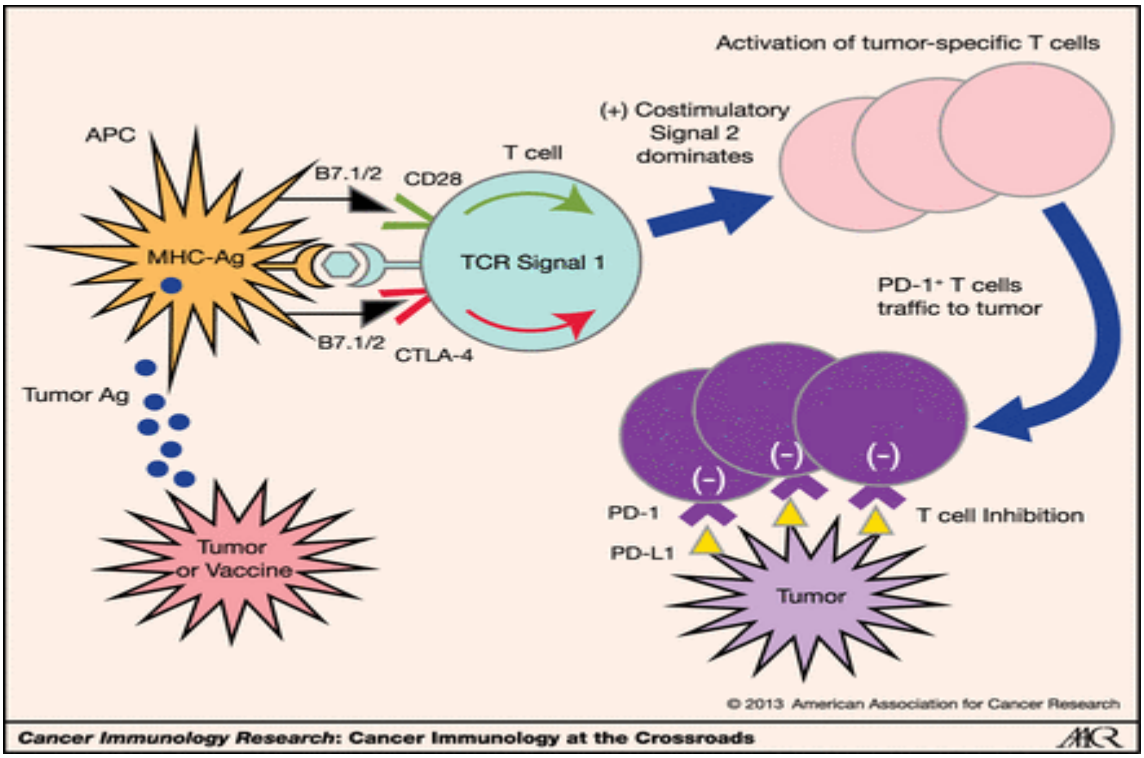
As part of its partnership strategy, the Company is exploring partnership opportunities for Tedopi®, its most advanced product in its development stage.

A SOLID RATIONAL FOR EVALUATING TEDOPI® IN COMBINATION WITH A CHECKPOINT INHIBITOR

Blocking checkpoint inhibitors is the most advanced approach in cancer immunotherapy to activate anti-tumor immunity, with two products registered, for example, in lung cancer (NSCLC) or melanoma (nivolumab and pembrolizumab). Even though this clinical activity is very promising, with an observed difference in survival compared to chemotherapy, other strategies are expected to increase the results in terms of survival, progression-free survival time, quality of life and control of observed autoimmune reactions. Effective tumor clearance requires coordinated immune mechanisms involving both the activation of immune effector cells and the blocking of suppressor mechanisms. Therefore, there is a strong rationale for combining "T lymphocyte specific therapeutic vaccines" with T lymphocyte-specific activation action, with non-specific checkpoint inhibitors that act as a brake on T lymphocytes.

To counter the immune system's attack, cancer cells use a wide variety of mechanisms, including low expression of histocompatibility molecules or MHC (MHC receptors are essential when they partner with peptides in the form of epitopes or neoepitopes to trigger a T lymphocyte response). Tumor cells also use the expression of T cell inhibitory molecules on which checkpoint inhibitors act, such as certain members of the family of molecules called B7, and where the PD-L1 ligand of PD1 (also PD-L2, B7-H3, VISTA) is found.

Combinations of specific cancer therapies with non-specific checkpoint inhibitors have been successfully tested in certain tumors, as already explained in pancreatic cancer (Le D.T. et al., 2013), and in prostate cancer [Jochems C. et al., 2014] and melanoma [Hodi F.S. et al., 2010].



The distinct roles of control points such as CTLA-4 and PD1 in the regulation of anti-tumor T response effector cells are described in the tumor microenvironment by J. R. Brahmer and D. M. Pardoll in the diagram above.

Interlocking mechanisms between specific and non-specific immunity:

MHC/epitope/TCR: this is the first signal for specific activation of T lymphocytes, it occurs via the epitope presented by the major histocompatibility complex (MHC) at the T lymphocyte receptor (TCR - signal 1). The interaction between the TCR and the peptide-MHC complex must be prolonged and of high intensity to be effective in the activation of the T lymphocyte. The affinity between the TCR receptor and the presented peptide in the groove of the MHC molecule plays a major role in the stability of this bond.

The tumor cell (or a "tumor" vaccine in the diagram) is the source of tumor antigens that must be processed and presented as epitopes by the MHC major histocompatibility complex to activate the T lymphocyte cells.

Tumor-specific T cell activation leads to T cell proliferation and effector function, but also to overexpression of PD1. In the tumor microenvironment, PD1-expressing T cells may encounter PD-L1 ligands, which may prevent them from expressing their cytotoxic killing function. The PD1 (programmed cell death-1) molecule is expressed after CTLA-4 and is recognized by two ligands (PD-L1 and PD-L2).

Currently, the checkpoint inhibitors that are the most advanced or registered in multiple clinical indications target CTLA4, PD1, PD-L1, al. of which are expressed on T lymphocytes. The PD1/PD-L1 axis is the main target of the checkpoint inhibitors that act on lymphocyte brakes in the tumor microenvironment.

However, there is a significant initial immunological escape from these biotherapies (response rate limited to a small number of treatment-naïve patients expressing the PD-L1 marker). For those patients who did respond, secondary immunological escape (after an initial response to treatment) became an emerging problem. Combining treatments that act on multiple targets is one way to combat that escape and overcome immune resistance, but these combinations must ensure manageable safety and intolerability. The elements that favor this type of combination are many:

- High expression of HLA and CD8 at the tumor level is a good prognostic factor (SD Brown et al.; Genome Research 2014);
- The increase of IFN-γ in tumor cells linked to the effect of therapeutic vaccines or neoepitopes facilitates immune recognition with an increase in Major Histocompatibility Complex or MHC-I receptors. This is observed at the same time as the increased expression of PD-L1 (Grenga I et al; Journal for ImmunoTherapy of Cancer 2014);
- Tumor neoantigens with a high tumor level are associated with longer overall survival (N McGranahan et al, Science 2016 - Clonal neoantigens elicit T cell immunoreactivity and sensitivity to immune checkpoint blockade).

Other actors in the tumor microenvironment are also involved with the generation of an immunosuppressive tumor microenvironment that include regulatory T lymphocytes (called Treg, identified as CD4+ CD25+ foxp3+) and the differentiation of

suppressive lines of myeloid origin (MDSC) that inhibit T effectors (via secretion of mediators such as TGF beta and IL-10). Tregs are T lymphocytes that suppress T immune responses. Tregs accumulate in the tumor, also preventing the killing functions. The interaction of CTLA-4, PD1 and PD-L1 molecules with their ligand is necessary for the suppressive function of the Tregs while the activating signals that pass through CD28 inhibit this suppressive function. Checkpoint inhibitors therefore also promote inhibition of the suppressive activity of the Tregs.

Suppressive myeloid cells may also accumulate in tumors and disrupt the function of cytotoxic lymphocytes. There are currently no treatments to eliminate them.

Key references related to Tedopi® and current lung cancer treatments:

Barve M, Bender J, Senzer N, Cunningham C, Greco FA, McCune D, Steis R, Khong H, Richards D, Stephenson J, et al. Induction of immune responses and clinical efficacy in a phase II trial of IDM-2101, a 10-epitope cytotoxic T-lymphocyte vaccine, in metastatic non-small-cell lung cancer.

J Clin Oncol. 2008; 26 (27):4418-25. doi: 10.1200 / JCO.2008.16.6462.

Beebe M, Qin M, Moi M, Wu S, Heiati H, Walker L, Newman M, Fikes J, Ishioka GY. Formulation and characterization of a ten-peptide single-vial vaccine, EP-2101, designed to induce cytotoxic T-lymphocyte responses for cancer immunotherapy. Hum Vaccin. 2008;4(3):210-8.

Brahmer J, Reckamp KL, Baas P, Crinò L, Eberhardt WE, Poddubskaya E, Antonia S, Pluzanski A, Vokes EE, Holgado E, Waterhouse D, Ready N, Gainor J, Arén Frontera O, Havel L, Steins M, Garassino MC, Aerts JG, Domine M, Paz-Ares L, Reck M, Baudelet C, Harbison CT, Lestini B, Spigel DR.

Nivolumab versus Docetaxel in Advanced Squamous-Cell Non-Small-Cell Lung Cancer. N Engl J Med. 2015;373 (2): 123-35. doi: 10.1056/NEJMoa1504627.

Bulut I, Meral M, Kaynar H, Pirim I, Bilici M, Gorguner M. Analysis of HLA class I and II alleles regarding to lymph node and distant metastasis in patients with non-small cell lung cancer. Lung Cancer. 2009;66(2):231-6.

Garon EB, Rizvi NA, Hui R, Leighl N, Balmanoukian AS, Eder JP, Patnaik A, Aggarwal C, Gubens M, Horn L, Carcereny E, Ahn MJ, Felip E, Lee JS, Hellmann MD, Hamid O, Goldman JW, Soria JC, Dolled-Filhart M, Rutledge RZ, Zhang J, Lunceford JK, Rangwala R, Lubiniecki GM, Roach C, Emancipator K, Gandhi L; KEYNOTE-001 Investigators. Pembrolizumab for the Treatment of Non-Small-Cell Lung Cancer. N Engl J Med. 2015;372(21):2018-28. doi: 10.1056/NEJMoa1501824.

Hanna N, Shepherd FA, Fossella FV, Pereira JR, De Marinis F, von Pawel J, Gatzemeier U, Tsao TC, Pless M, Muller T, Lim HL, Desch C, Szondy K, Gervais R, Shaharyar, Manegold C, Paul S, Paoletti P, Einhorn L, Bunn PA Jr. Randomized phase III trial of pemetrexed versus docetaxel in patients with non-small-cell lung cancer previously treated with chemotherapy. J Clin Oncol. 2004;22(9):1589-97.

Howlader N, Noone AM, Krapcho M, Garshell J, Miller D, Altekruse SF, Kosary CL, Yu M, Ruhl J, Tatalovich Z,Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER Cancer Statistics Review, 1975-2012, National Cancer Institute. Bethesda, MD,, based on November 2014 SEER data submission, posted to the SEER web site, April 2015

Iversen TZ, Engell-Noerregaard L, Ellebaek E, Andersen R, Larsen SK, Bjoern J, Zeyher C, Gouttefangeas C, Thomsen BM, Holm B, Thor Straten P, Mellemgaard A, Andersen MH, Svane IM.

Long-lasting disease stabilization in the absence of toxicity in metastatic lung cancer patients vaccinated with an epitope derived from indoleamine 2,3 dioxygenase. Clin Cancer Res. 2014 Jan 1;20(1): 221-32. doi: 10.1158/1078-0432.CCR-13-1560.

Masucci GV, Andersson E, Villabona L, Helgadottir H, Bergfeldt K, Cavallo F, et al. Survival of the fittest or best adapted: HLA-dependent tumor development. J Nucleic Acids Investig [Internet]. March 1, 2010 [Accessed Sept. 23, 2013]; 1 (1). Available at: http://www.pagepress.org/journals/index.php/jnai/article/view/1654 .

Nagata Y, Hanagiri T, Mizukami M, Kuroda K, Shigematsu Y, Baba T, Ichiki Y, Yasuda M, So T, Takenoyama M, Sugio K, Nagashima A, Yasumoto K . Clinical significance of HLA class I alleles on postoperative prognosis of lung cancer patients in Japan. Lung Cancer. 2009; 65(1):91-7.doi:10.1016/j.lungcan.2008.10.012.

Nemunaitis J, Cunningham, C, Bender, J, Ishioka, G, Maples, P, Pappen, B, Stephenson, J, Morse, M, Greco, A, McCune, D, Steis, R, Nugent, F, Khong, HT, Richards, D. Phase II trial of a 10-epitope CTL vaccine, IDM-2101, in metastatic NSCLC patients: Induction of immune responses and clinical efficacy. International Society for Biological Therapy of Cancer 2007, p 891-2.

Nemunaitis J, Nemunaitis M, Senzer N, Snitz P, Bedell C, Kumar P, Pappen B, Maples PB, Shawler D, Fakhrai H. Phase II trial of Belagenpumatucel-L, a TGF-beta2 antisense gene modified allogeneic tumor vaccine in advanced non small cell lung cancer (NSCLC) patients. Cancer Gene Ther. 2009; 16(8):620-4. doi: 10.1038/cgt.2009.15.

Nemunaitis J. et al., T-cytotoxic specific immunotherapy in NSCLC with brain metastases. P2.01-003 - Abstract 1202 16th world conference on lung cancer, September 2015

Paz-Ares L, Horn L, Borghaei H, Spigel DR, Steins M, Ready N, Quan Man Chow L, Vokes EE, Felip E, Holgado E, Barlesi F, Kohlhaeufl M, Rodriguez O, Burgio MA, Fayette J, Gettinger SN, Harbison C, Dorange C, Graf Finckenstein F, Brahmer JR. Phase III, randomized trial (CheckMate 057) of nivolumab (NIVO) versus docetaxel (DOC) in advanced non-squamous cell (non-SQ) non-small cell lung cancer (NSCLC). J Clin Oncol 33; 2015 (suppl; abstr LBA109).

Rizvi N, Brahmer J, Ou SH et al. Safety and clinical activity of MEDI4736, an anti-programmed cell death-ligand (PD-L1) antibody in patients with non-small-cell lung cancer. J Clin Oncol 2015; 33 (suppl; abstr 8032)

Rizvi NA, Garon E, Leighl N et al. Optimizing PD-L1 as biomarker of response with pembrolizumab as first-line therapy for PD-L1 positive metastatic non-small cell lung cancer: updated data from KEYNOTE-001. J Clin Oncol 2015;33 (suppl; abstr 8026)

So T, Takenoyama M, Sugaya M, Yasuda M, Eifuku R, Yoshimatsu T, Osaki T, Yasumoto K. Unfavorable prognosis of patients with non-small cell lung carcinoma associated with HLA-A2. Lung Cancer 2001; 32(1):39-46.

Spira AI, Park K, Mazières J et al. Efficacy, safety and predictive biomarkers results from a randomized phase II study comparing MPDL3280A vs docetaxel in 2/3L NSCLC (POLAR). J Clin Oncol 2015; 33 (suppl; abstr 8010)

Travis WD, Brambilla E, Noguchi, M, et al. International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society International Multidisciplinary Classification of Lung Adenocarcinoma. J Thorac Oncol. 2011; 6(2):244–285. doi: 10.1097/JTO.0b013e318206a221

Vansteenkiste JF, Cho B, Vanakesa T, De Pas T, Zielinski M, Kim MS, Jassem J, Yoshimura M, Dahabreh J, Nakayama H, Havel L, Kondo H, Mitsudomi T, zarogoulidis K, gladkov KA, Spiessens B, Brichard Y, Debruyne C, Therasse P, Altorki NK. MAGRIT, a double-blind, randomized, placebo-controlled phase III study to assess the efficacy of the recmage-a3 + as15 cancer immunotherapeutic as adjuvant therapy in patients with resected mage-a3-positive non-small cell lung cancer (NSCLC). Ann Oncol 2014;25(suppl_4):iv409-iv416. doi:10.1093/annonc/mdu347.

Viteri S., Vanel FR, Hilgers W. et al. Early signs of activity of Tedopi® (OSE2101), a multiple neoepitope vaccine, in a phase 3 trial in advanced lung cancer patients after failure to previous immune checkpoint inhibitors (Atalante-1)
https://www.abstractsonline.com/pp8/#!/6812/presentation/2375

Yadav M. et al., Predicting immunogenic tumor mutations by combining mass spectrometry and exome sequencing. Nature vol 515, Nov 2014

Yamaguchi Y, Yamaue H, Okusaka T, Okuno K, Suzuki H, Fujioka T, Otsu A, Ohashi Y, Shimazawa R, Nishio K, Furuse J, Minami H, Tsunoda T, Hayashi Y, Nakamura Y. Guidance for Peptide Vaccines for the Treatment of Cancer, The Japanese Society for Biological Therapy. Guidance for peptide vaccines for the treatment of cancer. Cancer Sci. 2014;105(7): 924-31.doi: 10.1111/cas.12443.

5.1.1.2 OSE-279, A PROPRIETARY ANTI-PD1 MONOCLONAL ANTIBODY

OSE-279 is a high affinity humanized anti-PD1 monoclonal antibody blocking both PD-L1 and PD-L2, the ligands of PD1 overexpressed by tumor cells. PD-L1 and PD-L2 are used by tumor cells to escape the immune system. Stimulation of PD-L1 and PD-L2 on tumor cells and other cell types of the tumor microenvironment is a mechanism of tumor immune escape.

OSE-279 is the key anti-PD1 backbone component of OSE's bifunctional checkpoint inhibitor BiCKI® platform that is targeting PD1 and other new immune targets, combined with new immunotherapy targets.

CLINICAL PHASE 1/2 ONGOING IN ADVANCED SOLID TUMORS AND LYMPHOMAS

OSE-279 is in Phase 1/2 clinical phase since December 2022. This first-in-human open label Phase 1/2 dose escalation and expansion study aims to determine the Maximum Tolerated Dose and/or the recommended Phase 2 dose of OSE-279 as a monotherapy in advanced solid tumors or lymphomas. Secondary objectives include assessment of OSE-279's antitumor activity, evaluation of the safety profile, pharmacokinetic and receptor occupancy or pharmacodynamic profile.

This first clinical study will also allow the Company, at a later stage, to explore OSE-279, the backbone of OSE's BiCKI® platform, in combination with other OSE drug candidates or with external assets accessed through potential new partnerships with biotech or pharmaceutical companies.

5.1.2 Clinical products developed in partnership

5.1.2.1 OSE-127/S95011, an immunomodulatory monoclonal antibody that targets the Interleukin-7 receptor alpha chain (IL-7R-alpha or CD127 receptor)

Publication of the first results with OSE-127 in the 'Journal of Immunology' 2023

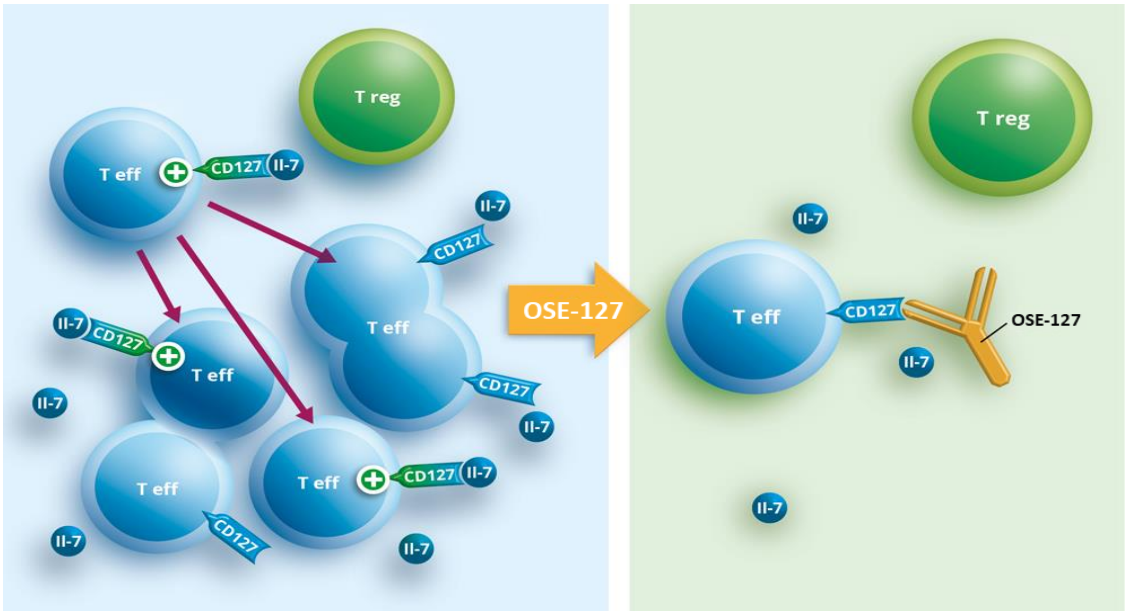
First-in-Human Study in Healthy Subjects with the Noncytotoxic Monoclonal Antibody OSE-127, a Strict Antagonist of IL-7Rα.

J Immunol. 2023 Mar 15;210(6):753-763.doi: 10.4049/jimmunol.2200635 Nicolas Poirier , Irène Baccelli , Lyssia Belarif , Riad Abès , Géraldine Teppaz , Caroline Mary , Sonia Poli , Claudia Fromond , Isabelle Girault , Sabrina Pengam , Emilienne Soma , Fanny De Sa , Jean-Pascal Conduzorgues , Cécile Braudeau, Regis Josien, Bram Volckaert , Dominique Costantini , Frédérique Corallo.

This publication reports on the Phase 1 trial positive results and on the understanding of the safety and tolerability profile for OSE-127, with a novel and differentiated mechanism of action of the only full-antagonist monoclonal antibody of IL-7 receptor for the treatment of chronic autoimmune diseases and also developed in hemato-oncology in lymphoblastic leukemia.

OSE-127/S95011 has an innovative mechanism of action that blocks Interleukin-7 and internalization of the receptor, inducing a powerful antagonist effect on pathogenic T lymphocytes involved in autoimmune diseases. This mechanism has been confirmed in in vivo models of autoimmune diseases that mimic human ulcerative colitis.

A strong antagonist effect on memory T lymphocytes while preserving the regulator T lymphocytes.



OSE-127/S95011, IL-7 receptor antagonist

Interleukin-7 (IL-7) is an interleukin involved in T cell survival, development and homeostasis. T lymphocyte proliferation requires the presence of Interleukin 7. IL-7 is the fuel for many autoimmune diseases. A major challenge in the treatment of inflammatory diseases could be the presence of pathogenic memory T lymphocytes in the tissues, likely to be resistant to conventional immunomodulatory therapy.

OSE-127/S95011 inhibits and blocks the IL-7 pathway. This interleukin plays an important role in the pathophysiology of autoimmune diseases such as ulcerative colitis, an inflammatory bowel disease in which T lymphocytes have a deleterious role destroying the lining of the colon.

OSE-127/S95011 is being developed under a two-step licensing option agreement with Servier until two Phase 2 clinical studies are completed, with exercise of the option upon successful completion of the one of the two studies.

The Phase 2 trial in ulcerative colitis, an autoimmune bowel disease started in December 2020, sponsored by OSE Immunotherapeutics. In parallel, another phase 2 in primary Sjögren's Syndrome, a systemic autoimmune disease characterized by damage to the exocrine glands, in particular the lacrimal and salivary glands, is sponsored and conducted by Servier. Patient enrollment was completed in November 2022 and the results are expected in 2023.

As part of the license option agreement, Servier has paid a €5 million milestone to OSE Immunotherapeutics (August 2021) upon enrollment of the first patient in the Phase 2 study in primary Sjögren syndrome. An additional €15 million payment is planned if Servier exercises the option upon completion of the two Phase 2 clinical studies.

In February 2019, Servier validated the first step of this agreement with the exercise of the first option after the validation of a previously defined development stage. Furthermore, this clinical development is currently being conducted as part of the EFFIMab

consortium funded by Bpifrance, of which OSE Immunotherapeutics is the leader and which includes public and private partners. Continued development after this Phase 2 will be fully ensured by Servier.

POSITIVE PHASE 1 CLINICAL TRIAL IN HEALTHY VOLUNTEERS

OSE-127/S95011 entered the clinical trial phase at the end of 2018, following the authorization granted by the Agence Fédérale des Médicaments et des Produits de Santé (AFMPS) and the Belgian Ethics Committee in November.

The purpose of the Phase 1 dose-escalation clinical study, the first administration to human, was to evaluate the safety and tolerability of single- and multiple-doses of OSE-127/S95011 through intravenous and subcutaneous administration. This randomized, double-blind, placebo-controlled trial was conducted in 63 healthy volunteers. Secondary endpoints included measures of pharmacokinetics, pharmacodynamics and immunogenicity to help assess and understand how the drug is absorbed and metabolized. In addition, exploratory biomarkers were used to assess the product's potential to treat inflammatory autoimmune diseases.

This Phase 1 clinical study of OSE-127/S95011 showed positive results, with a good safety and tolerability profile for the product. All pharmacokinetic and pharmacodynamic parameters were consistent and demonstrated dose proportionality throughout the dose escalation to 10 mg/kg. These data made it possible to determine the dosing and administration schedule for the two independent Phase 2 clinical trials, one in ulcerative colitis (OSE-sponsored) and one in primary Sjogren's Syndrome (Servier-sponsored).

PHASE 2 CLINICAL TRIAL UNDERWAY IN ACTIVE MODERATE TO SEVERE ULCERATIVE COLITIS (OSE IMMUNOTHERAPEUTICS AS SPONSOR)

This randomized, double-blind, placebo-controlled Phase 2 clinical trial aims to assess the efficacy and tolerability of OSE-127/S95011 in patients suffering from moderate to severe active ulcerative colitis after failure, loss of response or intolerance to previous treatment(s). The first patient was included in this study in December 2020, which expects to include 150 patients.

The primary endpoint of the study in ulcerative colitis is the change in the modified Mayo score from the baseline to the clinical symptoms at week 10 (stool frequency and rectal bleeding subscores) in addition to the endoscopic subscore (see www.clinicaltrials.gov).

The patient population (with moderate to severe ulcerative colitis, failure or intolerance to immunosuppressants, anti-TNFα, anti-integrins, ustekinumab and/or corticosteroids) was selected because of these patients' need for new treatment options to avoid disease-related complications for as long as possible and in which the safety profile of OSE-127/S95011 can be reliably assessed.

An interim futility analysis has been conducted according to the protocol on the first 50 patients (i.e., 33% of the total patient enrollment in the study) having completed the induction phase. The primary endpoint of the futility analysis was the efficacy of OSE-127/S95011 versus placebo assessed according to the reduction in the modified Mayo Score (an index used to assess the activity of ulcerative colitis).

In December 2021, based on the efficacy and tolerability results of this analysis, the Independent Data Monitoring Committee (IDMC) of the trial recommended the continuation of the study evaluating OSE-127/S95011, an Il-7 receptor antagonist, in patients with ulcerative colitis. Moreover OSE-127/S95011 has shown a good safety and tolerability profile in the whole patient population as already demonstrated in healthy volunteers in the Phase 1 study.

Based on the recommendation of the trial's IDMC, OSE Immunotherapeutics will proceed with the study.

ONGOING PHASE 2 CLINICAL TRIAL IN PRIMARY SJÖGREN SYNDROME (SERVIER AS SPONSOR)

This, randomized, double-blind, placebo-controlled Phase 2 trial aims to evaluate the efficacy and safety of OSE-127/S95011 in patients with Sjögren's Syndrome. The study includes 48 patients across a score of centers located in the United States, Australia and Europe. Results are expected in H1 2023.

The primary efficacy endpoint of the Sjögren study is the change in the total score of the ESSDAI index between the start of the study and week 13. The Eular Sjögren Syndrome Disease Activity Index (ESSDAI) is a physician-administered clinical index that has been validated to objectively assess systemic events in patients with primary Sjögren's Syndrome.

TARGET

The Interleukin-7 receptor is composed of two subunits, the alpha (or CD127) chain and the gamma (or CD132) chain, which is common to other interleukin receptors (IL-2, IL-4, IL-7, IL-9, IL-15 receptor). A mutation on the alpha chain of the Interleukin-7 receptor leads to immunodeficiency. The blocking of the Interleukin-7 receptor therefore represents a therapeutic target with multiple applications, particularly in autoimmune diseases. This cytokine is different from IL-2 and IL-15 because its presence is necessary and crucial for the generation and maintenance of memory T lymphocytes, as well as for IL-17 secreting cells (special helper T-cells). Consequently, IL-7 is considered the "fuel" for pathogenic T responses related to autoimmune and chronic inflammatory diseases (2) (Dooms, H. et al. 2013). Almost all T lymphocytes express IL-7R, with a major exception for regulatory T cells (Tregs) (3-5) (Michel, L. et al. 2008; Powell, N. et al. 2012), and this therapeutic approach provides an opportunity to selectively target effector T (eff T) while sparing regulatory T cells.

MECHANISM OF ACTION

OSE-127/S95011 has an innovative mechanism of action that blocks Interleukin-7 and internalization of the receptor, thus inducing a powerful antagonist effect on pathogenic T lymphocytes involved in autoimmune diseases. This mechanism has been confirmed in in vivo models of autoimmune diseases that mimic human ulcerative colitis.

PROOF OF CONCEPT CONFIRMED IN RELEVANT IN VITRO AND *IN VIVO* MODELS

OSE-127/S95011 has demonstrated its efficacy in preclinical inflammation models mediated by T cells, with both immediate and long-term effects, giving it a very novel mechanism of action.

This strategy, which differs from conventional or newer anti-inflammatory drugs used in the clinic, has demonstrated its efficacy in several preclinical models to restore altered immune balance in inflammatory bowel diseases (Powell, N. et al. 2012; Yamazaki, M. et al. 2003), type 1 diabetes, multiple sclerosis, and rheumatoid arthritis.

AN ONGOING PRECLINICAL RESEARCH PROGRAM IN COLLABORATION WITH THE KIEL UNIVERSITY IN ACUTE LYMPHOBLASTIC LEUKEMIA (ALL)

Targeting IL-7R CD127 is a promising novel strategy in B-cell Precursor ALL and T-ALL (T-cell lymphoblastic leukemia), since CD127 signalling is important for B- and T-cell development, and recent reports promote the view that CD127 is important for the development of BCP-ALL and T-ALL (T-cell lymphoblastic leukemia) *. Despite the favorable prognosis of BCP-ALL, relapse remains a clinical challenge and novel targeted immunotherapy options are urgently needed. T-ALL is an aggressive hematological cancer for which treatment options are limited at relapse.

This research program in leukemia have been selected for a presentation at the American Society of Hematology (ASH) 2022 annual meeting. This oral presentation has received the merit-based "Abstract Achievement Award" from the peer-review committee.

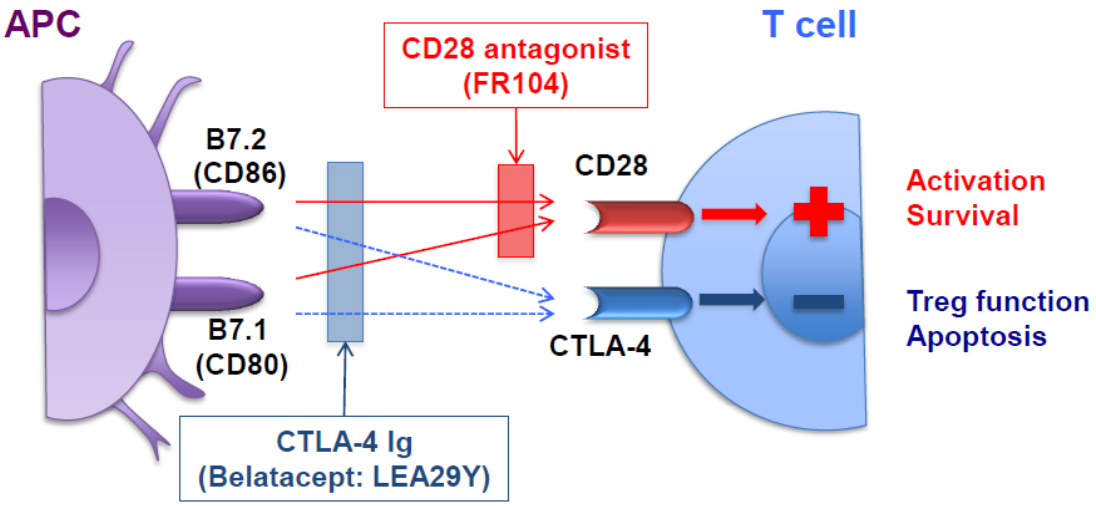
This prize results from the collaborative research program between conducted with the Kiel University to evaluate, in patient-derived samples and in-vivo xenograft models, the therapeutic potential of anti-IL-7R antagonist OSE-127 in targeting and blocking the high and dysregulated IL-7R-expression observed in 80% of B- or T-Acute Lymphoblastic Leukemia (ALL) patients.

*Thomas et al. Leukemia 2021 : "*Activated interleukin-7 receptor signaling drives B-cell acute lymphoblastic leukemia in mice*"
Silva et al. 2021 : "*Overexpression of wild-type IL-7Rα promotes T-cell acute lymphoblastic leukemia/lymphoma*"

5.1.2.2 FR104, monoclonal antibody, CD28 antagonist

This pegylated monovalent antibody selectively inhibits the CD28 receptor for potential clinical applications in autoimmune pathologies and transplantation.

The blocking of CD28 by FR104 makes it possible to control the effector T functions while maximizing the regulatory T cells. This novel control of immune synapses potentially offers new therapeutic options in many inflammatory and autoimmune diseases in which T cells are involved and where there is a significant medical need.



CD 28 delivers stimulation signals to the CTLA-4 and PDL-1 T cells and deliver inhibition signals to T-cells

Normally, the immune system defends the body against external aggression and tolerates its own constituents. An autoimmune disease occurs when the self-tolerance mechanisms fail, allowing auto-reactive lymphocytes to attack the body's constituents. The immune system then becomes pathogenic and induces tissue or cell damage. These diseases evolve chronically throughout life, with relapse and remission phases. Costimulatory signals are necessary to continue the harmful activation of the T lymphocyte. Blocking these costimulation signals is a new therapeutic pathway in which FR104 is involved.

In transplants and grafts, the immune system seeks to eliminate what it regards as foreign. In bone marrow transplants, the immunocompetent cells in the graft are able to recognize alloantigens in the host as foreign and reject them. This is called Graft Versus Host Disease (GVHD). Alloreactivity (antigens from an individual of the same species but with a different genetic and tissue structure) remains a major obstacle to organ and tissue transplantation because immunological rejection leads to relatively rapid graft loss without immunosuppressive treatment. Alloreactive lymphocytes are at the heart of these rejections and develop high-intensity immune responses one seeks to block.

PHASE 1 CLINICAL TRIAL: POSITIVE RESULTS

An initial Phase 1 trial with FR104 showed positive clinical results. The clinical and biological tolerability profile of this new product was very satisfactory in 64 healthy volunteers who received increasing doses of the product in single or repeated administrations. In addition, initial clinical activity data from this trial, using a KLH test, clearly showed a dose-dependent inhibition of the antibody response to KLH.

The results of the Phase 1 clinical study of FR104 showed good clinical and biological tolerability of the product. Its immunosuppressive activity in humans has demonstrated that the product has the potential to show clinical activity in the treatment of transplantation and immune-mediated diseases.

ONGOING PHASE 2 CLINICAL TRIAL IN RENAL TRANSPLANT

In December 2020, the French National Agency for Medicines and Health Products Safety and the Committee for the Protection of People gave their authorization to start a Phase 1/2 clinical trial evaluating FR104, administered for the first time in patients who have received a renal transplant. This study is carried out under a collaboration agreement between OSE Immunotherapeutics and the University Hospital Center in Nantes, which is the sponsor.

Professor Gilles Blancho, who heads the "Institut de Transplantation Urologie-Nephrologie" (ITUN) at the University Hospital Center, is the coordinating investigator.

The Phase 1/2 clinical trial aims to evaluate the safety, tolerance, pharmacokinetics, pharmacodynamics and efficacy of FR104 in patients who have received a renal transplant.

Long-term monitoring will be provided for one year after the end of the trial. The efficacy and long-term safety of the product will be measured according to criteria of renal function, incidence of rejection and adverse effects of FR104.

LICENSING AGREEMENT FOR FR104 IN ALL TRANSPLANT INDICATIONS

In April 2021, a global licensing agreement was signed with Veloxis Pharmaceuticals Inc. under which OSE Immunotherapeutics grants it the worldwide rights to develop, manufacture, register and market FR104 in all transplantation indications. At the same time, OSE Immunotherapeutics retains all rights to develop FR104 in autoimmune diseases. Through this agreement, Veloxis plans to develop FR104 to provide a potential therapeutic alternative for the prophylaxis of organ rejection in solid organ transplant patients.

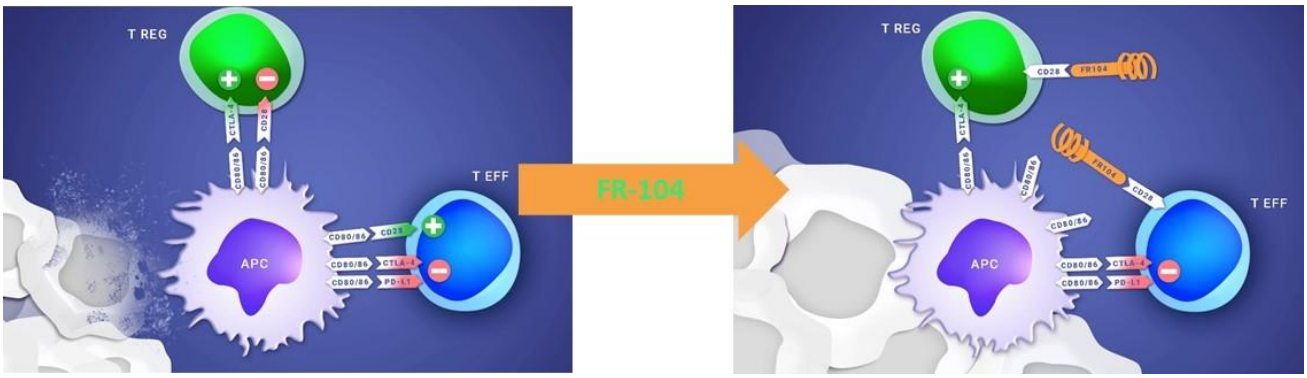
In January 2022, Veloxis has obtained acceptance of the Investigational New Drug (IND) by the Food & Drug Administration (FDA) for a clinical trial with VEL-101/FR104 in the prophylaxis of renal allograft rejection in recipients of kidney transplants.

A PHASE 1 CLINICAL TRIAL, SPONSORED AND CONDUCTED BY VELOXIS PHARMACEUTICALS, INC.

A Phase 1 clinical trial in the immunosuppression in renal transplant started in May 2022 in the United States under the sponsorship of Veloxis Pharmaceutical, Inc., OSE Immunotherapeutics' partner in transplantation. This study assesses the safety, tolerability, pharmacokinetics, and pharmacodynamics of single ascending doses of VEL-101 or placebo when administered subcutaneously (SC) or intravenously (IV). Approximately 56 healthy participants will be enrolled and will undergo monitoring for 50 days.

TARGET

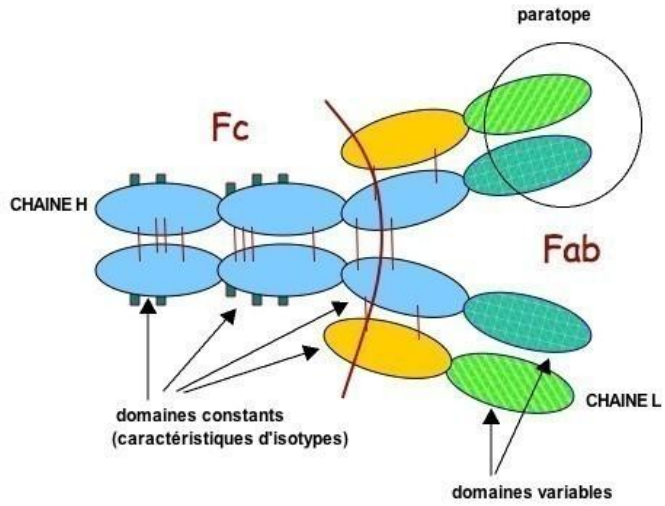
The binding of CD28, expressed on the surface of a lymphocyte, to B7-1 (also known as CD80) or B7-2 (also known as CD86) ligands, expressed on the surface of an antigen-presenting cell, provides the T lymphocyte with a costimulatory signal for it to become fully activated. Costimulatory signals regulate lymphocyte responses. The pharmacological effect on the costimulatory signal is a new therapeutic approach for modulating immune responses, in this present case to fight autoimmune reactions by reducing undesirable immune responses, and to prevent transplant rejection.



FR104 is an anti-CD28 monoclonal antibody, a pegylated humanized Fab' fragment in monovalent heterodimeric form.

It neutralizes CD28 interaction with its CD80/CD86 ligands (and also with CD275/ICOS-L). Due to its monovalent form, FR104 blocks CD28-CD80/86 interactions without activating T lymphocytes (see above Figure).

Unlike CD80/86 antagonists, FR104 does not prevent the powerful regulatory activity from CTLA4-CD80/86 interactions. These interactions are essential for the suppressive activity of regulatory T lymphocyte cells (Treg) [1]. FR104 thus reinforces the CTLA4-dependent suppressive activity while inhibiting effector T cells (Teff) [15]. FR104 is a bi-branched pegylated product; it is a chemical modification amplifying its pharmacokinetics to allow or an increased presence of the product at blood level. This addition is done on its C-terminal end (C-terminal cysteine 2). As a result of the chemical modification, the pegylated product leads to stable blood rate over time.



Overall dosing and administration schedule of an antibody with an Fc fragment and two Fab' fragments

IN VITRO MECHANISM OF ACTION

- FR104 selectively inhibits CD28-CD80/86 and CD28-CD275 interactions.
- It inhibits T-cell proliferation and cytokine synthesis (Interferon-gamma and Interleukin-2).
- It inhibits the responses of special effector T cells (memory effector T cells).
- It induces a response of CTLA-4-dependent regulatory T cells resulting in T-suppressive activity.
- It will not induce spontaneous activation of CD28-dependent T cells.

PROOF OF CONCEPT CONFIRMED IN MANY RELEVANT *IN VIVO* MODELS

In *in vivo* transplantation models (heart graft [3–5], liver graft [6] and kidney graft [1.7, 8]), CD28 antagonists act in synergy with other products, such as monoclonal antibodies and calcineurin inhibitors (CNIs). This class of CNI drugs is one of the reference treatments with cyclosporine as leading drug, often associated with corticosteroids. Alloreactivity or graft rejection is inhibited by FR104. Regulatory T cells are induced both in the periphery and in the graft, guaranteeing long-term conclusive graft outcomes. FR104, associated with calcineurin inhibitors (CNIs without added corticosteroids, or low-dose CNIs), is able to prevent graft rejection, inhibit the development of alloantibodies and extend graft survival [13] over the long term.

Other *in vivo* models of autoimmune pathologies have clearly proved the efficacy of FR104 (encephalomyelitis [14], rheumatoid arthritis (Vierboom et al., 2016), uveitis [10] and psoriasis [11]).

They have confirmed the significant therapeutic potential of this anti-CD28 monoclonal antibody.

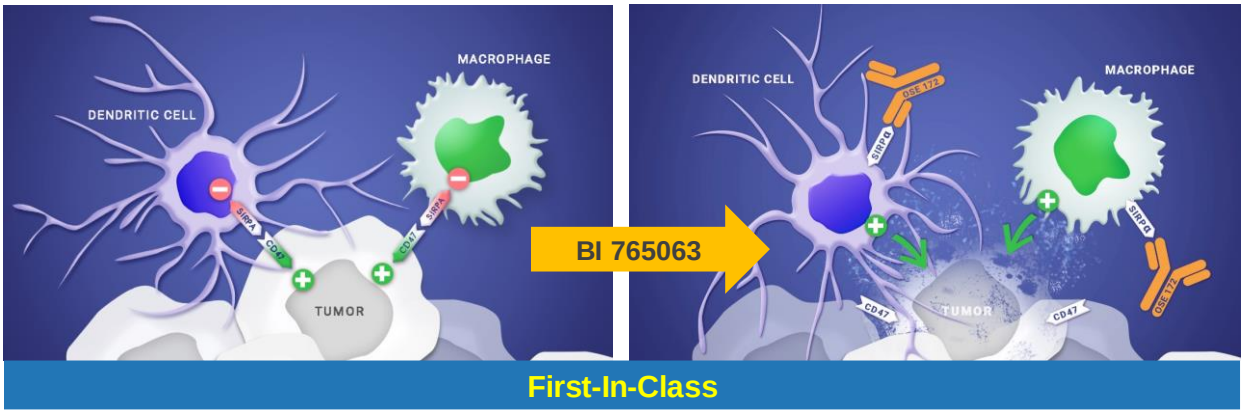
The FP7-HEALTH-2011 European program supported the preclinical development of FR104 in T dependent autoimmune diseases (TRIAD program: Tolerance Restoration In Autoimmune Diseases).

The major assets of FR104, one of the first products of this class, are:

- It is an immunomodulator and CD28 antagonist,
- The selection and patented optimization of this product candidate are key to ensure its efficacy and safety with the choice of developing a monovalent fragment (Fab'),
- The related humanization and pegylation processes, which increase its pharmacokinetic properties, also contribute to greater efficacy and good tolerability,
- It causes a decrease in effector T cells directly involved in the pathology of autoimmune diseases,
- It acts in synergy with suppressive regulatory T cells,
- It draws on a strong patent portfolio.

5.1.2.3 BI 765063 (OSE-172), selective monoclonal antibody antagonist targeting the SIRPα myeloid receptor

BI 765063 selectively blocks the SIRPα/CD47 interaction and thus increases the function of myeloid cells: phagocytosis of tumor cells and presentation of tumor antigens by dendritic cells. BI 765063 is also a selective inhibitor of SIRPα which, due to this property and the absence of binding and blocking by SIRPγ, a very similar receptor, guarantees the maintenance of a T lymphocyte response and the destruction of the T cell-mediated tumor.



SIRPα is expressed by Myeloid-Derived Suppressor Cells (MDSCs) and Tumor Associated Macrophages (TAMs) and controls their differentiation.

PHASE 1 CLINICAL TRIAL IN ADVANCED SOLID TUMORS

BI 765063 has been in Phase 1 clinical trial in patients with advanced solid tumors since June 2019. It is a dose finding study of BI 765063 administered as a single agent and in combination with Boehringer Ingelheim's monoclonal antibody PD1 antagonist BI 754091, a T-lymphocyte checkpoint inhibitor. The trial aims to characterize safety, pharmacokinetics, pharmacodynamics and preliminary efficacy of the immunotherapy in patients with advanced solid tumors.

The study is being conducted by OSE Immunotherapeutics under its license and collaboration agreement with Boehringer Ingelheim, which acquired the exclusive rights to BI 765063 in April 2018.

The dose escalation portion (Step 1) of the Phase 1 trial included genetically SIRPα homozygous V1/V1 or heterozygous V1/V2 patients with advanced solid tumors who had failed treatment or ineligible for standard therapy. Two doses of BI 765063 (18 and 24 mg/kg IV every 3 weeks) were evaluated in combination with BI 754091 (240 mg IV every 3 weeks).

As of April 2021, a total of 12 patients had received at least one dose or more of each treatment. The combination BI 765063 + BI 754091 presented a good tolerability profile and demonstrated clinical efficacy in two patients, with a decrease in the tumor in a patient with an adenocarcinoma of the colon, and a confirmed partial response in a patient with endometrial cancer. Both patients had stable microsatellite tumors (MSS) and were naive to any anti-PD1 checkpoint inhibitor therapy.

Checkpoint inhibitors used in monotherapy are recognized as effective in the presence of unstable micro-satellite biomarkers (MSI). However, the majority of colorectal and endometrial cancers are microsatellite stable (MSS) and the benefit of immune checkpoint inhibitors used as monotherapy is limited in these tumors.

The data presented at the 2021 ASCO meeting (in May) indicated that BI 765063 was well tolerated and showed monotherapy efficacy in heavily pre-treated solid tumor patients. In particular, a long-lasting partial response was observed in an advanced hepatocellular carcinoma (HCC) patient.

Updated data as of June 2021 from this Phase 1 dose escalation portion was presented as an ePoster at the ESMO 2021 conference (in September): 18 patients had been treated (16 evaluable for efficacy).

During the dose escalation, BI 765063 alone or in combination was well tolerated with no hematologic toxicity and the maximum tolerated dose (MTD) was not reached. The recommended Phase 2 dose and treatment schedule of BI 765063 was established with assays determining full receptor occupancy from cycle 1 and using a once every three weeks dosing schedule. In addition, promising early efficacy of BI 765063 was observed both alone and in combination, especially in advanced hepatocellular

carcinoma, endometrium and colorectal cancer, including microsatellite stable (MSS) tumors. Promising early efficacy was observed with one partial response (PR) in monotherapy in a patient with advanced hepatocellular carcinoma and three partial responses in combination in patients with MSS advanced endometrium or colorectal cancer.

Micro Satellite Instable (MSI) tumors can be effectively treated with immune checkpoint inhibitors alone. However, the majority of colorectal and endometrial cancers are microsatellite stable (MSS) and the benefit of immune checkpoint inhibitors used as monotherapy is limited in these tumors [(2).] This highlights the need for new effective treatment combinations such as BI 765063 and BI 754091 for MSS patients.

The trial expansion (Step 2 of Phase 1), with the first patient enrolled in May 2022, aims to further assess preliminary efficacy of BI 765063 in combination with ezabenlimab in two selected tumor types of V1/V1 homogygous patients from whom a clinical benefit has been observed: MSS advanced colorectal cancer (around 30 patients) and MSS advanced endometrial cancer (around 10 patients) whose disease relapsed after standard of care and who received no prior anti-PD-L1 inhibitors. It will determine the dose to be recommended for Phase 2 clinical use in advanced solid tumors.

On this basis, the Company plans, with its partner Boehringer Ingelheim, to continue the expanded Phase 1 and a Phase 2. The diseases for which BI 765063 could be developed concern all cancers where TAM (tumor-associated macrophages) cells and MDSCs (myeloid-derived suppressive cells) are involved. These TAM cells or MDSCs are key cells in the progression of inflammatory cancers. The cytokines secreted by these suppressor cells promote this climate (IL-10, IL-1β, TGFβ). Cancers related to chronic inflammation (primary liver cancer/colon cancer) could be, as an example, cancers of interest for such a strategy (Zamarron B.F. and 2011) (Mallmann MR et al. 2012).

BI 765063 (OSE-172), MYELOID CHECKPOINT INHIBITOR DESIGNED FOR IMMUNO-ONCOLOGY

The generation of an immunosuppressive tumor microenvironment is regularly observed in cancer progression and involves several cell lines with suppressive functions. Regulatory T lymphocytes (called Tregs) exert suppressive activity, and the first generation of checkpoint inhibitors acts on these regulatory T cells or Tregs (via the ligands of the CTLA-4, PD1 and PD-L1 molecules).

At the same time, differentiation of Myeloid-Derived Suppressor Cells that inhibit the functions of effector T lymphocytes (via secretion of mediators such as TGF beta and IL-10) can be seen. These MDSC myeloid cells can be widely observed in the tumor microenvironment. In parallel, tumor-associated macrophages (TAMs) also accumulate locally with suppressive functions that promote tumor growth.

There is currently no treatment to reduce or eliminate these myeloid suppressor cells or tumor-associated macrophages. A second generation of checkpoint inhibitors can be created by acting on these new suppressive immune cell targets.

TARGET

OSE Immunotherapeutics has identified the SIRPα (SIgnal Regulatory Protein alpha) target as a major checkpoint for myeloid cells. The Company has developed a selective SIRPα antagonist antibody, the checkpoint inhibitor BI 765063 (OSE-172), which transforms the tumor microenvironment by blocking suppressor cells and activating anti-tumor effector cells.

The optimization carried out on this product is the subject of three families of patents filed by the Company, the first of which was published on April 24, 2016.

MECHANISM OF ACTION

BI 765063 is a monoclonal antibody. A new-generation checkpoint inhibitor, it specifically blocks a function of tumor-associated myeloid/monocyte/macrophage suppressor cells (TAMs). These suppressor cells are very numerous in the tumor microenvironment and have a poor prognosis in aggressive cancers because they promote tumor growth (Chanmee T et al., Cancers 2014).

BI 765063 blocks SIRPα, a receptor that is highly expressed by myeloid cells and suppressor macrophage cells. BI 765063 restores the effector functions of these suppressor cells, and this activity encourages the restoration of immunosurveillance (Hanna R.N. et al.; Science 2015). It is also used in combination with other immunological therapies, in particular checkpoint inhibitors that act on T lymphocytes, such as those targeting the PD1/PD-L1 axis or products that stimulate the immune system.

This innovative product is part of the transformation of cells described as tumor-associated macrophages (TAMs) and suppressive myeloid suppressor cells (MDSCs) to block these poor-prognosis cells and transform them into good-prognosis effector cells.

Data from preclinical and translational studies, recently published (October 2020) in the Journal of Clinical Investigation (JCI), show, in in vivo models in rodents and ex vivo in humans, the efficacy and mechanism of action of BI 765063, the first selective antagonist of the "Don't Eat Me" signal mediated by SIRPα. For the first time, the OSE R&D team has identified the "Don't Find Me" signal, a complementary mechanism mediated by SIRPα whereby tumor cells evade immune detection by preventing T lymphocytes from entering the heart of the tumor.

The article entitled: *"Selective SIRPα blockade reverses tumor T cell exclusion and overcomes cancer immunotherapy resistance"* (https://www.jci.org/articles/view/135528/ga) relates to the work of the OSE R&D team, which discovered that the anti-SIRPα strategy reversed a major resistance and escape mechanism to immunotherapy. According to this mechanism, called "T lymphocyte exclusion", activated T lymphocytes cannot enter the site of the tumor and remain blocked at the periphery. Studies carried out in in vivo models of resistance to anti-PD1, PD-L1 or co-stimulation activators 4-1BB, have shown that the T lymphocytes initially blocked at the periphery of the tumor could effectively penetrate within the tumor when, in parallel, the SIRPα brake was blocked. Crossing this barrier is associated with a positive modulation of the expression of macrophages and the secretion of chemokines, allowing the penetration of T lymphocytes into the heart of the tumor.

PROOF OF CONCEPT OBTAINED IN *IN VIVO* MODELS

They have been obtained in aggressive cancer models such as primary liver cancer (HCC "Hepato Cell Carcinoma"), melanoma and breast cancer. These experiments have confirmed a therapeutic effect whenever BI 765063 (OSE-172) is used as monotherapy or in therapeutic combination with either another checkpoint inhibitor or an immune system stimulator, which may be long-lasting. The therapeutic effect is described as long-lasting because it was not possible to re-implant a tumor in animals treated with BI 765063 (OSE-172) that had developed anti-tumor immunization. Treatment with BI 765063 as a monotherapy and in combination with other immunotherapy treatments induces a powerful and long-lasting anti-tumor action.

The main preclinical results of BI 765063 have been presented at international conferences in the form of poster sessions and oral presentations (1-5) and have shown that this checkpoint inhibitor:

- Transforms the immunosuppressive tumor microenvironment in vivo and decreases tumor growth in a triple-negative breast cancer model;
- Slows the spread of metastases in a triple-negative breast cancer model;
- In combination with an anti-PD1/PD-L1 antibody, synergy for survival in hepatocellular carcinoma (HCC), which strengthens the rationale for combination therapy;
- In combination with other immunotherapies, BI 765063 induces a strong memory anti-tumor T immune response, which protects against tumor relapse.
- Modifies suppressive myeloid cells from ovarian cancer ascites to make them stimulative.
- BI 765063 selectively binds to SIRPα, not to SIRPɣ, a costimulatory receptor necessary for human T cell response.

(1) Dual targeting of adaptive and innate checkpoints induces potent memory anti-tumor response, Gauttier V. et al., EACR poster 2016
(2) Selective targeting of the SIRPα immune checkpoints, but not CD47, controls the polarization of macrophages, Gauttier V. et al., EACR poster 2016
(3) Control of immune tolerance by the SIRPα -CD47 pathway and Myeloid-Derived Suppressor Cells, Poirier N. et al., EACR poster ICI 2016
(4) Selective Targeting of the SIRP-α Immune Checkpoints to Dampen Suppression By Myeloïd-Derived Suppressor Cells And Control Polarization Of Human Macrophages, Vanhove B et al. 2016.
(5) Selective targeting of SIRPα induces potent memory anti-tumor immune responses without presenting haematological toxicity, Gauttier V et al., AACR poster 2017

5.1.3 Myeloid Platform

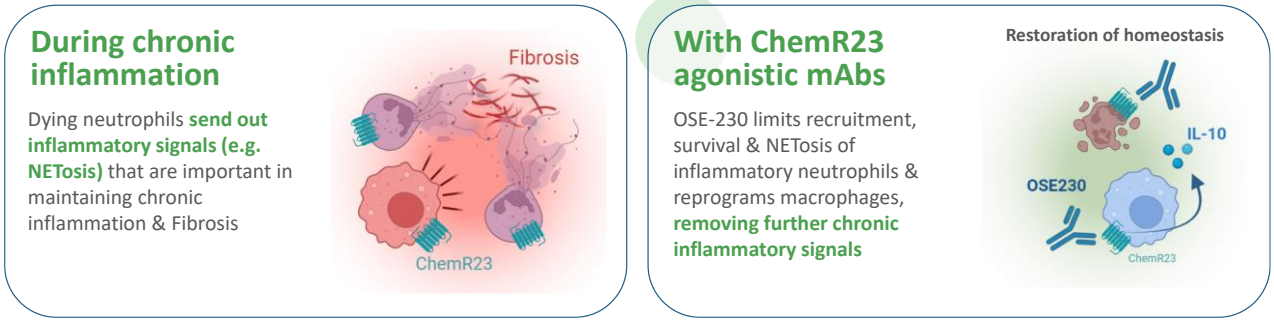
5.1.3.1 OSE-230, an antibody agonist of ChemR23, a therapy that triggers the resolution of chronic inflammation

OSE-230 is an agonist antibody against ChemR23, also known as chemerin chemokine-like receptor 1 (CMKLR1), a G-protein coupled receptor (GPCR) expressed on myeloid immune cells known to modulate inflammation.

Persistent inflammation is a hallmark of all chronic inflammatory and autoimmune diseases. If it is not controlled or resolved, it can lead to worsening tissue damage and cause tissue fibrosis, possibly associated with the loss of organ function. Most anti-inflammatory agents act using a mechanism that blocks pro-inflammation pathways. In contrast, OSE Immunotherapeutics is developing OSE-230 as a first-in-class therapeutic agent with the potential to resolve chronic inflammation by driving affected tissues to complete the inflammation program and restore tissue integrity. The product has a strong therapeutic potential in various chronic pathologies.

Resolution of inflammation is triggered by pro-resolving lipids activating GPCRs (G-Protein Coupled Receptor) targets. The ChemR23 GPCR is expressed on inflammatory myeloid immune cells, such as macrophages and neutrophils, and is over-expressed in tissues affected by chronic inflammatory diseases, such as lung inflammatory diseases or severe IBD (Inflammatory Bowel Disease) unresponsive to anti-TNF or anti-integrin therapies. ChemR23's over-expression is associated with chronic neutrophil accumulation in damaged tissues. OSE-230 is the first monoclonal antibody (mAb) to activate a pro-resolutive GPCR target (ChemR23). Its innovative mechanism of action drives inflammatory neutrophil tissue clearance through apoptosis and inhibition of the pathogenic NETosis* process. This mAb triggered resolution demonstrated positive preclinical efficacy in chronic colitis or chronic arthritis models with significant decrease in tissue fibrosis and restoration of tissue healing.

** NETosis is a program for formation of neutrophil extracellular traps (NETs), which consists of modified chromatin decorated with bactericidal proteins from granules and cytoplasm. Recent research has highlighted that neutrophils, and in particular NETs that can be released upon activation, have central roles in the initiation and perpetuation of systemic autoimmune disorders and trigger complex and chronic inflammatory responses that lead to organ damage and fibrosis.*

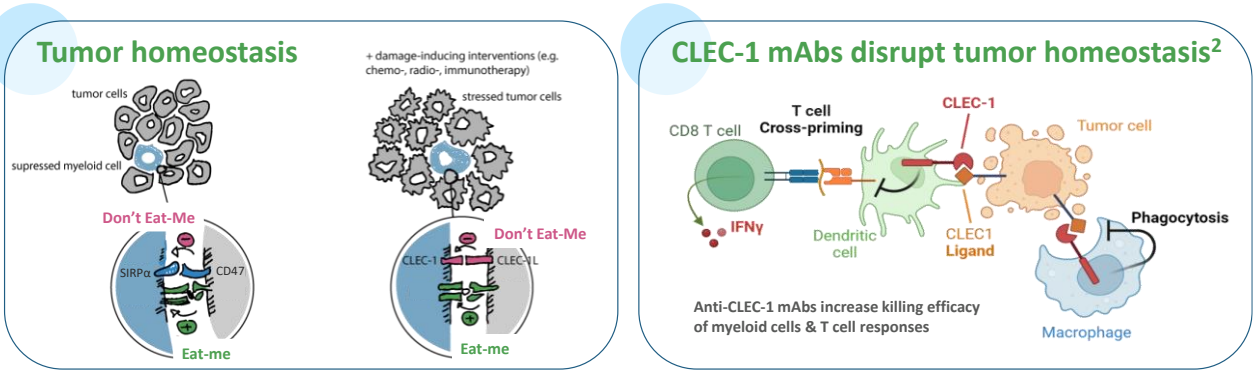


These data were presented in an oral session at the « Protein & Antibody Engineering Summit" (PEGS) 2022 annual meeting ("*Agonist Anti-ChemR23 Antibody for Inflammatory Diseases*").

The breakthrough innovation of the OSE-230 research program opens up development avenues in several chronic inflammation indications such as inflammatory bowel disease, inflammatory lung or kidney disease, arthritis or type 1 diabetes.

5.1.3.2 CLEC-1, a new immune myeloid checkpoint that regulates the anti-tumor response

The OSE Immunotherapeutics team in collaboration with Dr. Elise Chiffoleau's research team *(Center for Research in Transplantation and Translational Immunology at Nantes University Hospital)** have identified CLEC-1 (among CLR receptors-C-type lectin receptors) as a myeloid immune checkpoint and have identified antagonistic monoclonal antibodies that block this new signal "Don't Eat Me". CLEC-1 is a receptor expressed by myeloid cells, inhibiting the pro-phagocytosis and cross activation key functions of T-cells, thus limiting the antitumor immune response. The identification of CLEC-1 and its antagonists constitute an exciting innovative step in cancer immunotherapy.



Similar to the SIRPα/CD47 axis, the CLEC-1/CLEC-1 ligand pathway inhibits macrophage phagocytosis and the presentation of antigens by dendritic cells. The CLEC-1 ligand differs from CD47 because it is expressed by tumor cells under stress conditions, in particular when it is exposed to chemotherapy or radiotherapy. The new CLEC-1 monoclonal antibody antagonists developed by OSE Immunotherapeutics overcome this inhibition and act in synergy with the antibodies targeting tumor antigens currently on the market.

These CLEC-1 antagonistic monoclonal antibodies make it possible to remove new brakes on macrophage phagocytosis and dendritic cells and demonstrates synergistic anti-cancer effects, in particular when paired with chemotherapy.

**Collaborative academic program between OSE Immunotherapeutics and Dr Elise Chiffoleau's research teams (Center for Research in Transplantation and Translational Immunology (CR2TI), UMR1064, INSERM, Nantes University at Nantes University Hospital, https://cr2ti.univ-nantes.fr/research/team-1).*

In November 2022, an article, entitled "CLEC-1 is a death sensor that limits antigen cross-presentation by dendritic cells and represents a target for cancer immunotherapy" has been published in the peer-reviewed journal "Science Advances".

The results described in the research article highlight that:

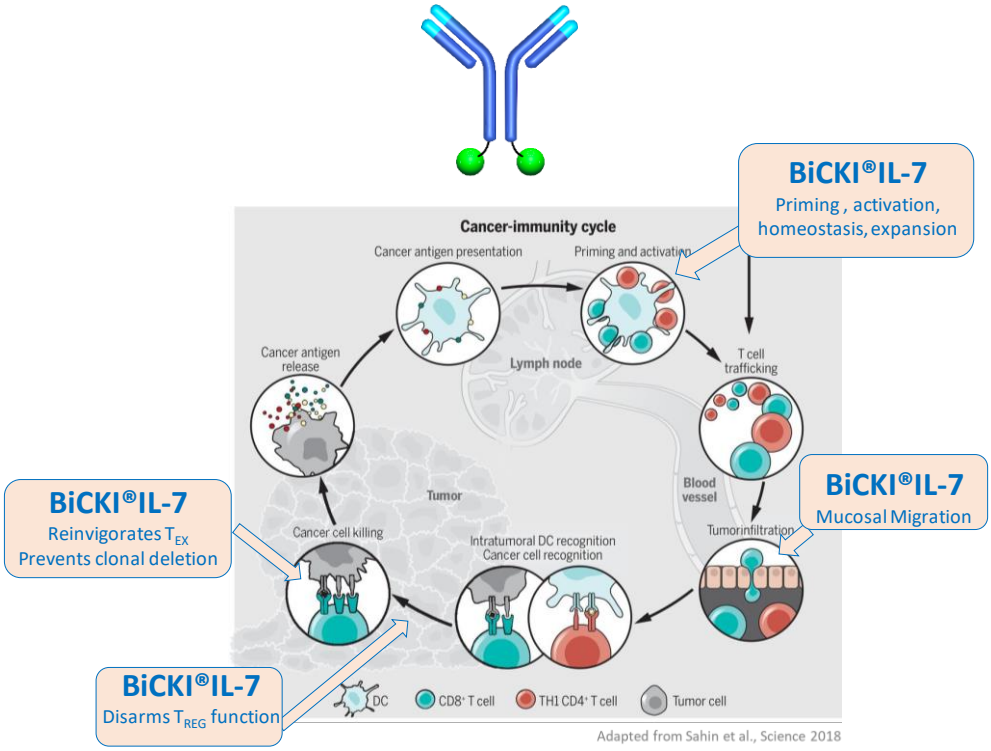
- Overall, CLEC-1 genetic deletion leads to a profound reinvigoration of the tumor immune microenvironment by enhancing infiltrates of dendritic cell (antigen presenting cells), increasing memory and activated T lymphocyte infiltrates, decreasing infiltrates of exhaustion marker PD1-expressing T lymphocytes and limiting the recruitment of immunosuppressive cells such as myeloid derived suppressor cells (MDSCs).
- Importantly, CLEC-1 blockade using monoclonal antibody treatment demonstrates robust anti-tumor activity, also by reinvigorating the tumor immune microenvironment in several preclinical oncology models, thereby faithfully recapitulating the effect of CLEC-1 genetic deletion in the context of human CLEC-1-expressing mice. Proprietary anti-CLEC-1 mAbs increase survival in monotherapy in orthotopic model of hepatocellular carcinoma while combination with chemotherapy increases preclinical tumor eradication in colon carcinoma model.
- Reports on fundamental discoveries and preclinical results showing that CLEC-1 is a novel myeloid checkpoint interacting with a new ligand TRIM-21 and highlighting the therapeutic potential of CLEC-1 antagonist antibodies (Abs) as innovative cancer immunotherapy.

These fundamental discoveries and preclinical results showing that CLEC-1 is a novel myeloid checkpoint interacting with a new ligand TRIM-21 confirm the therapeutic potential of CLEC-1 antagonist antibodies as an innovative cancer immunotherapy.

5.1.3.3 BiCKI®, a new platform of bispecific checkpoint inhibitors

The BiCKI® platform targets the PD1 receptor and other innovative targets. A bispecific fusion protein platform, it is built around a key backbone component anti-PD1 (OSE-279), chosen for its bioproduction ability, merged with innovative immunotherapy targets. The BiCKI® platform aims to inhibit key immune checkpoint inhibitors while simultaneously delivering cytokines capable of modulating regulatory T cells, and/or increasing the responses of exhausted T cells within the tumor. It can also incorporate other therapeutic methods to modify the tumor microenvironment by delivering, for example, costimulation signals to restore the activity of antitumor T lymphocytes or restore phagocytic functions and macrophage polarization.

Based on an anti-PD1 bifunctional antibody platform technology, BiCKI® is designed to expand the type of patients responding to immunotherapies. This is the second generation of PD-(L)1 inhibitors used to increase antitumor efficacy in hard-to-treat cancers by addressing untapped immune escape mechanisms.



BiCKI®-IL-7 is a bifunctional therapy which targets PD1 and at the same time provides IL-7 cytokine to restore exhausted T cell function, to disarm Treg suppressive activity and to extend stem-like memory T cells able to reconstitute the memory and effector T cells. This immunotherapy has potential to address the high medical need of patients with cancers with primary or secondary resistance or that are refractory to immune checkpoint inhibitor treatments.

In addition, the BiCKI®-IL-7v immunocytokine significantly improves the quality and durability of memory T lymphocytes in the tumor microenvironment (with T lymphocyte stem cells without immune exhaustion).

The Company has been invited to present the latest preclinical progress on BiCKI®-IL-7 : *« Anti-PD1/IL7v immunocytokine promotes durable T-cell responses and overcomes anti-PD1 resistance »* in oral presentation at the American Association Cancer for Research (AACR) 2022 annual meeting.

CoVepiT, multi-target and long-term protective vaccine against COVID-19

CoVepiT was developed from epitopes to fight infections caused by SARS-CoV-2, the virus responsible for COVID-19. The vaccine incorporates peptide fragments (epitopes) selected and optimized using artificial intelligence algorithms to increase immune response and induce strong memory T cell responses.

CoVepiT is generated using OSE's proprietary Memopi® technology which has been validated for both safety and efficacy through the step-1 of Phase 3 clinical phase of neoepitope vaccine Tedopi® in patients with non-small lung cancer.

The results of the peptide selection were published in **BioRxiv** in August 2020 in an article entitled*: "Tissue-resident memory CD8 T-cell responses elicited by single injection of a multi-target COVID-19* vaccine".

PHASE 1 CLINICAL

On April 1, 2021, OSE Immunotherapeutics received authorization from the Belgian Federal Agency for Medicines and Health Products and the Belgian Ethics Committee to initiate a Phase 1 clinical trial to evaluate the safety, reactogenicity and immunogenicity of CoVepiT in 48 healthy adult volunteers.

In July 2021, the Company voluntarily suspended enrollment and administration of CoVepiT in this trial as a precautionary measure due to a limited number of grade 1 adverse events (nodule-like indurations at the injection site) and one grade 2 adverse event in one participant. The data were then analyzed regularly with the independent Safety Monitoring Committee and the investigating center in Ghent.

On November 30, 2021, the Company announced the positive analysis of the first clinical data of CoVepiT confirming the good tolerability of the vaccine and a very good level of T cell response in vaccinated healthy volunteers. Indurations had resolved within a few weeks for most participants (no systemic reaction, no fever, no inflammation, no local ulceration), with continued follow-up showing a good tolerability profile. This profile with frequent indurations is close to that of vaccines that induce a T cell response (1, 2, 3) and is regularly linked to this T mechanism of action.

In March 2022, the positive analysis of the long-term immune T response of CoVepiT showed positive immunological results at 6 months on the memory T response in vaccinated subjects:

- Positive long-term immunological results at 6 months in healthy volunteers with strong memory T responses against the virus proteins.
- CoVepiT, based on 13 peptides, induces long-lasting immunity against a wide variety of structural and non-structural viral proteins.
- The vaccine remains independent of the mutations identified in current and emerging variants.

These sustainability and longevity results of the memory T response at 6 months are in addition to the initial immune T cell results obtained at week 6, the primary endpoint for all subjects in the clinical trial. This long-term positive immune response is of great interest [(4)] because multi-specific memory T cells are expected to be protective in immunocompromised patients should new coronaviruses or variants of concern emerge.

OSE Immunotherapeutics has thus validated the concept in clinic with a long-term T immunity against coronavirus thanks to its T cell-based vaccine platform inducing long-lasting memory T cells.

However, in immunocompromised patients, the studies conducted show that on average, a third vaccine dose induces antibodies and gives a protection in about 40 to 50% of seronegative patients (non-present antibodies) after a second dose, according to the type of pathology. Hence, regular booster shots of registered vaccines are recommended for this fragile population with a deficient antibody response. Moreover, in addition to vaccines, new treatments are now available such as monoclonal antibodies or antiviral treatments, prophylactic treatments with anti-SARS-CoV2 monoclonal antibodies and antiviral treatments against SARS-CoV2.

With the new available treatments and the recommended regular boosters, the French "*Haute Autorité de Santé*" and the experts recommend a booster vaccine against Covid-19 during the autumn 2023 for persons at high risk of severe disease, in particular immunocompromised or at very high-risk people. These populations targeted by CoVepiT now have many new registered treatments available. In such conditions, pursuing the clinical development of CoVepiT to show a vaccine efficacy is made very complex and the Company suspended the product's development.

(1) Pleguezuelos et al. 2020
(2) Rodo et al. PLoS Pathog 2019
(3) Heitmann, J. S. et al. Nature 2021
(4) Swaddling et al. Nature 2022
(5) Heitmann, J. S. et al. Nature 2022

5.1.2 Research and Development

The Company continues to identify new targets and optimize product candidates selected for immuno-oncology and immuno-inflammation. In particular, other checkpoint inhibitors and immunomodulators will be selected and optimized, based on proof-of-concept substantiated during research and development, to enter the development phase.

The Company plans to add new products to its portfolio, continue to develop its pre-clinical research programs and move them to the clinical trial phase, either by its own resources, or in co-development as part of a partnership, for broad indications or niche indications.

5.2 Principal markets

5.2.1 Immuno-oncology market

IN IMMUNO-ONCOLOGY: ASSESSMENT OF THE IMMUNOTHERAPY MARKET IN CANCER AND ASSESSMENT OF THE TEDOPI® MARKET IN LUNG CANCER

The global immuno-oncology market is evaluated at $40 billion for 2022 and is projected at $127 billion by 2028, i.e. a 21% per annum increase over the period 2022 – 2028 (ref. Evaluatepharma). Checkpoint inhibitors are expected to post an increase of 14.2% to reach $143.5 billion at the end of the same period.

The first cancer immunotherapy products registered were checkpoint inhibitors acting on T cells (Opdivo® BMS, Keytruda® Merck, Tecentriq® Roche, Yervoy® BMS, Bavencio® Merck Serono/Pfizer, Imfinzi® AstraZeneca).

Opdivo® (nivolumab, monoclonal antibody, anti-PD1 checkpoint inhibitor from BMS)/

Revenue (based on data published by the companies): 2022 = $8.2 billion

Keytruda® (pembrolizumab, monoclonal antibody, anti-PD- checkpoint inhibitor from Merck MSD)

Revenue: 2022 = $31. 5 billion

Tecentriq® (atezolizumab, anti-PD-L1 checkpoint inhibitor from Roche)

Revenue: 2022 = $3.9 billion.

Yervoy® (ipilimumab, monoclonal antibody targeting CTLA-4, from BMS)

Revenue: 2022 = $2.1 billion.

Bavencio® (avelumab, monoclonal antibody targeting anti-PD-L1, from Merck Darmstadt or EMD Serono in collaboration with Pfizer-Javelin program): this antibody is an IgG1, a cytotoxic antibody.

Revenue: 2022 = $666 million.

Imfinzi® (durvalumab, humanized monoclonal antibody targeting the PD-L1 ligand, checkpoint inhibitor MEDI 4736d).

In 2018, registration in non-small cell lung cancer, non resecable in patients who have not progressed after chemo and radiotherapy. In 2022, Imfinzi associated with Imjudo and chemotherapy was approved in the US in NSCLC. Associated to chemotherapy, he has been approved in the US in advanced biliary tract.

Revenue 2022 = $2.8 billion.

The prices in immuno-oncology are:

Checkpoint inhibitors registered for NSCLC: nivolumab (Opdivo® - BMS), pembrolizumab (Keytruda® - Merck &Co), atezolizumab (Tecentriq® - Roche), durvalumab (Imfinzi® AstraZeneca) all cost $150,000 a year.

In Europe, the price of Opdivo® ranges between €5,000 and €6,000 a month (i.e. around €72,000 a year). The price of a treatment for a 75 kg man would exceed €7,000 per month for Keytruda®, the Merck & Co product. Yervoy® in melanoma is the same price.

ASSESSMENT OF THE TEDOPI® MARKET IN LUNG CANCER

Every year, more deaths are recorded from lung cancer than from colon, breast and prostate cancers put together.

Risk factors are cigarettes, air pollution and family history.

In 2020, 2.2 million new cases (incidence) were recorded worldwide (11.4% of the total number of new cancers) and 1.8 million deaths (mortality) (18% of the total). The global mortality-to-incidence ratio was high at 0.82. The number of new cases is estimated at 3.6 million in 2040, with a rise in the average annual incidence rate of 2.51%*.

Non-small cell lung cancer (NSCLC) accounts for around 85 to 88% of lung cancers. The 5-year overall survival rate was 23% according to cancer.net 2019 (Doctor Approved Patient Information from ASCO®). For the vast majority of patients, this cancer is

discovered at an advanced stage (Yang et al., 2005) (Govindan et al., 2006) (American Cancer Society, 2012). NSCLC is considered to be a major public health issue due to its poor prognosis.

The HLA-A2 population accounts for 45% of the population suffering from NSCLC (similar figures in Asia, the United States and the European Union).

In the United States in 2022, the incidence of lung cancer was 264,000 patients. This impact included 145,000 patients with metastatic NSCLC, of which 89,000 were non-respondent to checkpoint inhibitors, and out of these, 44,000 were HLA-A2 positive*.

In the five major European countries, the incidence of lung cancer was 202,000 patients. This impact included 149,000 patients with metastatic NSCLC, of which 63,000 were non-respondent to checkpoint inhibitors, and out of these, 28,000 were HLA-A2 positive*.

In total, a potential of 72,000 patients are candidates for treatment with Tedopi® in the United States and Europe.

Source: WHO International Agency for Research on Cancer - 2020 Lung Fact Sheet*

Checkpoint inhibitors are becoming a standard treatment and are increasingly used in different lines of early through to late treatment. Tedopi's® positioning as a post-checkpoint inhibitor is not a restriction on its potential market. By focusing exclusively on patients whose treatment with PD1/PD-L1 immune checkpoint inhibitors has failed, Tedopi® meets a very high therapeutic need since no product has, to date, been registered for this population in immune escape.

At this stage, no estimates have been made for any other clinical applications in other cancers or therapeutic combinations with other products.

ASSESSMENT OF THE TEDOPI® MARKET IN PANCREATIC CANCER

The incidence of pancreatic ductal adenocarcinoma is steadily increasing in Western countries and is likely to become the 2nd greatest cause of death by cancer in 2030, after lung cancer and before liver cancer (Rahib L et al: Projecting cancer incidence and deaths to 2030: the unexpected burden of thyroid, liver, and pancreas cancers in the United States. Cancer Res 2014). The prognosis for this disease is very poor with a 5-year survival rate of less than 5%. As to the prognosis, most patients have metastases (50%) or a locally advanced cancer (one third). If the disease is operable, surgical resection followed by adjunctive chemotherapy can be used to treat a minority of patients, with 80% of cases relapsing during the follow-up period.

Standard treatment for metastatic pancreatic adenocarcinoma is still gemcitabine monotherapy for up to 15 years. For more than 10 years, dozens of Phase 3 randomized clinical trials assessed combinations of cytotoxics, or cytotoxics with targeted therapies, without managing to demonstrate that these treatments were in any way superior to gemcitabine alone. Since 2011, treatments with folforinox (Conroy T et al: FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer. N Engl J Med 2011) and then by nab-paclitaxel + gemcitabine demonstrated their superiority over gemcitabine alone in terms of response rate, progression-free survival and overall survival. Progression-free survival rates at 6, 12 and 18 months were 52.8%, 12.1% and 3.3%, respectively, in the folforinox group.

Preliminary results for therapeutic vaccines targeting tumor antigens directly (telomerase, KRAS proteins or mesothelin) and GVAX (granulocyte-macrophage colony-stimulating factor - secreting allogeneic pancreatic tumor cells) showed moderate clinical activity and a good tolerability profile [Middleton G et al. Gemcitabine and capecitabine with or without telomerase peptide vaccine GV1001 in patients with locally advanced or metastatic pancreatic cancer (TeloVac): an open-label, randomized, Phase 3 trial. Lancet Oncol 2014; DT et al. A live-attenuated Listeria vaccine (ANZ-100) and a live-attenuated vaccine expressing mesothelin (CRS-207) for advanced cancers: Phase I studies of safety and immune induction. Clin Cancer Res 2012). DT et al. Safety and survival with GVAX pancreas prime and Listeria Monocytogenes-expressing mesothelin (CRS-207) boost vaccines for metastatic pancreatic cancer. J Clin Oncol 2015].

Pancreatic adenocarcinoma is associated with significant number of neoantigens which justify the use of immunotherapy. The somewhat moderate outcomes reported with the checkpoint inhibitors or therapeutic vaccines used in this type of cancer can be explained by the pivotal role played by the tumor microenvironment (the stroma) in the development and progression of this type of cancer. A dense, fibrous stroma combined with a pancreatic adenocarcinoma forms a physical and chemical double barrier, involved in immunosuppression. To reverse this immunosuppression, induction chemotherapy is an interesting option. Cytotoxics may reduce the tumor load and activate the immune system by destroying tumor cells. The activation of tumor neoantigens and pro-inflammatory cytokines is also a promising means of awakening the immune defenses.

ASSESSMENT OF THE TEDOPI® MARKET IN OVARIAN CANCER

Worldwide, ovarian cancer is the seventh most common cancer and the eighth leading cause of cancer death in women. The five-year survival rate for ovarian cancer worldwide is 30-40%. In 2021, there were nearly 43,000 new cases diagnosed (Europe and US). Once the first relapse has occurred, ovarian cancer is managed as a chronic disease, requiring iterative lines of platinum-based chemotherapy. Chemotherapy is stopped after six cycles. A major priority is to extend chemotherapy-free intervals by offering patients a maintenance strategy with targeted therapy (PARP inhibitors or bevacizumab). At their first or second relapse; patients have received both a PARP inhibitor and bevacizumab. Those who progress after PARP inhibitors and bevacizumab represent an unmet medical need: they are then offered chemotherapy alone, with no maintenance strategy: the TEDOVA trial is aimed at these women.

5.2.2 Immuno-inflammatory disease market

The immuno-inflammatory disease market is a key market that includes major pharmaceutical industry players.

Ulcerative colitis affects 1.8 million patients in the US (920,000, Europe (690,000) and Japan (170,000). Approximately 50% of patients suffer from moderate to severe disease and use methotrexate, corticosteroids, anti-TNFa, JAK, etc. Despite the many treatments available, 25 to 30% of patients remain without satisfactory treatment *(Drugs Context. 2019; 8: 212572 – doi: 10.7573/dic.212572).* 15% of patients do not respond to treatment and require surgery (Scientific *Reports volume 10, Article number: 12546, 2020).*

In 2021, the global ulcerative colitis market amounted to $9.5 billion. This market is growing and could reach $11.5 billion in 2028 (*EvaluatePharma 2020*).

Sjögren's Syndrome: it affects around 600,000 patients in the United States, Europe and Japan, half of them in the United States. This is the 3rd most prevalent autoimmune disease affecting the salivary and lacrimal glands, lungs, kidneys and the nervous system (*EvaluatePharma 2020*).

More than 75% of patients suffering from Sjögren's Syndrome are treated. The only registered drug is cevimeline (Exovac®) and the other main treatments used are generics of Exovac®, lubricants and products for local use and T-lymphocyte modulators (Rituxan®, Benlysta®) (Context *Drugs. 2019*; 8: 212572 – *doi: 10.7573/dic.212572*).

For example, revenue from leading treatments for autoimmune diseases is as follows (information provided by the websites of pharmaceutical companies):

Humira® (adalimumab, AbbVie): $21.6 billion in 2022(in particular, for Crohn's disease, ulcerative colitis and rheumatoid arthritis).

Remicade® (infliximab, Merck and Janssen biotech/J&J): $ $2.4 billion in 2021 in autoimmune diseases.

Enbrel® (etanercept, Pfizer, Amgen, Takeda): 2022 = $4.1.

Xeljanz® (tofacitinib citrate, Pfizer) : 2022 = $1.8.More often than not, the original patents protecting these biotechnology products, such as Humira®, Enbrel®, Remicade® and Mabthera® have expired. Generic products are known as “biosimilar” products and must have documentation as comprehensive as the original product developed by pharmaceutical players such as, for example: Mylan (Glactect®, generic form of Copaxone®), Celltrion Healthcare (Remsima™, biosimilar form of Remicade®; Truxima™, biosimilar form of Rituxan®), Samsung Bioepis (Benepali™, biosimilar form of Enbrel®; Imraldi™, biosimilar form of Humira®).

The key players in the autoimmune disease market are Johnson & Johnson (J&J), AbbVie, Amgen, Genentech/Roche, Astellas, UCB, Eli Lilly, Sanofi, AstraZeneca, Novartis and Biogen.

5.2.3 Renal Transplant Market

The global transplant market was estimated at $12.8 billion in 2019 and is expected to reach $25.8 billion in 2027, an annual growth rate of 9.3%.

Globally, these figures were 92,532 renal transplants, i.e. 62% of the total of 129,681 organ transplants (*Global Observatory on Donation and Transplantation*)

The market for immunosuppressants, a lifelong treatment for the transplanted patient, is expected to grow by 4% per year in renal transplants (*Grandviewresearch.com, June 2020*). As transplant rejection is a major problem for patients who require lifelong immunosuppressive treatment, and despite the progress made in immunosuppressive treatments, the need for medical advances for patients receiving a renal transplant remains very important (Grand *View Research, 2019*).

5.2.4 Chronic Inflammation Market

Chronic inflammatory diseases are the most significant cause of death worldwide and their incidence is growing, highlighting the patients' need for disruptive innovations to manage such complex diseases. The prevalence of diseases associated with chronic inflammation is expected to increase over the next 30 years, particularly in the United States. In 2014, approximately 60% of Americans suffered from at least one chronic condition, 42% from more from one chronic condition, and 12% of adults suffered from at least five chronic conditions. Globally, three in five people die from chronic inflammatory diseases such as stroke, chronic respiratory diseases, heart disease, cancer, obesity and diabetes*.

Examples:

Diabetes: the number of diabetics worldwide increased from 108 million in 1980 to 422 million in 2014. In the same period, the prevalence among adults over the age of 18 increased from 4.7% to 8.5% (*World Health Organization data, June 2020*).

Arthritis and joint diseases: these diseases affect around 350 million people worldwide*.

Chronic obstructive pulmonary disease: in 2014, it was the third-highest cause of death in the United States with 15.7 million Americans diagnosed*.

(**Chronic inflammation*, *Roma Pahwa; Amandeep Goyal; Pankaj Bansal; Ishwarlal Jialal, updated November 2020*)

In chronic inflammatory diseases, rarer diseases are also described. As an example, the global prevalence of hidradenitis suppurativa, or Verneuil disease, would be of 40% (Jfri A. et al., JAMA Dermatol. 2021). This an invalidating chronic inflammatory cutaneous disease, painful and suppurative, affecting large skin folds. Neutrophils are involved in this disease.
The global market for anti-inflammatory drugs amounted to $93.88 billion in 2019 and is expected to reach $191.42 billion in 2027, an increase of 9.3% (https://www.globenewswire.com/news-release/2020/05/28/2040417/0/en/Anti-Inflammatory-Drugs-Market-to-Exhibit-9-3-CAGR-by-2027-Owing-to-Rising-Prevalence-of-Inflammatory-Health-Conditions-Fortune-Business-Insights.html).

5.3 Important events in the development of the Company's business

APRIL 2012	Creation of OSE Pharma
MARCH 2015	IPO of the Company and capital increase of almost €21.1 million.
MAY 2015	First licensing and distribution agreement with Israel entered into with Rafa Laboratories, a pharmaceutical company specializing in oncology and rare lung diseases, with longstanding presence in the country and longstanding expertise in the industry.
FEBRUARY 2016	START of Phase 3 registration clinical trial (Atalante-1 trial) of Tedopi® in Europe and the United States, in advanced non-small cell lung cancer in second-line treatment.
MAY 2016	Merger of OSE Pharma (Paris) with Effimune (Nantes). Change of name to OSE Immunotherapeutics and registered office located in Nantes.
JULY 2016	Option exercised by Janssen Biotech Inc. (Johnson & Johnson group) as part of the global licensing agreement between Janssen and OSE Immunotherapeutics (signed in October 2013), triggered by the positive Phase 1 results of FR104. According to the terms of this agreement, Janssen was responsible for all clinical development, registration and international marketing of FR104 in autoimmune diseases and transplantation.

DECEMBER 2016 Signature of a two-step worldwide licensing option agreement with Servier, an international independent pharmaceutical company, to develop and market Interleukin-7 receptor antagonist OSE-127/S95011.

APRIL 2018 Signature of a worldwide licensing and collaboration agreement in immuno-oncology with Boehringer Ingelheim to develop the anti-SIRPa monoclonal antibody, BI 765063 (OSE-172), a new checkpoint inhibitor. OSE Immunotherapeutics could receive up to €1.1 billion if all planned milestones achieved.

NOVEMBER 2018 Worldwide rights for FR104 taken over from Janssen Biotech by OSE Immunotherapeutics, according to which the Company has exclusive access to all intellectual property, data, files and materials developed by Janssen Biotech as part of the FR104 program. Janssen Biotech's decision to return the FR104 program to OSE Immunotherapeutics was motivated by an internal strategy review and prioritization of its own product portfolio.

Authorization from the ANSM (French National Agency for Medicines and Health Products Safety) and the CCP (French equivalent of the Institutional Review Board) to start a Phase 2 clinical trial to assess the use of Tedopi® alone or in combination with Opdivo® (nivolumab) versus maintenance standard-of-care treatment with Folfiri (chemotherapy combining folinic acid, fluorouracil and irinotecan), in advanced or metastatic pancreatic cancer (clinical trial sponsored and conducted by the oncology group GERCOR, with the support of Bristol-Myers Squibb which provided Opdivo®).

Authorization from the Belgian Federal Agency for Medicines and Health Products (FAMHP) and the Belgian Ethics Committee to initiate a Phase 1 clinical trial of OSE-127/S95011, aiming to assess the safety and tolerability of intravenous and subcutaneous administered single- and multiple-doses of OSE-127/S95011.

FEBRUARY 2019 Exercise by Servier of the first option of the two-step worldwide licensing agreement for the continuation of the clinical development and potential marketing of OSE-127/S95011 in autoimmune diseases. Under the terms of the licensing agreement, exercise of this first option resulted in the payment, by Servier, of a milestone payment of €10 million (excluding tax) to the Company, after validation of a previously defined development stage.

JUNE 2019 First patient treated in the Phase 1 clinical trial to evaluate BI 765063, the selective antagonist targeting SIRPα, in patients with advanced solid tumors; milestone payments worth €15 million were made by Boehringer Ingelheim to OSE Immunotherapeutics upon clinical trial authorization and treatment of the first patient.

NOVEMBER 2019 Licensing agreement with Chong Kun Dang (CKD) Pharmaceuticals Corp. for the development of Tedopi® in Korea. Under the terms of the agreement, OSE Immunotherapeutics will receive milestone payments totaling €4.3 million, including €1.2 million upon signature and achievement of a short-term milestone, as well as royalties on product sales and a transfer pricing margin of slightly less than 30 percent.

DECEMBER 2019 Positive results of the Phase 1 clinical trial of OSE-127/S95011 which show a good safety and tolerability profile of the product.

MARCH 2020 Signature of an amendment to the two-step worldwide licensing option agreement on the exclusive rights of OSE-127/S95011, Interleukin-7 receptor antagonist, signed with Servier in December 2016. This amendment modifies the arrangements for the potential exercise of the licensing option agreement's second step. OSE Immunotherapeutics will thus receive a milestone payment of €5 million from Servier on enrollment of the first patient in Phase 2a clinical study scheduled to start in Sjögren's Syndrome and an additional payment of €15 million on exercise of the option at the end of the two scheduled Phase 2 studies, with priority being given to the study in Sjögren's Syndrome. The initial agreement provided for a total payment of €20 million at the end of Phase 2 in ulcerative colitis.

APRIL 2020 Announcement of positive result of step 1 of the Phase 3 clinical trial of Tedopi®, Atalante-1, in non-small cell lung cancer: Primary endpoint of stage 1 achieved with a survival rate at 12 months in patients treated with Tedopi®.

MAY 2020 Announcement of a COVID-19 prophylactic vaccine program that leverages the Company's expertise in the selection and optimization of peptides, and its patented Memopi® technology to explore a T-lymphocyte response with immune memory in COVID-19.

SEPTEMBER 2020 Oral presentation at the European Society for Medical Oncology (ESMO) virtual annual meeting of the positive results of step 1 of the Phase 3 Tedopi® trial in patients with non-small cell lung cancer (NSCLC) after failure of an immune checkpoint inhibitor treatment. These results show a clearly improved overall survival time with Tedopi® compared to the standard treatment, a significant increase in survival after progression, the maintenance of a good ECOG score reflecting the change in the general health of the patient, and the confirmation of a better tolerability profile for Tedopi®. Overall, the benefit/risk ratio is favorable to Tedopi® and better than that of standard treatment in these patients previously treated with checkpoint inhibitors.

**The ECOG score is a performance scale used to assess the overall state of health of the patient. It is subdivided into 5 grades from 0 to 5, ranging from fully active (0) to completely disabled and then to death (5).*

NOVEMBER 2020 €18.6 million capital increase launched on November 16 through a private placement.

DECEMBER 2020 Authorization from the French National Agency for Medicines and Health Products Safety (Agence Nationale de Sécurité du Médicament) and the Committee for the Protection of People of a Phase 1/2 clinical trial evaluating FR104, a CD-18 antagonist monoclonal antibody, in patients who have received a renal transplant. This study will be conducted as part of a collaboration agreement between OSE Immunotherapeutics and the Centre Hospitalier de Nantes, the study sponsor.

Inclusion of the first patient in the Phase 2 clinical trial evaluating OSE-127/S95011/S95011, an IL-7 receptor antagonist, in patients with moderate to severe active ulcerative colitis. This clinical trial is being sponsored by OSE Immunotherapeutics.

FEBRUARY 2021 Signature of a €25 million financing agreement with the European Investment Bank to expand the clinical development of its leading immunotherapy programs. This financing will consist of three tranches divided into two tranches of €10 million and one of €5 million.

MARCH 2021 Authorization of the French National Agency for Medicines and Health Products Safety (ANSM) and the Committee for the Protection of People (CPP) of a Phase 2 clinical trial evaluating Tedopi® in patients with relapsing ovarian cancer (TEDOVA trial)) carried out under the promotion of the French cooperative group ARCAGY-GINECO.

APRIL 2021 Signature of a worldwide licensing agreement with Veloxis Pharmaceuticals for the development, manufacturing and marketing of FR104, a CD28 antagonist, in the organ transplantation market. OSE Immunotherapeutics may receive up to €315 million in potential milestone payments, including a €7 million due at signature and royalties on sales. At the same time, OSE Immunotherapeutics retains all rights to develop FR104 in autoimmune diseases.

MAY 2021 Positive Phase 1 results of BI 765063, a first-in-class SIRPα inhibitor, in solid tumors, presented at the ASCO 2021 meeting. The data show good tolerability of BI765063 and efficacy as monotherapy in heavily pretreated patients with solid tumors.

Launch of a Phase 2 clinical study evaluating Tedopi® in combination with Opdivo® (nivolumab) in non-small cell lung cancer, sponsored by ForT Foundation.

JULY 2021 Payment of €10 million for the first tranche of the loan granted by the European Investment Bank (EIB) on February 12, 2021.

AUGUST 2021 Inclusion of the first patient in the Phase 2 clinical trial evaluating OSE-127/S95011 in Sjögren's Syndrome, sponsored by Servier. Under the collaboration agreement with licensing option, the inclusion of this first patient triggered a payment of €5 million from Servier to OSE Immunotherapeutics.

SEPTEMBER 2021 Escalation dose PHASE 1 results of BI 765063 in advanced solid tumors, presented at the ESMO (European Society for Medical Oncology) annual meeting. Data from Phase 1 dose escalation indicated that BI 765063 monotherapy or in combination with anti-PD1 ezabenlimab is well tolerated and shows promising activity in heavily pre-treated solid tumor patients.

Positive final results of the Phase 3 trial of Tedopi® (Atalante-1) in HLA-A2 positive patients with non-small cell lung cancer after failure of an immune checkpoint inhibitor (PD1/PD-L1), presented at the ESMO (European Society for Medical Oncology) annual meeting.

JANUARY 2022 — Appointment of Dominique Costantini as Interim Chief Executive Officer following the departure of Alexis Peyroles.

Acceptance of the IND obtained by Veloxis Pharmaceuticals, Inc. from the Food & Drug Administration (FDA) for VEL-101/FR104. As part of the global license agreement signed in April 2021, this first step triggers a €5 million from Veloxis Pharmaceuticals, Inc. to OSE Immunotherapeutics.

MAY 2022 — Initiation of the expansion Phase 1 clinical trial of BI 765063 in endometrium and colorectal cancer and payment of a €10 million milestone from Boehringer Ingelheim to OSE Immunotherapeutics.

First participant dosed in a Phase 1 study of VEL-101/FR104 evaluated in renal transplantation, a study sponsored and conducted by OSE Immunotherapeutics' partner, Veloxis Pharmaceuticals, Inc.

JUNE 2022 — Creation of an Advisory Board (SAB) composed of six leading international experts to guide the Company in its next phases of growth and scientific orientations.

JULY 2022 — Appointment of Alexis Vandier as Chief Executive Officer.

OCTOBER 2022 — Appointment of Nicolas Poirier as new Chief Executive Officer following the decision of the Board of Directors to terminate the mandate of Alexis Vandier.

Update on Tedopi® with authorizations for compassionate use in non-small cell lung cancer (NSCLC) by Health agencies in Europe. Regulatory meetings planned with the regulatory Agencies to validate the new confirmatory Phase 3 clinical trial in NSCLC.

DECEMBER 2022 — First patient dosed in the Phase 1/2 clinical trial evaluation OSE-279, a high affinity anti-PD1 blocking monoclonal antibody in patients with advanced solid tumors or lymphomas.

Payment of €10 million as part of the second tranche of the loan granted by the European Investment Bank on December 16, 2022.

5.4 Strategy and objectives

OSE Immunotherapeutics is an integrated biotechnology company that develops, on its own or in partnership, immunotherapies aimed at controlling the immune system for immuno-oncology and immuno-inflammation.

The Company's objective is to become a leading international player in the field of immunotherapy. OSE Immunotherapeutics aims to broaden and accelerate the development of its product portfolio at the clinical stage and to explore new therapeutic indications with strong medical need.

It controls the technologies of immunoregulation and immuno-activation of the immune system with complementary international teams and expertise involved in the research and optimization of drug candidates, pharmaceutical development of biotherapies, clinical development and registration. The Company has an innovative technological foundation, expertise in selection and optimization of receptor targeting, enabling significant therapeutic advances.

OSE Immunotherapeutics has a portfolio of five immunotherapy products in clinical trials from Phase 3 to Phase 1. The Company is also developing its technological platforms and selects the most innovative candidates to enter the preclinical and clinical development phases, on its own or as part of a partnership with a pharmaceutical group, for products targeting several indications and a larger market. It is developing immunological activation or regulation (suppression) products to identify and select the most relevant targets to produce agonists or antagonists in immuno-oncology or immuno-inflammation.

To achieve these objectives, the Company plans to increase the number of clinical and preclinical projects to create a richer portfolio and accelerate the transition of its research programs from preclinical to the clinical phase. It plans to advance its development programs either by its own resources or by co-development under new collaboration and licensing agreements with the industrial

players involved in the field of activating or regulating immunology. Its products may be developed in therapeutic combinations of high clinical interest, in broad indications in partnership or in niche indications on its own.

5.4.1 A dynamic partnership development strategy based on a portfolio of innovative products

Partnerships with international pharmaceutical groups enable OSE Immunotherapeutics to accelerate the clinical development of its products. The Company aims to find the "right" partners, as with Boehringer Ingelheim, Servier and Veloxis, who will include the product candidate in their portfolio as a valuable program and commit the resources required to co-develop the product and ultimately address patients' needs.

Partnerships are also a strong component of the Company's business model, generating non-dilutive revenues to finance R&D programs on innovative therapeutic targets and entities.

Due to the potential of its most advanced programs, the Company signed worldwide strategic partnerships with leading international pharmaceutical companies to conduct the clinical development of key products:

OSE-127/S95011

Two-step optional licensing agreement for OSE-127/S95011 signed with Servier in December 2016: the Company will develop the product until the completion of Phase 2 clinical trials in ulcerative colitis. After that, Servier will continue the development, as part of its licensing option.

This agreement amounts to a total of €272 million, including a payment of €10.25 million on signature (received in early 2017) and a payment of €30 million on exercise of a two-step licensing option, including €10 million at option 1, exercised in February 2019 (following validation of a pre-defined step of development) and €20 million on exercise of option 2.

In March 2020, OSE Immunotherapeutics and Servier signed an amendment covering the terms of the potential exercise of the licensing option by modifying Step-2 of this option. This amendment provides for:

- An initial milestone payment of €5 million upon inclusion of the first patient in the Phase 2a clinical trial (sponsored by Servier) in Sjögren's Syndrome, a systemic autoimmune disease characterized by an exocrine gland condition affecting the tear and salivary glands. The study is ongoing and the inclusion of the first patient, in August 2021, triggered the payment of this first milestone payment of €5 million by Servier to OSE Immunotherapeutics in September 2021.
- A second payment of €15 million on exercise of the option, at the end of the two planned Phase 2 studies. Servier, the sponsor of the Sjögren Syndrome study, is primarily interested in the results of this study. Nevertheless, all options remain open depending on the results of the two studies on Servier's decision. The second payment of €15 million is indivisible.

FR104

Collaboration and exclusive license agreement (signed on April 26, 2021) with Veloxis Pharmaceuticals for the development, manufacturing and marketing of FR104, a CD28 antagonist, in the organ transplantation market. Through this agreement, Veloxis plans to develop FR104 to provide a new therapeutic option for the prophylaxis of organ rejection in solid organ transplant patients.

Under the agreement, OSE Immunotherapeutics will receive up to €315 million in potential milestone payments from Veloxis, including a €7 million due on signature, development, registration and marketing milestones, and tiered royalties on potential future sales. Veloxis will assume all production, development and marketing costs of FR104 in transplantation indications.

At the end of January 2022, Veloxis Pharmaceuticals, Inc. received acceptance of the New Investigational Drug (IND) application in the United States for VEL-101/FR104 to conduct a clinical trial in the US under Veloxis' sponsorship. As part of the global licensing agreement signed in April 2021, this first step triggered a €5 million payment from Veloxis Pharmaceuticals, Inc. to OSE Immunotherapeutics. Since then, a Phase 1 sponsored and conducted by Veloxis, started in the US in May 2022.

BI 765063 (OSE-172)

Collaboration and exclusive licensing agreement (signed in April 2018) with Boehringer Ingelheim to jointly develop BI 765063 (OSE-172): Boehringer Ingelheim finances the product candidate's development in various types of cancer, its approval and international marketing.

According to the terms of this agreement, OSE Immunotherapeutics will receive from Boehringer Ingelheim a potential amount of more than €1.1 billion according to predefined development steps, marketing authorization, and sales, plus royalties on net worldwide sales of the product. This amount includes a payment of €15 million on signing the agreement (received in April 2018), a milestone payment of 15 million (received in June 2019) following the authorization of the clinical trial (in March 2019) and a milestone payment of €8 million (received in October 2021) for the treatment of the first patient in the expansion phase 1 of the trial in endometrium or colorectal advanced cancer (in September 2021) and a €10 million (in May 2022) upon initiation of the expansion Phase 1 conducted by Boehringer Ingelheim in advanced hepatocellular carcinoma and in head and neck cancer.

BI 765063 is in Phase 1 clinical trial in patients with advanced solid tumors.

The dose escalation phase (Step 1 of Phase 1) has been completed. BI 765063 in monotherapy and in combination showed good tolerability, without hematological toxicity and without reaching the maximum tolerated dose (MTD).

The expansion phase (Step 2 of Phase 1) is ongoing and aims to continue the evaluation of the first signs of efficacy of BI 765063 in combination with ezabenlimab in MSS advanced colorectal cancer (around 30 patients) and MSS advanced endometrium cancer (around 10 patients) whose disease relapsed after standard treatment and who received no prior anti-PD(L)1 inhibitors.

On this basis, the Company plans, with its partner Boehringer Ingelheim, to continue the expansion Phase 1 and a Phase 2.

The Company could accelerate the development of some of its products in co-development as part of new collaboration and licensing agreements with industrial players involved in the field of activating or regulatory immunology. Its products may be developed in therapeutic combinations of high clinical interest, in broad indications.

5.4.2 Clinical development of proprietary products

TEDOPI®

- **Final positive results of the Phase 3 clinical study of Tedopi® in non-small cell lung cancer (NSCLC) – A confirmatory Phase 3 in preparation to position Tedopi® in second line treatment in secondary resistance post-immunotherapy**
  The results from the first Phase 3 trial (Atalante-1) have shown significant survival benefit with Tedop® versus a chemotherapy standard treatment (docetaxel or pemetrexed) in HLA-A2 positive patients with non-small cell lung cancer (NSCLC) in secondary resistance after failure to immune checkpoint inhibitors. Patients included in this trial had failed second-line checkpoint inhibitor treatments, and represent a patient population in 3rd line treatment, hard-to-treat and with high medical need.

Based on these results and following the positive outcomes from the « Food & Drug Administration » (FDA) Type C meeting and to the "European Medicines Agency" (EMA) favorable scientific advice, OSE Immunotherapeutics is preparing a new Phase 3 clinical trial to support the registration of Tedopi®. This confirmatory study will evaluate Tedopi® versus the standard in second line treatment in HLA-A2 positive patients with advanced NSCLC.

Furthermore, licensing agreements have also been concluded in two countries to make Tedopi® available to the broadest audience globally and maximizing its potential:

- Licensing agreement (entered into in 2015) with RAFA Laboratories in Israel, which benefits from strong knowledge of and expertise in immunology.
- Licensing agreement (signed in 2019) with Chong Kun Dang (CKD) Pharmaceuticals Corp. for the development of Tedopi® in Korea. Under the terms of the agreement, OSE Immunotherapeutics will receive milestone payments totaling €4.3 million, including €1.2 million upon signature (€700,000) and upon the positive outcome of Atalante-1 step 1 (€500,000 already paid following the positive results of step 1 of Atalante-1). The milestone payments for an additional €3.1 million are related to Tedopi® registration and marketing milestones. The agreement also provides for royalties on sales of the product and a margin as part of the transfer price at a level slightly below thirty percent. The deal applies specifically to development and licensing of Tedopi® in the Korean market which accounts for approximately 1% of the total global oncology market.

  At the same time, given that the positive Phase 3 results significantly strengthened the value of Tedopi®, the Company is continuing to explore potential partnering opportunities for the product.

- **Tedopi®, in combination with Opdivo®, in Phase 2 in NSCLC**: a trial sponsored by the Italian oncology foundation, FoRT, with the support of Bristol Myers Squibb and OSE Immunotherapeutics.

  This Phase 2 clinical trial, initiated in 2021, aims to evaluate Tedopi® in combination with Opdivo® (nivolumab), a checkpoint inhibitor targeting the PD1 receptor of Bristol Myers Squibb, or with chemotherapy as a second-line treatment in HLA-A2 positive patients. with metastatic non-small cell lung cancer after a first-line chemo-immunotherapy.

- **Tedopi® is in a Phase 2 clinical trial for pancreatic cancer patients:** a trial sponsored by the GERCOR cooperative group in oncology in HLA-A2 positive patients with locally advanced pancreatic cancer.

  Due to COVID-19, enrollment of new patients in the TEDOPaM study of Tedopi® evaluated in monotherapy and in combination with Opdivo® (nivolumab, BMS) in pancreatic cancer has been suspended. Based on the analysis of the first 29 patients, the Independent Data Monitoring Committee (IDMC) for the trial recommended to stop the treatment with Opdivo® and proposed to add a chemotherapy to Tedopi®. As an interruption of chemotherapy could be harmful for patients, the evaluation of Tedopi® alone or combined with Opdivo® was stopped and a Tedopi® + chemotherapy treatment arm with FOLFIRI * was introduced. The trial resumed in the first quarter of 2021 with an amended protocol comparing Tedopi® in combination with FOLFIRI versus FOLFIRI as a maintenance treatment after induction treatment with FOLFIRINOX **. The main criteria remain the one-year survival rate.

  **FOLFIRINOX: a chemotherapy regimen combining folinic acid, fluorouracil, irinotecan and oxaliplatin*

  ***FOLFIRI: a chemotherapy regimen combining folinic acid, fluorouracil and irinotecan.* An interim analysis performed on the 29 first patients has shown interesting results for Tedopi® in monotherapy versus FOLFIRI. These results were presented at the American Society of Clinical Oncology (ASCO) meeting in June 2022.

  Patient recruitment is ongoing since it resumed in 2021.

  Tedopi®, in combination with Keytruda®, is in a Phase 2 clinical trial as maintenance treatment in ovarian cancer: a trial sponsored by the cooperative group ARCAGY-GINECO.

  This Phase 2 clinical trial (TEDOVA trial) aims to evaluate Tedopi® as a monotherapy maintenance treatment or in combination with the anti-PD1 Keytruda® (provided by MSD, Merck Sharp & Dohme Corp, a subsidiary of Merck & Co., Inc.) versus the reference treatment in platinum-sensitive ovarian cancer patients whose disease is controlled after platinum-based chemotherapy. It is planned to include 180 patients in the trial-in-progress, the first of which was randomized in August 2021.

OSE-279

OSE-279, a humanized anti-PD1 monoclonal antibody is under Phase 1/2 clinical Phase since December 2022 in advanced solid tumors and lymphomas. The Company owns its proprietary anti-PD1. This first clinical study also allows, at a later stage, to explore OSE-279 in combination with other OSE Immunotherapeutics' drug candidates or with external assets accessed through potential new partnerships with biotech or pharmaceutical companies.

5.4.3 Research & Development: active pursuit of new innovative research programs, proprietary research platforms, evolution of the product portfolio to clinical phase

Research and development is the Company's core business. To carry out its research programs, the Company uses in-house resources as well as partnerships with public research institutes and specialized subcontractors. The Company uses its own research laboratory at its Nantes (France) site where the teams conduct various optimization activities and preclinical studies.

The Company relies on in-house and international expertise in immunotherapy with, in particular, *ad hoc* models of vaccination based on T cells, the tumor microenvironment (immuno-oncology based on T cells), autoimmune and inflammatory diseases, to accelerate development. It also grows via its network of clinical experts in these immune-related pathologies.

OSE Immunotherapeutics expects to be able to generate further significant value from its two proprietary drug discovery platforms:

- **BiCKI® platform**, focused on immuno-oncology (IO) is a bispecific fusion protein platform relying on the proprietary anti-PD1 backbone (OSE-279) to increase anti-tumor efficacy. The most advanced BiCKI® candidate is targeting anti-PD1xIL-7.

- **Myeloid platform**, focused on optimizing the therapeutic potential of myeloid cells in IO and immuno-inflammation (I&I). **OSE-230** (ChemR23 agonist mAb) is the most advanced candidate generated by the platform, with the potential to resolve chronic inflammation by driving affected tissues to tissue integrity.

The Company will continue to develop innovative products in preclinical and R&D development through research collaborations with centers of excellence or collaborative programs conducted in consortia financed as part of calls for proposals.

5.5 Research & Development, patents and licenses

5.5.1 Industrial property

OSE Immunotherapeutics is assisted in its initiatives and actions to protect its intellectual property rights by specialist intellectual property firms.

5.5.1.1 Memopi® technology and the product, Tedopi® (OSE-2101)

The Company, together with OPI (its wholly owned subsidiary), owns the worldwide rights to OSE-2101.

OSE-2101 is specifically the subject of a patent family, the original patent family, and the protection is supplemented by other patent families.

Original patent family

Claims for patents granted for this family cover a composition comprising the combination of different types of peptides (CTL peptides optimized for greater interaction with the HLA-A2 receptor, CTL peptides optimized for greater interaction with cytotoxic T cells, HTL peptides) for OSE-2101 as well as the therapeutic applications of this composition for the treatment of cancer, in particular, to delay remissions of cancer after surgery, chemotherapy or radiotherapy.

This family is based on an international application, WO 04/094454, filed on April 16, 2004, that claims the priority of an American order filed on April 18, 2003, under number US 60/463,724.

It includes the following patents delivered:

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
AU2010214701	Australia	AU2010214701	AU2010214701	2/2/2012	April 2024
CA 2 522 812	Canada	CA2522812	CA2522812	8/21/2012	April 2024
EP04759962.6	Europe	EP 1 620 456	EP 1 620 456	2/26/2014	April 2024
(validated in all contracting states of the European Patent Office)					
US14081086	United States	US2010209493	US 8,007,810	8/30/2011	April 2024
	United States	US2014141064	US 9,394,350	7/19/2016	April 2024 + 64 days
	United States	US2017028041	US 9,913,884	3/13/2018	April 2024
JP5156882	Japan	JP2006526628	JP5156882	12/21/2012	April 2024

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

Complementary families

T-cell immune therapy and the treatment of brain metastases (HLA-A2 positive patients)

On November 6, 2014, the Company filed an international application for a specific T-cell immune therapy for use in the treatment of brain metastases in HLA-A2 positive patients. This patent application opens the way to new potential indications within the field of brain metastases, a metastatic localization complicating a number of cancers.

This family includes the following patents and patent applications:

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
AU2014410466	Australia	AU2014410466	AU2014410466	1/2/2020	November 2034
KR10-2017-7015327	South Korea	KR20170098811	KR102043725	11/6/2019	November 2034
US15/524,278	United States	US2017319672	US 10,434,157	10/8/2019	November 2034 + 157 days
IL250576	Israel	IL250576	IL250576	12/27/2019	November 2034
JP2017-518779	Japan	JP2017533898	JP6474893	2/8/2019	November 2034
TW104135282	Taiwan	TW201625287	TW I703982	9/11/2020	October 2035
CA 2,963,184	Canada	CA 2,963, 184	CA 2,963,184	11/24/2020	November 2034
EP-14796049.6	Europe	EP-3215184	EP-3215184	3/3/2021	November 2034
Valid in Belgium, Switzerland, Germany, Spain, France, the United Kingdom, Italy					
BR 11 2017 009 358 8	Brazil	BR112017009358		Pending	November 2034
CN 201480082351.X	China	CN107073087A	ZL201480082351.X	9/8/2020	November 2034
EA 201790990	Eurasia	EA 201790990	EA037271	3/2/2021	November 2034
MX/a/2017/005807	Mexico	MX/a/2017/005807	MX386458	9/24/2021	November 2034
NZ 729514	New Zealand	NZ729514	NZ 729514	3/24/2020	November 2034

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

Immune therapy and an early memory T-cell response

On June 29, 2015, OSE Pharma filed an international patent application with a specific T-cell immune therapy capable of inducing an early memory T-cell response in HLA-A2 positive patients. This patent covers the product's method of administration.

This family includes the following patents and patent applications:

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
PCT/EP2015/06474	International application	WO2017/000983			
ZA2018/00434	South Africa	ZA201800434	ZA2018/00434	12/19/2018	June 2035
JP 2017-567729	Japan	JP2018525343	JP 6654207	1/30/2020	June 2035
EP 15 733431.9	Europe	EP-3 313 431		Pending	June 2035
US 15/578,721	United States	US-2018-0169200	US11191820	12/7/2021	June 2035 + 308 days
AU2015400687	Australia	AU2015400687	AU2015400687	8/5/2021	June 2035
BR 11 2017 0 27653 4	Brazil	BR112017027653		Pending	June 2035
CA 2,990,299	Canada	CA2990299		Pending	June 2035
EA 201890148	Eurasia	EA201890148	EA041118	9/15/2022	June 2035
IT 255722	Israel	IL255722		Pending	June 2035
KR 10-2022-7002805	South Korea			Pending	June 2035
NZ 737717	New Zealand	NZ737717	NZ737717	11/30/2021	June 2035

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

Method of preparing a stable emulsion

On January 24, 2018, OSE Pharma filed an international patent application for an industrial-scale method of preparing a stable emulsion and for the ready-to-use product.

This family includes the following patents and patent applications:

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
PCT/EP2018/051647	International application	WO 2018/138110			
TW 107102651	Taiwan	TW 201840331	1793099	02/21/2023	January 2038
AR 20180100167	Argentina	AR113209		Pending	January 2038
EP 18 710760.2	Europe	EP 3 573 600	EP 3 573 600	3/2/2022	January 2038
Validated in Albania, Austria, Bosnia-Herzegovina, Belgium, Bulgaria, Switzerland, Cyprus, Czech Republic, Germany, Denmark, Estonia, Spain, Finland, France, United Kingdom, Greece, Croatia, Hungry, Ireland, Island, Italy, Lithuania, Luxemburg, Leetonia, Monaco, Montenegro, Macedonia, Malta, Netherlands, Norway, Poland, Portugal, Romania, Serbia, Sweden, Slovenia, Slovakia, Saint-Marin and Turkey.					
US 16/477,534	United States	US-2019-0345213	US11, 325,959	05/10/2022	January 2038
US 17/736,113	United States	US-2022-0259277-A1		Pending	January 2038
EP 22 153774,9	Europe	EP 4 029 494		Pending	January 2038
AU 2018213890	Australia	AU2018213890		Pending	January 2038
BR 11 2019 014917 1	Brazil	BR112019014917		Pending	January 2038
CA 3,047,492	Canada	CA3047492		Pending	January 2038
CN 201880007527.3	China	CN110191703A	ZL201880007527.3	04/08/2022	January 2038
CN 202210293478.2	China	CN114917189A		Pending	January 2038
J/6205	Macao			10/11/2022	January 2038
IL 267237	Israel	IL267237		Pending	January 2038
JP 2019-560481	Japan	JP2020505464	JP7140778	09/12/2022	January 2038
KR 10-2019-7024340	South Korea	KR10-2019-0107113		Pending	January 2038
MX/a/2019/008878	Mexico	MX395840		09/22/2022	January 2038
NZ 745571	New Zealand			Pending	January 2038
ZA 2019/05487	South Africa		ZA 2019/05487	5/27/2020	January 2038
62020006780.4	Hong Kong	40016682A	HK40016682	08/26/2022	January 2038
42023067136.4	Hong Kong			Pending	January 2038

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

Treatment in combination with an immune checkpoint inhibitor

On November 27, 2017, OSE Pharma filed an international patent application for a cancer treatment method involving sequential administrations of Tedopi® and an immune checkpoint inhibitor.

This family includes the following patents and patent applications:

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
PCT/EP2017/080543	International application	WO2019/101347			
AU 2017440798	Australia	AU2017440798		Pending	November 2037
BR 11 2020 010656 9	Brazil	BR112020010656		Pending	November 2037
CA 3,081,774	Canada	CA3081774		Pending	November 2037
CN 201780097101.7	China	CN111727051A		Pending	November 2037
EP 17 811880.8	Europe	EP 3 716 999		Pending	November 2037
IL 274748	Israel	IL274748		Pending	November 2037
JP 2020-528928	Japan	JP2021504378	JP6999035	12/23/2021	November 2037
KR 10-2020-7018440	South Korea	KR10-2020-0093005		Pending	November 2037
MX/a/2020/005454	Mexico	MX2020005454		Pending	November 2037
NZ 765655	New Zealand			Pending	November 2037
US 16/767,144	United States	US2020-0384067		Pending	November 2037
ZA 2020/03829	South Africa			Pending	November 2037

* The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

5.5.1.2. OSE-1101

This family concerns the application/use of the OSE-1101 product in the treatment of cystic fibrosis or its complications, such as inflammatory disorders or infection.

This family is based on international application WO2013/164204, filed on April 19, 2013, that claims the priority of a European application filed on April 30, 2012, under number 12 305487.6.

This family includes the following patents and patent applications:

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
US14/397,743	United States	US2015/133487	US 9,301,955	4/5/2016	April 2033
IL235358	Israel	IL235358	IL235358	12/27/2019	April 2033

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

5.5.1.3 FR104

The portfolio relating to FR104 on anti-CD28 antagonist antibodies includes the following patent families.

Family 1

This family, in the name of INSERM, concerns the CD28.3 antibody and its derivatives.

This family is based on international application, WO 2002/051871, filed on December 26, 2001, that claims the priority of a French patent application filed on December 26, 2000, under number FR0017025.

This family includes the following patents:

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
EPO1995797.6	Europe	EP1345969	EP1345969	08/11/2010	December 2021
Validated in Austria, Belgium, Switzerland, Germany, Denmark, Spain, Finland, France, United Kingdom, Greece, Ireland, Italy, Luxemburg, Monaco, Netherlands, Portugal, Sweden and Turkey.					
US10/450,832	United States	US2008/0038273	US 7723482	1/18/2008	December 2021 + 1,419 days
JP2002552964	Japan	JP2004-516034	JP4066166	05/25/2010	December 2021

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

Family 2

This family, co-owned with INSERM, concerns a specific recombinant monovalent antibody structure, a derivative of the CD28.3 antibody.

This family is based on international application, WO2010/082136, filed on January 13, 2010, that claims the priority of a European patent application filed on January 14, 2009, under number EP09290029.9.

This family includes the following patents:

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
CA2749627	Canada	CA2,749,627	CA2,749,627	5/14/2019	January 2030
CA3037902	Canada	CA3037902	CA3037902	8/31/2021	January 2030
US13/144,471	United States	US2011/0313135	US 9,587,023	3/7/2017	January 2030 + 949 days
JP2011-545812	Japan	JP2012-514997	JP 5755148	6/5/2015	January 2030
US15/416513	United States	US2017166643	US 10689444	6/23/2020	January 2030

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

Family 3

This family, co-owned with INSERM, concerns a monovalent ligand of the human CD28 receptor capable of binding to the epitope of the CD28.3 antibody.

This family is based on international application, WO2011/042891, filed on October 8, 2010, that claims the priority of a French patent application filed on October 9, 2009, under number FR0904866.

This family includes the following patents:

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
EP10785516.5	EP	EP2486059	EP2486059	11/11/2015	October 2030
Valid in Belgium, Switzerland, Germany, Spain, France, the United Kingdom, Ireland, Italy and the Netherlands.					
US13/501015	United States	US2013/0058933	US 8785138	7/22/2014	October 2030

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

Family 4

This family, co-owned with INSERM, concerns humanized antibodies derived from the CD28.3 antibody and their use as a drug.

This family is based on international application, WO2011/101791, filed on February 16, 2011, that claims the priority of two European patent applications filed on February 18, 2010, and July 13, 2010, under number EP10290080.0 and EP 10290389.5, respectively.

This family includes the following patents:

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
EP11707918.6	EP	EP2536764	EP2536764	7/4/2018	February 2031
Valid in all European Patent Convention Contracting States					
EP18177022.3	EP	EP3428192	EP3428192	8/11/2021	February 2031
Valid in Belgium, France, Germany, Italy, Spain, Switzerland/ Liechtenstein, the United Kingdom					
CA 2,788,544	Canada	CA 2,788,544	CA 2,788,544	3/5/2019	February 2031
JP2012-553431	Japan	JP2013-519389	JP5992340	8/26/2016	February 2031
US13/577103	United States	US2013/0078236	US 8785604	7/22/2014	February 2031
US14/326119	United States	US20150071916	US 9,562,098	2/7/2017	February 2031 + 180 days
US15/386998	United States	US2017/114136	US10364287	7/30/2019	February 2031 + 149 days

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

Family 5

This family, in the name of OSE Immunotherapeutics, concerns a regime for the administration of humanized antibodies derived from the CD28.3 antibody.

This family is based on an international application WO2017/103003 filed on 12/15/2016 and claiming the priority of two European patent applications filed on December 15, 2015, and November 22, 2016 under numbers EP 15200281.2 and EP16306537.8, respectively.

This family includes the following patents and patent applications:

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
EP16822423.6	Europe	EP3390450	EP3390450	1/20/2021	December 2036
Validated in: Albania, Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Monaco, the Netherlands, Norway, Poland, Portugal, Macedonia, Romania, San Marino, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Liechtenstein, Turkey, United Kingdom.					

EP21150940.1	Europe	EP-3868785		Pending	December 2036
US17/668.969	United States	US-2022-0411510A1		Pending	December 2036
JP2018-532040	Japan	JP2018538309	JP6923528	8/18/2021	December 2036
CN201680080258.4	China	CN108699148		Pending	December 2036
KR10-2018-7020218	South Korea	KR20180087428		Pending	December 2036
HK 19120836.2	Hong Kong	HK1260979	HK1260979	9/17/2021	December 2036
HK 42022048901.7	Hong Kong	HK40058111		Under registration	December 2036

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

5.5.1.4 OSE-127 or EFFI-7

The portfolio of project Effi-7 covering anti-IL-7Rα antagonist antibodies includes two patent families.

Family 1

This family bears on anti-IL-7Rα antagonist antibodies of the IL7 receptor. It concerns in particular the antibody being developed.

This family is based on an international application WO2015189302 filed on June 10, 2015 that claims the priority of two applications, a provisional American application US 62/010117 filed on June 10, 2014 and a European patent application EP15305078.6 filed on January 23, 2015.

It includes applications pending review before 34 Patent Offices based on the PCT application, including Europe and the United States. 19 patents have been granted in particular in China, the United States (2), Australia, Colombia, Mexico, Russia, Israel and Singapore.

Filing no.	**Country**	**Publication no.**	**Patent no.**	**Delivered on**	**Theoretical expiration date***
US15/317355	United States	US2017/0129959	US 10,428,152	10/1/2019	June 2035
US16/532000	United States	US-2019-0382497-A1	US11440964	09/13/2022	June 2035 + 7 days
US17/941.885	United States			Pending	June 2035
NC2016/0005101	Colombia		CO34155	8/13/2018	June 2035
EP15727989.4	Europe	EP3155014		Pending	June 2035
17104912.8	Hong Kong	1231487		Under registration	June 2035
2016/08275	South Africa			Pending	June 2035
170005	Algeria			Pending	June 2035
AU 2015273532	Australia	AU2015273532	AU2015273532	07/08/2021	June 2035
SA 516380455	Saudi Arabia		SA7395	12/22/2020	June 2035
AP/P/2016009599	ARIPO	AP2016009599	AP5847	10/28/2021	June 2035
BR1120160287550	Brazil			Pending	June 2035
1242/2016	United Arab Emirates			Pending	June 2035
EA201692460	Eurasia	EA201692460	EA3903	01/11/2022	June 2035
CA 2,950,823	Canada	CA2950823		Pending	June 2035
JP 2017-517406	Japan	2017-522903		Pending	June 2035
JP 2021-128846	Japan	JP2021-184731		Pending	June 2035
KR 10-2017-7000724	South Korea	KR10-2017-0019417		Pending	June 2035
3172-2016	Chile	3172-2016		Pending	June 2035
CN 201580043066.1	China	CN106715471A	106715471	4/9/2021	June 2035
NC2016/0005101	Colombia		34155	08/13/2018	June 2035
CR2016-000576	Costa Rica	CR2016-000576	4268	10/31/2022	January 2036
PCT 1982/2016	Egypt			Pending	June 2035
201617042413	India			Pending	June 2035
IL 249449	Israel	IL 249449	IL 249449	10/1/2020	June 2035
SG11201610036P	Singapore	SG11201610036P	SG 11201610036P	10/17/2020	June 2035
P12016002094	Malaysia	MY-1900889	MY-1990889-A	05/17/2022	June 2035
MX/a/2016/016236	Mexico	MX2016016236	376066	11/2/2020	June 2035

NZ7726932	New Zealand	NZ7726932	NZ7726932	05/26/2022	June 2035
NZ765238	New Zealand			Pending	June 2035
1201600468	OAPI		20097	07/23/2021	June 2035
2699-2015	Peru		10980	11/16/2021	June 2035
1-2016-502445	Philippines			Pending	June 2035
RU2016151265	Russia	RU2016151265	2734076	10/12/2020	June 2035
RU2020131068	Russia			Pending	June 2035
SA2016005336	Salvador	SA2016005336	SV20160021048	04/28/2022	June 2035
1601007372	Thailand	171839		Pending	June 2035
TN2016/0528	Tunisia	TN2016/0528	25334	6/7/2018	June 2035
2016 13258	Ukraine		125366	03/02/2022	June 2035
VN-2016-05015	Vietnam		VN29307	07/22/2021	June 2035
National/regional phases entered in: Europe, United States, South Africa, Algeria, Saudi Arabia, ARIPO (African Regional Intellectual Property Organization), Australia, Brazil, Canada, Chile, China, Colombia, Republic of Korea, Costa Rica, Egypt, United Arab Emirates, Eurasia, Hong Kong, India, Israel, Japan, Malaysia, Mexico, New Zealand, Peru, Philippines, Russia, El Salvador, Singapore, Thailand, Tunisia, Ukraine, AIPO (African Intellectual Property Organization), Vietnam.					

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

Family 2

This family concerns humanized antibodies directed against CD127, the alpha chain of the IL-7 receptor. It concerns in particular the antibody being developed.

This family is based on an international application WO 2018/104483 filed on December 7, 2017, that claims the priority of a European patent application filed on December 9, 2016, under number EP16306655.8.

Direct extensions were made in several countries including Argentina, Bolivia, Paraguay, Pakistan, Taiwan, Venezuela, Lebanon and Uruguay.

It includes patents and applications pending review before 34 Patent Offices based on the PCT application, including Europe and the United States. 22 patents have been delivered including in the United States, in Europe, Africa (ARIPO, OAPI), China, Korean Republic, Eurasia, Hong Kong, Japan, Mexico, Malaysia, New Zealand, Salvador, Ukraine, Russia, Pakistan, Taiwan, Lebanon, Colombia and Israel.

Filing no.	**Country**	**Publication no.**	**Patent no.**	**Delivered on**	**Theoretical expiration date***
National/regional phases entered in: Europe, United States, South Africa, Algeria, Saudi Arabia, ARIPO (African Regional Intellectual Property Organization), Australia, Brazil, Canada, Chile, China, Colombia, Republic of Korea, Costa Rica, Egypt, United Arab Emirates, Eurasia, Hong Kong, India, Israel, Japan, Malaysia, Mexico, New Zealand, Peru, Philippines, Russia, El Salvador, Singapore, Thailand, Ukraine, AIPO (African Intellectual Property Organization), Vietnam.					
20170103427	Argentina	AR110326A1		Pending	December 2037
2019/02743	South Africa			Pending	December 2037
190278	Algeria			Pending	December 2037
519401906	Saudi Arabia			Pending	December 2037
AU2017373819	Australia	AU2017373819	AU 2017373819	07/14/2022	December 2037
AP/P/2019/011639	ARIPO		AP5638	06/29/2021	December 2037
1120190105956	Brazil			Pending	December 2037
3.042.582	Canada			Pending	December 2037
CL 1530 2019	Chile	1530-2019	64203	02/08/2022	December 2037
2019-000273	Costa Rica			Pending	December 2037
11306	Lebanon	11306	11306	3/8/2018	December 2037
PCT 869/2019	Egypt			Pending	December 2037
P6000785/2019	United Arab Emirates			Pending	December 2037
US16/467284	United States	US20190375844	US11098128	8/24/2021	December 2037
US17/363,260	United States	US20210395376 US2022-033834		Pending	December 2037
EA 201991005	Eurasia	EA201991005	EA 041126	09/16/22	December 2037
EP17835592.1	Europe	EP3551664	EP3551664	2/17/2021	December 2037

Valid in all European Patent Convention Contracting States					
JP 2019-530803	Japan	JP2020500542	JP6986559	12/1/2021	December 2037
KR 10-2019-7019889	South Korea	KR10-2019-0090005	KR10-2306366	03/02/2021	December 2037
CN 201780076086.8	China	CN 110392695	CN201780076086.8	2/2/2021	December 2037
62020002274.4	Hong Kong		HK40012892	06/04/2021	December 2037
201917022344	India			Pending	December 2037
IL 266837	Israel	IL266837	IL266837	10/1/2020	December 2037
NC2019/0005909	Colombia		37628	9/15/2020	December 2037
PI20199003245	Malaysia	MY190770	MY-190770-A	05/12/2020	December 2037
MX/a/2019/006577	Mexico	MX2019006577	MX396014	09/29/2022	December 2037
NZ753213	New Zealand	NZ753213	NZ7532131	09/30/2022	December 2037
1201900214	OAPI		19665	12/02/2020	December 2037
1794093	Paraguay			Pending	December 2037
PK626/2017	Pakistan	PK626/2017	143833	03/01/2022	December 2037
001201-2019/DIN	Peru	2019-1152		Pending	December 2037
1-2019-501285	Philippines			Pending	December 2037
RU2019115610	Russia	RU2019005905	RU276352	03/30/2022	December 2037
2019005905	Salvador	SV2019005905	SV2019005905	03/02/2021	December 2037
11201904953X	Singapore			Pending	December 2037
TW106142933	Taiwan	TW201833137	177996	09/21/2022	December 2037
1901003402	Thailand			Pending	December 2037
37511	Uruguay			Pending	December 2037
a 2019 05605	Ukraine		UA126386	09/28/2022	December 2037
2017-000463	Venezuela			Pending	December 2037
1-2019-03642	Vietnam			Pending	December 2037

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

Family 3

This family concerns a treatment method of CD127+ cancers with anti-CD127 agents, in particular antibodies with an ADCP+ activity but without ADCC.

This family is based on an international application WO 2022/248940 filed on May 27, 2022, that claims the priority of a European patent application filed on May 28, 2021, under number 17/334,158.

This family includes the following applications:

Filing no.	**Country**	**Publication no.**	**Patent no.**	**Delivered on**	**Theoretical expiration date***
US17/334,158	United States	US20220389104		Pending	May 2041
PCT/FR2022/051003	International application	WO 2022/248940			May 2042
US18/060129	United States			Pending	May 2042

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

Family 4

A fourth family concerns anti-CD127 antibodies with an ADCP effect (cellular phagocytosis depending on antibodies) on CD127+ tumor cells and without ADCC (cellular toxicity induced by antibodies) on immune cells, in particular for cancer treatment.

This family is based on an international application WO2022/248940 filed on May 27, 2022, which claims the priority of the US patent application filed under number US17/334158. The national/regional phases are to be engaged in November 2023. This family's theorical date of expiration is May 2042.

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
PCT/IB2022/000365	International application	WO2022/248940			May 2042
18/060129	United States	US2022389104		Pending	May 2042

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

5.5.1.5 MD-707 and OSE-703 or EFFI-3

Family 1

This family concerns antagonist anti-IL-7Rα antibodies of the IL7 receptor.

This family is based on international application WO2013056984 filed on October 4, 2012 that claims the priority of a European patent application filed on October 19, 2011 under number EP11306353.1.

This family includes the following patents:

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
PCT/EP2012/069670	International application	WO2013056984			
US 14/352992	United States	US2014-0308281	US 9,447,182	9/20/2016	October 2032 + 20 days
JP2017106295	Japan	JP2017184753	JP6621778	12/18/2019	October 2032
EP17200006.9	Europe	EP3299392	EP3299392	11/18/2020	October 2032
Validated in: Germany, Spain, France, United Kingdom, Italy.					

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

Family 2

This family designed for immuno-oncology concerns a non-antagonistic anti-IL-7Rα antibody of the IL7, presenting a cytotoxic activity.

This family is based on international application WO 2017/149394 filed on February 28, 2017, that claims the priority of a provisional American application filed on February 29, 2016 under number 62/301271.

This family includes the following patents and patent applications:

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
EP 17716593.3	Europe	EP3423496	EP3423496	7/3/2019	February 2037
Validated in: Germany, Austria, Belgium, Bosnia and Herzegovina, Bulgaria, Cyprus (Greek part), Croatia, Denmark, Spain, Estonia, Finland, France, Greece, Hungary, Ireland, Iceland, Italy, Latvia, Lithuania, Luxembourg, Macedonia, Malta, Morocco, Moldova, Monaco, Montenegro, Norway, the Netherlands, Poland, Portugal, Romania, United Kingdom, San Marino, Serbia, Slovakia, Slovenia, Sweden, Switzerland, Czech Republic, Turkey.					
US16/080572	United States	US 2020-0308288	US11230602	1/25/2022	February 2037
CN 201780014099.2	China	CN109195987	ZL201780014099.2	5/27/2022	February 2037
KR 7028377	South Korea	KR20180118746		Pending	February 2037
JP 2018-545380	Japan	JP2019-515648	JP7053479	4/04/2022	February 2037
IL 261330	Israel	IL261330	IL261330	11/01/2022	February 2037
AU 2017225495	Australia	AU2017225495		Pending	February 2037
BR 1120180674796	Brazil	BR112018067479		Pending	February 2037
CA 3014313	Canada	CA3014313		Pending	February 2037
IN 17030581	India	IN201817030581		Pending	February 2037
HK19123912.8	Hong Kong		HK 40000684	9/25/2020	February 2037

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

Family 3

This family covers reagents, anti-CD127 compounds used for a T cell eff/T reg cellular sorting method.

This family is co-owned with the AP-HP and the *Etablissement Français du Sang* (French blood agency).

This family is based on an international application WO2019043065 filed on August 29, 2018, that claims the priority of a European patent application filed on August 29, 2017 under number EP17306109.4.

This family includes the following patent applications:

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
EP 18762082.8	Europe	EP3676292		Pending	August 2038
US 16/643,550	USA	US-2020-0362300-A1		Pending	August 2038

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

5.5.1.6 BI 765063 (OSE-172) or EFFI-DEM

The portfolio relating to BI project 765063 relates to antibodies directed against SIRPα and their uses. It includes several patent families.

Family 1

The first patent family concerns anti-SIRPα antibodies able to induce the differentiation of MDSC for the treatment of cancer and infectious diseases. This family also concerns more broadly the use of anti-SIRPα antibodies for some therapeutic indications.

This family includes an international application WO2016/063233 filed on October 21, 2015, that claims the priority of a European application filed on October 24, 2014 under number EP14190370.8

This family includes the following patents and patent applications: It includes patents granted in Europe and Japan.

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
EP 15794641.9	Europe	EP3209691	EP 3209691	7/15/2020	October 2035
Validated in Austria, Belgium, Switzerland, Germany, Denmark, Spain, France, United Kingdom, Italy, the Netherlands, Hungary, Poland, Czech Republic, Slovakia, Sweden, Turkey. Pending opposition					
EP 20177260.5	Europe	EP3783027		Pending	October 2035
HK 18102829.3	Hong Kong		HK1243428	2/26/2021	October 2035
CA 2964203	Canada	CA 2964203		Pending	October 2035
JP 2017-520986	Japan	JP2017538669	JP6918279	7/27/2021	October 2035
JP 2021-102148	Japan	JP2021155432		Pending	October 2035
US 17/79.45	United States	US2022028199		Pending	October 2035

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

Family 2

The second patent family concerns the use of anti-SIRPα antibodies capable of inhibiting the polarization of M2-type anti-inflammatory macrophages and/or promoting M1-type pro-inflammatory macrophages for the treatment of cancer.

This family also concerns the use of anti-SIRPα antibodies in combination with check point inhibitor compounds for some therapeutic indications (solid cancers).

This family includes an international application WO 2017/068164 filed on October 21, 2016, that claims the priority of a European patent application filed on October 21, 2015 under number EP15190918.1.

This family includes the following patents and patent applications:

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
EP16785163.3	Europe	EP3365370		Pending	October 2036

US17/747.798	United States	US20220298259		Pending	October 2036
JP2018-521040	Japan	JP2018531274	JP7078533	05/23/2022	October 2036
JP2022007399	Japan	JP2022040378		Pending	October 2036

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

Family 3

The third patent family concerns a humanized anti-SIRPα antibody.

This family includes an international application WO 2017/178653 filed on April 14, 2017, that claims the priority of a provisional American application US 62/322,707 and a European patent application EP 17305182.2.

This family includes patents and applications under review before 30 Patent Offices on the basis of the PCT application. It includes patents granted in the United States, in China, in South Korea, Colombia and Nigeria.

Filing no.	**Country**	**Publication no.**	**Patent no.**	**Delivered on**	**Theoretical expiration date***
National/regional phases undertaken in Europe, the United States, China, Japan, Republic of Korea, Canada, Israel, Eurasia, ARIPO, United Arab Emirates, Australia, Brazil, Chile, Colombia, Egypt, Hong Kong, India, Indonesia, Malaysia, Mexico, New Zealand, Nigeria, Peru, Philippines, Thailand, Saudi Arabia, Singapore, Ukraine, Vietnam, South Africa.					
2018/06293	South Africa			Pending	April 2037
518400237	Saudi Arabia			Pending	April 2037
2017248626	Australia	AU 2017248626		Pending	April 2037
201891882	Eurasia			Pending	April 2037
EP 17718881.0	Europe	EP3443010		Pending	April 2037
AP/P/2018/011048	ARIPO	AP 6589	12/13/2022	Pending	April 2037
P6001432/2018	United Arab Emirates			Pending	April 2037
US 16/093062	United States	US 2019-0127477	US11279766	03/22/2022	April 2037
US-17681219	United States	US20220281991		Pending	April 2037
201891882	Eurasia			Pending	April 2037
PCT 1633/2018	Egypt			Pending	April 2037
19125023.2	Hong-Kong			Pending	April 2037
BR- 112018070823-2	Brazil			Pending	April 2037
CN 201780023581.2	China	CN109071664A	ZL 201780023581.2	02/21/2023	April 2037
CN 202310060526.8	China			Pending	April 2037
JP 2018-550322	Japan	JP2019520034		Pending	April 2037
JP 2022-0112873	Japan	JP2022169504 A		Pending	April 2037
KR 10-2018-7032968	South Korea	KR 10-2018-0134397	KR102355240	01/20/2022	April 2037
CA 3020373	Canada	CA 3020373		Pending	April 2037
2018-02898	Chile	42,229		Pending	April 2037
IN-17038715	India	IN201817038715		Pending	April 2037
P00201808100	Indonesia	2018/12882		Pending	April 2037
IL 262251	Israel	IL262251		Pending	April 2037
PI 2018703774	Malaysia		MY-195448-A	01/22/2023	April 2037
MX-PA12434	Mexico	MX2018012434		Pending	April 2037
NC2018/0010855	Colombia	NC2018/0010855	38015	11/30/2020	April 2037
F/P/2018/338	Nigeria		F/P/2018/338	05/30/2019	April 2037

746545	New Zealand			Pending	April 2037
1974-2018/DIN	Peru	2018-1921		Pending	April 2037
1-2018-550160	Philippines	1-2018-550160		Pending	April 2037
11201808465U	Singapore			Pending	April 2037
1801006381	Thailand			Pending	April 2037
a201809487	Ukraine	a201809487	126658	01/11/2023	April 2037
1-2018-05049	Vietnam	62572		Pending	April 2037

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

Family 4

The fourth patent family concerns the use of anti-SIRPα antibodies (including BI 765063) in particular for targeting patients designated V1 (one of the main categories of SIRP); and capable of increasing the "cross-presentation" of antigens to T cells.

This family is based on an international application WO2019/175218 filed on March 13, 2019 that claims the priority of a European application EP 18 305 271.1. The theoretical expiration date of this family is March 2039.

This family includes the following patent applications:

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
AU 2019233577	Australia	AU2019233577		Pending	March 2039
BR 11 2020 017709 1	Brazil	BR112020017709		Pending	March 2039
CA 3 091 468.	Canada	CA3091468		Pending	March 2039
CN 201980031527.1	China	CN112105646		Pending	March 2039
CL 2305-2020	Chile	CL2020002305		Pending	March 2039
EA 202091859	Eurasia	EA202091859		Pending	March 2039
EP 19711862.3	Europe	EP3765512		Pending	March 2039
KR 10-2020-7029293	South Korea	KR20210006338		Pending	March 2039
JP 2020-546939	Japan	JP2021517130		Pending	March 2039
MX/a/2020/009121	Mexico	MX2020009121		Pending	March 2039
PH 1-2020-551491	Philippines	PH12020551491		Pending	March 2039
NZ 767618	New Zealand			Pending	March 2039
US 16/979,627	United States	US2021040206		Pending	March 2039
ZA 2020/05451	South Africa			Pending	March 2039

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

Family 5

A fifth patent family concerns a bifunctional compound including, on the one hand, an anti-SIRPα antibody (including BI 765063), and, on the other hand, coupled with this antibody, an immune agent such as PD1.

This family is based on an international application WO2019/073080 filed on October 15, 2018, that claims the priority of a European application EP 17 306 396.7. The theoretical expiration date of this family is October 2038.

This family includes the following patent applications:

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
EP18789355.7	Europe	EP3694881		Pending	October 2038
CN201880079823.4	China	CN111511766		Pending	October 2038
JP2020-546939	Japan	JP2020536573		Pending	October 2038
US16/754,285	United States	US20210179728		Pending	October 2038
HK 6202025276.8	Hong Kong	HK 40035592		Pending	October 2038

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

5.5.1.7 BiCKI®, a new platform of bispecific checkpoint inhibitors targeting the PD1 receptor and other innovative targets

The new bispecific fusion protein platform is built around a key backbone component anti-PD1 (OSE-279) merged with innovative immunotherapy targets.

A portfolio relating to this platform includes several patent families.

5.5.1.7.1 OSE-279 and variants

These antibodies are PD1 antagonists (immune checkpoint inhibitor) and are the subject of a patent family.

This family is based on an international application WO2020/127366 filed on December 17, 2019 that claims the priority of a European application filed on December 21, 2018 under number EP 18 306801.4. The theoretical expiration date of this family is December 2039.

This family includes the following patent applications and patents:

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
EP 19 829506.5	Europe	EP 3 883 966		Pending	December 2039
US 17/414,967	USA	US20210355225	US11352430	06/07/2022	December 2039
US 17/830,381	USA	US-2022-0332826		Pending	December 2039
AR 20190103789	Argentina	AR117465		Pending	December 2039
TW 108146725	Taiwan	TW 202037608 A		Pending	December 2039
AU2019406452	Australia	AU2019406452	AU2019406452	09/16/2021	December 2039
BR 11 2021 011982 5	Brazil	BR112021011982		Pending	December 2039
CA3122526	Canada	CA3122526	CA3122526	01/03/2023	December 2039
CL202101628	Chile	CL2021001628		Pending	December 2039
CN201980092699	China	CN113557245	ZL 201980092699.X	10/25/2022	December 2039
CN 202211259346.4	Chine			Pending	December 2039
NC2021/0007956	Colombia	CO2021007956	CO40654	10/24/2022	December 2039
EA202191751	Eurasia	EA202191751		Pending	December 2039
HK62022050704.5	Hong-Kong	HK 40060816A		Pending	December 2039
IL283812	Israel	IL283812	IL283812	01/02/2023	December 2039
IL 296038	Israel			Pending	December 2039
202117029423	India	IN202117029423		Pending	December 2039
JP2021536204	Japan	JP2022513528	JP7043685	03/18/2022	December 2039
JP202240264	Japan			Pending	December 2039
KR10-2021-7022357	Korea	KR10-2021-0097197	KR10-2371173	03/04/2022	December 2039
KR10-2022-7007041	Korea			Pending	December 2039
MX/a/2021/007290	Mexico		MX390775	03/17/2022	December 2039
NZ777390	New Zealand			Pending	December 2039
1-2021-551426	Philippines			Pending	December 2039
11202106347P	Singapore			Pending	December 2039
1-2021-03887	Vietnam	VN82644 A		Pending	December 2039
2021/04246	South Africa			Pending	December 2039

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

5.5.1.7.2 BiCKI® OSE-279

This family covers the OSE-279 targeting platform for PD1 (anti-PD1) onto which is grafted at least one biological ligand such as another immune checkpoint inhibitor.

This family is based on an international application WO2020/127369 filed on December 17, 2019 that claims the priority of a European application filed on December 21, 2018 under number EP 18 306799.0. The theoretical expiration date of this family is December 2039.

This family includes the following patent applications:

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
CA3122899	Canada	CA3122899		Pending	December 2039
BR112021012027	Brazil	BR112021012027		Pending	December 2039
AU2019406453	Australia	AU2019406453		Pending	December 2039
IL284052	Israel	IL284052		Pending	December 2039
KR10-2021-7022787	South Korea	KR10-2021-0107058		Pending	December 2039
CN201980092706.6	China	CN113573782		Pending	December 2039
EP19818165.3	Europe	EP3897845		Pending	December 2039
HK620220500713.6	Hong Kong	HK400608824A		Pending	December 2039
US17/414,968	USA	US20220025050		Pending	December 2039
IN202117031144	India	IN202117031144		Pending	December 2039
JP2021-536194	Japan	JP2022515223		Pending	December 2039

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

5.5.1.7.3 BiCKI IL7

The portfolio is being built with several families.

A first family relates to bifunctional composite antibodies comprising a first anti-PD1 antibody part, fused to a second interleukin 7 (IL7) part. IL7 is in native form or in mutated form with preferred IL7 mutants.

This family is based on an international application WO2020/127377 filed on December 17, 2019 that claims the priority of a European application filed on December 21, 2018 under number EP 18 306808.9 The theoretical expiration date of this family is December 2039.

This family includes the following patent applications:

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
TW 108147053	Taiwan	TW 20039572 A		Pending	December 2039
CA3123338	Canada	CA3123338		Pending	December 2039
BR112021012037.8	Brazil	BR112021012037		Pending	December 2039
AU2019407814	Australia	AU2019407814		Pending	December 2039
IL284002	Israel	IL284002		Pending	December 2039
KR10-2021-7022838	South Korea	KR20210108978		Pending	December 2039
EP19818167.9	Europe	EP3898677		Pending	December 2039
HK62022050714.4	Hong Kong	HK40060825A		Pending	December 2039
CN201980092752.6	China	CN113614109		Pending	December 2039
IN202117031145	India	IN202117031145		Pending	December 2039
JP2021-536209	Japan	JP2022514702		Pending	December 2039
US17/414,970	United States			Pending	December 2039

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

5.5.1.7.4 BiCKI SIRP

This family covers bifunctional compound antibodies comprising a first anti-PD1 antibody part, fused to a second SIRP part, in particular SIRP-alpha and SIRP-alpha variants.

This family is based on an international application WO2020/127373 filed on December 17, 2019 that claims the priority of a European application filed on December 21, 2018 under number EP 18 306810.5 The theoretical expiration date of this family is December 2039.

This family includes the following patent applications:

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
National/regional phases undertaken in Europe, United States, Australia, Brazil, Canada, Chile, China, Eurasia, Israel, India, Japan, South Korea, Mexico, New Zealand, Philippines, Singapore, and South Africa.					
CA3122914	Canada	CA3122914		Pending	December 2039
BR112021012040.8	Brazil	BR112021012040		Pending	December 2039
AU2019409805	Australia	AU2019409805		Pending	December 2039
IL283992	Israel	IL283992		Pending	December 2039
KR10-2021-7022853	South Korea	KR20210107062		Pending	December 2039
JP2021-536199	Japan	JP2022514698		Pending	December 2039
EP19818166.1	Europe	EP3898676		Pending	December 2039
HK62022051225.0	Hong Kong	HK40065033A		Pending	December 2039
CN201980092872.6	China	CN113574067		Pending	December 2039
SG11202106251U	Singapore	SG11202106251U		Pending	December 2039
US 17/414,971	United States	US 2022-0056135		Pending	December 2039

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

5.5.1.7.5 Mutated IL7

This family concerns variants of IL-7 and various forms of bifunctional antibodies including these variants of IL-7.

This family is based on an international application WO 2021/122866 filed on December 17, 2020 that claims the priority of a European application filed on December 17, 2019 under number EP19306671.9. The theoretical expiration date of this family is December 2040.

This family includes the following patent applications:

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
National/regional phases undertaken in ARIPO, Australia, Brazil, Canada, Chile, China, Colombia, Costa Rica, Eurasia, Europe, Hong King, Israel, India, Japan, South Korea, Mexico, Malaysia, New Zealand, Philippines, Peru, Saudi Arabia, Singapore, Ukraine, United States, Vietnam and South Africa.					
TW109144676	Taiwan	TW202136287		Pending	December 2040*
AU2020406083	Australia	AU2020406083		Pending	December 2040*
BR112022011945	Brazil	BR112022011945 -3 A2		Pending	December 2040*
CA3159555	Canada	CA3159555		Pending	December 2040*
CN202080088470.1	China	CN114829385A		Pending	December 2040*
EP20842208.9	Europe	EP4077364		Pending	December 2040*
IL293745	Israel	IL293745		Pending	December 2040*
IN202217038057	India	IN202217038057		Pending	December 2040*
KR10-2022-7024683	South Korea	KR10-2022-0114637		Pending	December 2040*

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

5.5.1.7.6 Mono Mono IL7 muted

This family concerns an antibody format including one single domain of link to PD1 and one single muted IL7.

This family is based on an international application WO 2022/129512 filed on December 17, 2021, which claims the priority of an international patent applications and two European patent applications, these applications had been delivered on December 17, 2020, on April 9, 2021, and on September 30, 2021, under numbers PCT/EP2020/086600, EP21305462.0 and EP21200350.3 respectively. The national/regional phases are to be engaged in June 2023. The theorical expiration date of this family is April 2041.

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
PCT/EP2021/086471	International application	WO2022/129512			December 2041*

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

5.5.1.7.7 Mono Mono cytokine

This patent concerns an antibody format including one signe domain of link to a specific antigen of immune cells and a single cytokine.

This family is based on a single international application WO 2022/214653 filed on April 8, 2022 which claims the priority of two European patent applications filed on April 9, 2021 under number EP21305462.0 and on September 20, 2021 under number EP21200350.3. The national/regional phases are to be engaged in October 2023. The expiration theorical date of this family is April 2042*.

Filing no.	Country	Publication no.	Patent no.		Delivered on	Theoretical expiration date*
PCT/EP2022/059414	International application	WO2022/214653				April 2042*

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

5.5.1.7.8 Mono Mono SIRP

This family concerns an antibody format including one single domain of link to a specific antigen of immune cells and a single immuno-activating molecule as SIRPa or SIRPg.

This family is based on an international application WO 2022/214652 filed on April 8, 2021, which claims the priority of a European patent application filed on April 9, 2021 under number EP21305463.8. The national/regional phases are to be engaged in October 2023. The expiration theorical date is April 2042*.

Filing no.	Country	Publication no.	Patent no.		Delivered on
PCT/EP2022/059411	International application	WO2022/214652			April 2042*

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

5.5.1.8 New antibodies targeting Chem R23, in particular intended to treat inflammatory diseases

These antibodies target the mechanism of inflammation resolution, with action on the CMKLR1 (ChemR23) receptor of myeloid cells. Two patent families relate to these antibodies.

Family 1

The first family of patents covers anti-ChemR23 antibodies.

This family is based on an international application WO2019/193029 filed on April 3, 2019 that claims the priority of a European application filed on April 3, 2018 under number EP 18 305 395.8. The theoretical expiration date of this family is April 2039.

This family includes the following patent applications:

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
AU 2019247068	Australia	AU2019247068		Pending	April 2039
CN20198037001.4	China	CN112218894		Pending	April 2039
CA 3102607	Canada	CA 3102607		Pending	April 2039
EP 19715092.3	Europe	EP3774899		Pending	April 2039
IL 277701	Israel	IL277701		Pending	April 2039
IN 202017043525	India	IN202017043525		Pending	April 2039
KR 10-2020-7031788	South Korea	KR20210006359		Pending	April 2039
JP 2020-554298	Japan	JP2021520210		Pending	April 2039
BR11 2020 020118.9	Brazil	BR112020020118		Pending	April 2039
US 17/045,130	United States	US2021147558A		Pending	April 2039

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

Family 2

The second patent family covers improved anti-ChemR23 antibodies.

This family is based on an international application WO 2021069709 filed on October 9, 2020 claiming the priority of a European patent application filed on October 9, 2019 under number 19306322.9 and a European patent application filed on October 9, 2019 under number 19306323.7. The theoretical expiration date of this family is October 2040.

This family includes the following patent applications:

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
National/regional phases engaged in the following countries: Australia, Brazil, Canada, Chili, Colombia, China, Costa Rica, Algeria, Saudi Arabia, United Arab Emirates, Egypt, Europe, Eurasia, Hong Kong, India, Indonesia, Israel, South Korea, Japan, Malaysia, Mexico, New Zealand, ARIPO, OAPI, Peru, Philippines, Singapore, Thailand, Ukraine, United States, South Africa and Vietnam.					
19306323.7	Europe	EP3804754		Pending	October 2039
AU2020365034	Australia	AU2020365034		Pending	October 2040
BR112022006760-7	Brazil	BR112022006760		Pending	October 2040
CA3156835	Canada	CA3156835		Pending	October 2040
CN202080084501.6	China	CN114786722		Pending	October 2040
EA202291105	Eurasia	EA202291105		Pending	October 2040
EP20789120.1	Europe	EP4041302		Pending	October 2040
IL292029	Israel	IL292029		Pending	October 2040
202217021274	India			Pending	October 2040
KR10-2022-7015533	South Korea	KR10-2022-0087466		Pending	October 2040
JP 2022-521452	Japan			Pending	October 2040
US 17/767606	United States			Pending	October 2040

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

5.5.1.9 New antibodies targeting SIRP gamma

Two patent families relate to antibodies directed against SIRP gamma and their therapeutic uses.

Family 1

A first family concerns the use of antibodies directed against SIRP gamma for treatment of various diseases.

This family is based on an international application WO 2018149938 filed on February 15, 2018 that claims the priority of a European application filed on February 17, 2017 under number EP 17305184.8. The theoretical expiration date of this family is February 2038.

This family includes the following patent applications:

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
AU 2018221774	Australia	AU2018221774		Pending	February 2038
BR 11 2019 016356 5	Brazil	BR112019016356		Pending	February 2038
CA 3051318	Canada	CA3051318		Pending	February 2038
CN 201880012199.6	China	CN 110300764		Pending	February 2038
EP 18707306.9	Europe	EP 3583128		Pending	February 2038
HK 62020002193.4	Hong Kong	HK 40012839		Pending	February 2038
IL 268731	Israel	IL268731		Pending	February 2038
IN 201917030178	India	IN 201917030178		Pending	February 2038
JP 2019-544888	Japan	JP2020510643	JP7179743	Pending	February 2038
JP 2022-182731	Japan			Pending	February 2038
KR 10-2019-7027076	South Korea	KR20190117670		Pending	February 2038
US 17/571,499	United States	US20220242951		Pending	February 2038

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

Family 2

Family 2: a second family concerns the use of antibodies directed against SIRP gamma (and in particular the epitope of SIRP gamma; interaction with CD47), for the treatment of various diseases.

This family is based on an international application WO2020/039049 filed on August 22, 2019, that claims the priority of a European application filed on August 22, 2018 under number EP 18 306 131.6. The theoretical expiration date of this family is August 2039.

This family includes the following patent applications:

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
JP 2021-509919	Japan	JP2021534204		Pending	August 2039
EP19755925.5	Europe	EP 3 841 122		Pending	August 2039
US 17/270,028	USA			Pending	August 2039
CA3110139	Canada	CA3110139		Pending	August 2039

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

5.5.1.10 New antibodies targeting CLEC-1

These products target C-type lectin 1, designated CLEC-1 for treatment of various diseases. They involve several families of patents.

Family 1

The first family, co-held with the INSERM and the University of Nantes, covers the use of antibodies directed against CLEC-1 for the treatment of various diseases.

This family is based on an international application WO2018/073440 filed on October 20, 2017, and claims the priority of two European applications filed under numbers EP16306381.1 and EP17305988.2.

This family includes the following patent applications:

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
AU 2017345286	Australia	AU2017345286		Pending	October 2037
BR1120190079246	Brazil	BR112019007924		Pending	October 2037
CA3039348	Canada	CA3039348		Pending	October 2037
CN 201780065072.6	China	CN 110291102		Pending	October 2037
EP 17797066.2	Europe	EP3529262	EP3529262	7/21/2021	October 2037
Valid in : Albania, Austria, Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, Cyprus (Greek part), Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lichtenstein, Lithuania, Luxembourg, Macedonia, Malta, Moldova, Monaco, Montenegro, Morocco, the Netherlands, Norway, Poland, Portugal, Romania, San Marino, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey, the United Kingdom.					
HK 19130492.2	Hong Kong	HK40007035	HK40007035	11/28/2021	October 2037
EP 21178847.6	Europe	EP 3950709		Pending	October 2037
IL 266111	Israel	IL266111	IL266111	12/02/2022	October 2037
IN 201917014926	India	IN201917014926		Pending	October 2037
JP 2019-521034	Japan	JP2020503252	JP7032396	02/282022	October 2037
JP 2022-25697	Japan			Pending	October 2037
KR 10-2019-7014209	South Korea	KR20190068605		Pending	October 2037

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

Family 2

This family relates to chimeric anti-CLEC1 antibodies.

This family is based on an international application WO 2021/110990 filed on December 4, 2020 that claims the priority of a European application filed on December 5, 2019 under number EP 19306583.6. The theoretical expiration date of this family is December 2040.

This family includes the following patent applications:

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
CA3159155	Canada	CA3159155		Pending	December 2040
CN202080095475.7	China	CN115151309		Pending	December 2040
EP20819741.8	Europe	EP4069372		Pending	December 2040
JP2022-533579	Japan			Pending	December 2040
US17/779428	United States	US-2022-0281983		Pending	December 2040

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

Family 3

A third family, co-hold with INSERM and Nantes University, concerns humanized antibodies targeting CLEC-1 in the treatment of various diseases.

This family is based on an international application WO2022/258714 filed on June 8, 2022, which claims the priority of the European patent application filed under number EP 21305777.1. The national/regional phases are to be engaged in December 2023. The theorical expiration date of this family is June 2042.

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
PCT/EP2022/065600	International application	WO2022/258714			July 2042

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

5.5.1.11 Biomarkers of anti-TNF alpha treatment

This family concerns biomarkers used to evaluate the response to therapeutic treatment with anti-TNF alpha agents.

This family is held as co-property with the Nantes CHU (University Hospital).

This family is based on an international application WO2019025624 filed on August 3, 2018, that claims the priority of a European patent application filed on August 3, 2017 under number EP17306039.3. The theorical expiration date of this family is June 2042.

This family includes the following patent applications:

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
EP 18746241.1	Europe	EP3662081		Pending	August 2038
US 16/636,162	United States	US-2020-0181706		Pending	August 2038

5.5.1.12 COVEPIT

Two families concern a vaccine against SARS-CoV-2.

Family 1

This family is based on an international application WO 2021/228853 filed on May 11, 2021, claiming the priority of a European patent application filed on May 11, 2020, under number EP20305469.7, a European patent application filed on August 14, 2020 under number EP20305930.8 and a European patent application filed on January 20, 2021 under number EP21305071.9. The theoretical expiration date of this family is May 2041.

Filing no.	Country	Publication no.	Patent no.	Delivered on	Theoretical expiration date*
PCT/EP2021/062481	International application	WO2021/228853			May 2041
EP21724179.3	Europe	EP4149531		Pending	May 2041
17/924,371	United States			Pending	May 2041

(*) The expiration date may be extended in some countries up to five years (via supplementary protection certificates) if marketing authorizations have been obtained in the countries considered, or as part of certain procedures specific to these countries (such as "patent term extension/adjustment" in the U.S. – the additional duration is indicated when granted and known).

5.5.1.13 Comment

The strategy followed by OSE Immunotherapeutics concerning patents is to ensure the existence and protect the intellectual property rights that are the foundation of its drug research programs, and, as necessary, to take legal recourse against any harm to its intellectual property rights.

Family 2

This patent is based on an international application WO2022/268916 filed on June 23, 2022 which claims the priority of a European patent application filed under number EP 21 305866.2. The expiration theorical date of this family is June 2042. The national/regional phases are to be engaged in December 2023.

5.5.2 Brands and domain names

At the date of this Universal Registration Document, the Company has protected the trademarks "OSE PHARMA", "OSE IMMUNOTHERAPEUTICS", "MEMOPI", "TEDOPI" by registering them in France, then they were registered in countries where it was considered useful, including in the European Union (European Union brand), the United States, China or South Korea.

The names "OSE-172" and "OSE-127" were chosen by OSE Immunotherapeutics to designate its technologies. In most countries, including the European Union and the United States, an initial approval of the commercial name of a pharmaceutical product by the supervisory authorities is mandatory, and these names may therefore be modified.

The trademark "Atalante-1" designating the phase 3 clinical trial of Tedopi® was filed in January 2016 and registered in May 2016 in France. It was extended to the United States in July 2016 and has been registered there since June 2017.

The trademark "OSE IMMUNOTHERAPEUTICS" was filed in February 2016 and registered in June 2016 in France.

The Chinese trademark OSE No. 22180371 was filed in December 2016 and registered on April 7, 2019.

The trademarks "BiCKI", "B-Cool", "B-TIC" and "BiCKAN" were filed in May 2018 in France and the European Union and filed in September 2018 in the United States. The BiCKI, B-TIC and BiCKAN brands were registered in October 2018 in France and in the European Union.

The trademark "B-COOL" was contested in France and the European Union. In France, this trademark was registered in February 2019 only for certain services. In the European Union, this trademark was registered in December 2019 for certain products and services. In the United States, the trademark “B-COOL” was registered in June 2021 for certain products and services.

In the United States, the BiCKI brand was registered on September 10, 2019. The B-TIC and BiCKAN brands were registered on June 23, 2020.

The Company reserved various domain names, including the following: osepharma.com, osepharma.fr, effimune.com, ose-immuno.com, oseimmunotherapeutics.com, oseimmunotherapeutics.fr, oseimmuno.com, oseimmuno.fr, ose-immuno.com and ose-immuno.fr.

5.6 Competitive position

5.6.1 Non-small cell lung cancer treatments

Despite the new treatments, the five-year survival rates are around 7% for patients with metastatic cancer (Cancer.Net® / ASCO, November 2021).

For non-small cell lung cancer, a classification known as “TMN” is used which takes into consideration the appearance of the lung tumor, any presence of tumor cells in the Nodes and any Metastasis. Depending on the result of this classification, non-small cell lung cancers are referred to as “stage 0, Ia, Ib, IIa, IIb, IIIa, IIIb or IV”, in increasing order of severity.

Small cell lung cancers are classed as being “localized” Ia to IIIa and “diffuse” IIIb or “metastatic” IV.

Current treatments vary depending on the stage and the various treatment lines:

The treatment of NSCLC-type lung cancers varies according to their type and stage of development. Histological types are most often adenocarcinomas (40.8%), squamous cell carcinomas (21.4%), large-cell carcinomas (3%) and other forms of carcinomas (20.4%) (Howlader N et al., 2013):

- Stage I: surgery consisting of removing the part of the lung that is affected or the entire lung. If surgery is not possible, radiotherapy is given
- Stage Ib: surgery possibly followed by chemotherapy. If surgery is not possible, radiotherapy is given.
- Stage IIa and IIb: surgery followed by chemotherapy. If surgery is not possible, radiotherapy is given.

- Stage IIIa: chemotherapy, possibly combined with surgery or radiotherapy.
- Stage IIIb: chemotherapy combined with radiotherapy, surgery is highly unlikely.
- Stage IV: chemotherapy which may be combined with other types of treatment ("targeted therapy" when a gene is expressed, for example EGFR, with a particular mutation, tyrosine kinase inhibitors act on the gene mutations observed).

Two-thirds of non-small cell bronchial cancers are diagnosed at the metastatic stage.

Three types of existing treatments are mainly used to treat bronchial cancers: surgery, radiotherapy and medical treatments (chemotherapies and targeted therapies). Immunotherapy is becoming a clinical reality with checkpoint inhibitors proving to be more effective than chemotherapy in some cancer subtypes and considered a revolutionary therapeutic breakthrough for the first time at ASCO 2015.

Generally speaking, lung cancer chemotherapy consists of intravenous infusion sessions (cures) every one to four weeks depending on the drugs used. The treatment lasts between three and four months, sometimes longer. The choice of drugs used depends on the tumor's characteristics. Chemotherapy is, therefore, the mainstay treatment for the majority of patients. Other factors to be considered when selecting treatments are general health, age and medical history. The main products are cisplatin, carboplatin, paclitaxel (Taxol®), albumin bound paclitaxel (nab-paclitaxel, Abraxane®), docetaxel (Taxotere®), gemcitabine (Gemzar®), vinorelbine (Navelbine®), irinotecan (Camptosar®), etoposide (VP-16®), vinblastine and pemetrexed (Alimta®).

Chemotherapy-related treatments include anti-angiogenic-type therapies that act on the blood vessels. Vargatef® (nintedanib, Boehringer Ingelheim) combined with chemotherapy (docetaxel) is an anti-angiogenic therapy, i.e. blocking angiokinase receptors such as the VEGF, FGF or PDGF receptors, expressed on the vessels nourishing the tumor. This product was registered at the end of November 2014 in Europe in adenocarcinoma-type NSCLC cancer after first-line therapy (EPAR - EMA). Likewise, ramucirumab, another anti-angiogenic (Cyramza®, acting on a VEGF R2 receptor, from Eli Lilly) was registered in December 2014 in lung cancer (NSCLC) after first-line therapy failed. Median survival time was improved in the group combining ramucirumab with docetaxel versus docetaxel (10.5 months vs. 9.1 months); hemorrhagic-type side-effects have been described.

An important deciding factor is the search for a particular molecular anomaly for non-squamous cell carcinomas: finding out if there is a molecular anomaly on the tumor cell enables patients presenting with this anomaly to receive targeted therapy. Currently, the existence of an EGFR gene mutation (approximately 10 to 15% of the population) impacts the treatment from the first-line therapy with the option to treat with EGFR tyrosine kinase inhibitors like erlotinib (Tarceva®), gefitinib (Iressa®), afatinib (Gilotrif®), osimertinib (Tagrisso®) or dacomitinib (Vizimpro®). They inhibit an enzyme, vital to many cell membrane receptors. In addition, there is necitumumab (Portrazza®) which targets EGFR in squamous cell cancers. They are prescribed in lung cancers where the EGFR gene is mutated (EGFR+); their adverse effects include diarrhea and skin disorders.

Another targeted therapy is indicated in the event of the molecular rearrangement of the ALK gene (approximately 4% of the population) which enables treatment with a product acting on ALK from second-line therapy onwards. As a result, crizotinib (Xalkori® Pfizer), ceritinib (Zykadia® Novartis), alectinib (Alecensa®), brigatinib (Alunbrig®) and lorlatinib (Lorbrena®) were registered. In addition, Zykadia® was approved for patients with an ALK gene mutation after treatment with Xalkori® has failed, in the United States and Europe, in May 2015. In practice, this targeted therapeutic approach only affects the minority of patients with identified mutations, often those with little exposure to smoking, and the treatment frequently fails.

At the diffuse or metastatic stage, platinum-based first line therapies are administered: this is called platinum-based combination chemotherapy. Those who respond or who have a stable disease may receive a first-line maintenance therapy such as, for example, pemetrexed for particular non-squamous cell histological-type cancers and docetaxel for other patients.

Keytruda® was the first checkpoint inhibitor registered as a first-line therapy after its superiority over chemotherapy was established for patients strongly expressing the PD-L1 marker (with approximately 25% of NSCLC patients at the invasive or metastatic stage expressing the PD-L1 marker at > 50% at tumor level). It was also registered as a first-line therapy in combination with chemotherapy for all patient types, irrespective of their PD-L1 marker level. In 2020, it was registered in combination with Opdivo® as a first-line therapy in metastatic NSCLC with PD-L1 expression ≥ 1%. In January 2023, the Food & Drug Administration approved Keytruda® as adjuvant treatment following surgical resection and platinum-based chemotherapy for patients with stage IB (T2a ≥4 centimeters), II, or IIIA Non-Small Cell Lung Cancer (NSCLC).

The Yervoy® + Opdivo® combination was registered in 2020 as a first-line therapy for NSCLC whose PD-L1 expression is ≥ 1%.

Tecentriq® has now been registered as a first-line therapy, in combination with Avastin® and chemotherapy. In 2020, it obtained registration as a first-line therapy for metastatic NSCLC in patients with high PD-L1 expression (TC ≥ 50% or CI ≥ 10%), without tumor aberration of the AGFR or ALK gene. A second-line therapy will be offered in the event of intolerance or progression of the disease (if no EGFR or ALK-type mutation or molecular anomaly can be accessed by a targeted therapy).

In the same year, Tecentriq® was registered as an adjuvant treatment after surgery and platinum chemotherapy in stage II-IIIA NSCLC, in patients with PD-L1 expression ≥ 1%.

Libtayo® (cemiplimab) (anti-PD1, Regeneron) was registered in 2021 in first-line treatment of lung cancer in metastatic patients with strong tumor expression of PD-L1 score ≥50%.

In November 2022, this product was also registered in combination with a platinum-based chemotherapy in advanced or metastatic lung cancer, in patients without identified genetic abnormality for whom a targeted therapy is available (genes EGFR ALK ROS-1).

5.6.2 Existing second-line therapies for advanced lung cancer and choice of comparator for Phase 3

Treatments registered as second-line therapies (after a first-line treatment fails) are checkpoint inhibitors such as pembrolizumab and nivolumab, and two chemotherapies: docetaxel and pemetrexed (+ erlotinib, a targeted therapy for patients with a particular mutation). The median survival rate is between five and eight months for chemotherapy and the one-year survival rate is 33% (Hanna N 2004; Shepherd FA 2005; Ciuleanu T 2012; Garassino MC 2013). Docetaxel and pemetrexed are considered to be benchmark second-line therapies and are used as third-line treatments if checkpoint inhibitors have failed. They were the comparators used in the Phase 3 trial of Tedopi®.

Four checkpoint inhibitor-type treatments producing a non-specific activation of cytotoxic T lymphocytes by releasing the brakes of immunity are now registered as second-line therapies: nivolumab (Opdivo® BMS) registered in squamous cell cancers and non-squamous cell cancers in progression as a second-line therapy, pembrolizumab (Keytruda® Merck) registered as a second-line therapy in patients expressing the PD1 ligand known as PD-L1 (approximately 20% of patients expressing the PD-L1 marker) whatever the histology, atezolizumab (Tecentriq®) registered in squamous cell and non-squamous cell cancers in patients expressing PD-L1 and durvalumab (Imfinzi®) registered as a second-line therapy in inoperable tumors in patients whose cancer has progressed after chemotherapy and radiotherapy, targeting the PD1/PD-L1 signaling pathway. The survival rate for these new checkpoint inhibitor therapies acting on the PD1/PD-L1 axis is three to four months longer than with chemotherapy and this survival rate is observed as a median between nine and thirteen months for the four checkpoint inhibitor therapies.

More recently, checkpoint inhibitors have been compared to chemotherapy. Opdivo® (nivolumab, registered in 2015 as a second-line treatment for squamous cell NSCLC cancers), obtained a median survival of 9 months (versus a median of 6 months for docetaxel in this subgroup of patients who have a particular histology). In 2019, an analysis, presented to the AACR (American Association for Cancer Research) conference, on pooled data from four trials showed that 14% of patients treated with Opdivo® were still alive after four years. Data from two Phase 3 clinical trials showed an overall survival of 14% in patients treated with Opdivo® versus 5% in patients treated with docetaxel (CT195 abstract: Long-term survival outcomes with nivolumab (NIVO) in patients with previously treated advanced non-small cell lung cancer (NSCLC): Impact of early disease control and response; Julie Brahmer et al., DOI: 10.1158/1538-7445.AM2019-CT195 Published July 2019).

The other checkpoint inhibitors recorded since 2015 also published a median survival of around nine to thirteen months in patients with squamous or non-squamous cell cancer as a second-line treatment (nivolumab: Brahmer J. and al NEJM 2015; Paz-Ares L. et al., J Clin Oncol 33, 2015; atezolizumab: Spira A et al. J Clin Oncol 33, 2015 - abs 801.0; Keytruda®, pembrolizumab: Garon et al. NEJM 2016 in PD-L1 positive patients in second line NSCLC). Tecentriq® (atezolizumab), within the context of the annual European Society of Medical Oncology conference (ESMO 2016) showed that median survival of patients under atezolizumab was 13.8 months, i.e. 4.2 months longer than patients receiving chemotherapy with docetaxel (overall survival rate of 13.8 months versus 9.6 months) irrespective of their PD-L1 marker expression rates.

(A Rittmeyer et al., the Lancet 2016; Atezolizumab versus docetaxel in patients with previously treated non-small-cell lung cancer (OAK): a Phase 3, open-label, multicenter randomized controlled trial).

Third-line treatments are offered but are essentially palliative.

In short, there is still a great need for active and well-tolerated treatments for advanced-stage NSCLC cancers, in particular, after checkpoint inhibitors have failed.

With final positive Phase 3 results (Atalante-1 trial), Tedopi® is positioned in T-specific cytotoxic immunotherapy, in HLA-A2 positive patients with non-small cell lung cancer at stage IIIB invasive and non resectable or metastatic stage IV after tumor progression with PD1 or PD-L1 checkpoint inhibitor.

Final positive results of the Atalante-1 trial were presented in oral session at the 2021 ESMO congress: "*Activity of OSE-2101 in HLA-A2+ non-small cell lung cancer (NSCLC) patients after failure to immune checkpoint inhibitors (IO): Final results of Phase 3 Atalante -1 randomised trial"* and were completed with results at the 2022 ASCO and ESMO annual meetings.

A total of 219 patients were included in the Atalante-1 trial. Of these patients, 183 (84%) received sequential immunotherapy/chemotherapy of which 118 (54%) met the definition of "population of interest" and otherwise had similar baseline characteristics to the overall Atalante 1 population.

The phase 3 clinical trial results of Atalante-1 have shown significant survival benefit of Tedopi® versus a standard chemotherapy treatment (docetaxel or permetrexed) in positive HLA-A2 patients with non-smalll cell lung cancer with secondary resistance to immune checkpoint inhibitors. The patients included in this trial had failed second-line checkpoint inhibitor treatments and represent a hard-to-treat patient population with high medical need.

Based on these results and following the positive recommendations from the FDA "Type C" meeting and to the scientific advice from the EMA, OSE Immunotherapeutics is preparing a new confirmatory Phase 3 trial to support the regulatory registration of Tedopi® in second line. This clinical trial will evaluate Tedopi® versus standard of care in second line treatment in HLA-A2 positive patients with advanced NSCLC.

In addition to non-small cell lung cancer, Atalante-1 is pioneering a possible new therapeutic vaccine strategy that, by activating T lymphocytes, would make it possible to optimize treatment by checkpoint inhibitor or chemotherapy.

THERAPEUTIC COMBINATIONS WITH CHECKPOINT INHIBITORS ARE NOW A VAST FIELD OF STUDY

Immuno-oncology products under development according to their mechanisms of action

Immune defenses against cancer

When the immune system recognizes tumor cells as foreign bodies, it triggers an immune response involving a series of cells (lymphocytes and antigen-presenting dendritic cells) and specialized proteins (antibodies, cytokines). The coordinated action of these different elements should end in the destruction of the tumor cells, and this is what happens in cancer immunosurveillance.

This response is characterized by two levels of defense: the first level is non-specific; it is innate immunity; the second level is called specific or adaptive immunity. This defense system can be overridden. In fact, some tumor cells present few characteristics that betray their true nature; they are neither recognized, nor attacked by the immune system. They present tumor antigens, but these are also present on other healthy organs and the immune reaction will not be triggered against these "self"-antigens. They will not be recognized as being alien. Other tumor cells may also use strategies to escape detection, for example, by multiplying very rapidly and overwhelming the immune system's reaction capacity. Oncogenes (tumor genes) are expressed at the surface of the tumor by tumor antigens (macromolecules or proteins). They themselves can directly inhibit the normal functioning of the immune system by deregulating it, thereby blocking immunosurveillance.

NON-SPECIFIC IMMUNOTHERAPY: NON-SPECIFIC T CELL ACTION CHECKPOINT INHIBITORS

Immune checkpoints regulate the breadth of the T-lymphocyte response and are key to avoiding auto-immunity. However, they also limit the robustness and duration of the anti-tumor immune responses. The molecules that play a role in regulating these checkpoints are currently in clinical development in many cancers. They include molecules regulating T-cell activity: CTLA-4, PD1/ PD1-L1, TIM 3 and LAG-3. These molecules can be blocked by monoclonal antibodies (MAb) which are capable of releasing the brakes on these molecules from T lymphocytes, not only preventing them from attacking tumors, but also from attacking other self-cells. Since 2011, this non-specific approach has led to a number of checkpoint inhibitors being marketed (see "Competition and immuno-oncology products" table).

THERAPEUTIC COMBINATIONS WITH CHECKPOINT INHIBITORS

The research has moved into a completely new phase with the search for better combinations for each patient that are more efficient and less toxic. The combination of a specific T-cell therapy and a non-specific therapy is logical and holds great therapeutic promise. These combinations are very interesting. (Pardoll D, Nature Reviews Drug Discovery, 12, 489-492, 2013).

Other treatments targeting cells in the tumor micro-environment or new, second-generation checkpoint inhibitors are expected in this field as a result of interesting tumor responses observed in 20% of patients on average in patients at the metastatic stage. Time without progression and survival rate are observed, but still over a limited period, when these products are used on their own. Auto-immune reactions are observed for around 10% of patients treated. Primary or secondary resistance was described for these products used alone. All these reasons encouraged researchers and clinicians to explore new therapeutic combinations.

Keytruda® (Merck & Co) a checkpoint inhibitor acting on PD1, registered in melanoma, advanced lung cancer (second- and first-line therapy in combination with pemetrexed and carboplatin), metastatic lung cancer (in first-line therapy in combination with pemetrexed and carboplatin, whatever the PD-L1 expression), as first-line treatment in metastatic non-small cell lung cancer whose PD1 expression is ≥ 1% (in combination with Opdivo®), bladder cancer (urothelial carcinoma), squamous cell head and neck cancer, and advanced gastroesophageal junction/stomach/colorectal cancer, Hodgkin's Lymphoma, large B cell lymphoma, uterine cancer, hepatocellular carcinoma, Merkel cell carcinoma, renal cancer, endometrial cancer, advanced renal cancer, squamous skin carcinoma and triple negative breast cancer.

It is associated in clinical development, for example, with many other therapies such as:

Ramucirumab, an Anti-VEGF-2 monoclonal antibody (MAb) studied in multiple tumors (Eli Lilly); Epacadostat IDO1 inhibitor, in solid tumors of the NSCLC type (Incyte) with negative results in 2018; MK-4166, an Anti-GITR MAb in solid tumors (Merck); Ipilimumab, an Anti-CTLA4 Mab in many cancers (BMS).

Opdivo® (Bristol-Myers Squibb), a checkpoint inhibitor acting on PD1 recorded in melanoma, lung cancer (squamous cell cancer), metastatic kidney cancer, recurrent or metastatic head and neck cancer, relapsed Hodgkin's lymphoma to a bone marrow transplant, metastatic bladder cancer, metastatic colorectal cancer and hepatocellular carcinoma, small cell lung cancer, squamous esophageal carcinoma. It is associated in clinical development, for example, with many other therapies such as:

ALT-803 IL-15 superagonist / IL-15Rα-Fc, fusion protein in NSCLC lung cancer (Altor BioScience); Urelumab Anti-CD137 MAb in solid tumors; Ipilimumab Anti-CTLA-4 MAb in many cancers (Bristol-Myers Squibb; Lirilumab Anti-KIR MAb in multiple myelomas, lymphomas and solid tumors (Bristol-Myers Squibb / Innate); Epacadostat IDO1 inhibitor in multiple tumors (Incyte).

THERE ARE ALSO MANY CLINICAL COMBINATIONS OF CHECKPOINTS WITH THERAPEUTIC VACCINES

Keytruda® — Merck & Co (PD1 MAb) was studied in combination, notably:

With ADXS-PSA, a therapeutic vaccine against cancer targeting a prostate tumor antigen (PSA), in resistant prostate cancer (Advaxis); (Phase *1/2 results in 2020*: overall *median survival rate of 16.4 months with ADXS-PSA versus 11 months with standard treatment*); with G100, a therapeutic vaccine in non-Hodgkin's lymphoma (Immune Design); with BCG in bladder cancer (Merck); with a viral vaccine expressing p53, MVA, a vaccine virus expressing this target for solid tumors (NIH); with autogene cevumeran, a personalized therapeutic vaccine developed by BioNtech in first line melanoma; withc mRNA-5671, a therapeutic vaccine targeting KRAS mutations, developed by Moderna Therapeutics.

Opdivo® — Bristol-Myers Squibb (PD1 mAb) was studied in combination, notably:

with Viagenpumatucel, a cell-based therapeutic vaccine (Heat Biologics) in non-small cell lung cancer; with ISA101, a therapeutic vaccine against the HPV virus in solid tumors (ISA Pharmaceuticals); with GVAX, a therapeutic vaccine against pancreatic cancer (Pancreatic cancer Sidney Kimmel Cancer Center).

Personalized Off the shelf	Company	Product Name	Platform	Indication	Stage	Combo	NCT
	OSE Immuno	Tedopi®	Peptide-based	NSCLC	3	n.a.	NCT02654587
Off-the-shelf	Northwest	DCVax-L	Dendritic-based	Glioblastoma	3	n.a.	NCT00045968
	UbiVac	DPV-001		NSCLC	2	n.a.	NCT02234921
	BioNTech	FixVac (BNT113)	mRNA	HPV16+ H&N cancer	2	n.a.	NCT03418480
		FixVac (BNT111)		Advanced Melanoma	2	n.a.	NCT02410733
	NuGenerex	AE37	Peptide-based	Breast Cancer	2	Pembrolizumab	NCT04024800
	Ultimovacs	UV1		Melanoma	2	n.a.	NCT04382664
				Melanoma	2	n.a.	NCT03538314
				Melanoma	2	n.a.	NCT02275416

			NSCLC	2	n.a.	NCT01789099
			Mesothelioma	2	Nivolumab	NCT04300244
			HNSCC	2	Pembrolizumab	NCT05075122
	Thaio Pharma	TAS0313	Urothelial Carcinoma	2	Pembrolizumab	JapicCTI-183824
	Vaccitech	VTP800/850	Prostate cancer	2	Nivolumab	NCT03815942
	Advaxis	ADXS-503	NSCLC	1/2	Pembrolizumab	NCT03847519
	Gritstone Bio	Slate	KRASmut-driven tumor types	1/2	Nivolumab + Ipilumab	NCT03953235
	Aston Sci	AST-301	TNBC	1	Pembrolizumab	NCT05163223
	Innovio	INO-5401	glioblastoma	1	Cemiplimab	NCT03491683
	BioNTech	FixVac (BNT112)	Prostate	1	n.a.	NCT04382898
		FixVac (BNT116)	NSCLC 2L	1	Cemiplimab	NCT05142189
	Moderna	mRNA-5671	KRAS mutant tumors	1	Pembrolizumab	NCT03948763
	Aston Sci	AST-021p	Solid tumors	1	n.a.	NCT04864418
	Ultimovacs	UV1	Prostate	1	n.a.	NCT04701021
	OncoPep	PVX-410	MM	1	Pembrolizumab / Atezolumab	NCT02886065
	Nouscom	NOUS-209	dMMR/MSI tumours	1	Pembrolizumab	NCT04041310
	Vaccitech	VTP-600	NSCLC	1	Pembrolizumab	NCT04908111
	Bavarian Nordic	TAEK-VAK	HER2 cancers	1	Traztuzumab	NCT04246671

	Viral/bacterial vector	
	DNA-based	
	mRNA	
	Peptide-based	
	Viral/bacterial vector	

SPECIFIC IMMUNOTHERAPY: COOPERATION BETWEEN CELLS IS NECESSARY

The response may be humoral (antibodies) or cellular (cytotoxic T).

The adaptive immunity acquired is specific and endowed with memory. This specific characteristic is the result of an activation process, during which certain lymphocytes learn to recognize tumor antigens via their epitopes.

T lymphocytes ensure a specific cellular response. Cooperation between lymphocytes is necessary to trigger an immune response. A distinction is made between T8 lymphocytes (identified by a T-CD8 marker), activated into cytotoxic lymphocytes which will directly attack tumor cells, and T4 cells (T-CD4 marker); auxiliary T lymphocytes mainly function to stimulate/regulate the immune response. Initially naive (i.e. not informed), these cells are educated by antigen-presenting cells which teach them to specifically recognize tumor antigens.

Cancer immunotherapy aims, therefore, to trigger or stimulate the body's own immune system to fight the disease. This type of immunotherapy combines B-cell antigen stimulation or T-cell antigen stimulation approaches. They involve a single antigen or a group of particular antigens, designed to activate the patient's immune system so that it recognizes and kills cells carrying the same antigen. The immunocompetence of a lymphocyte is dependent on the synthesis of a membrane receptor specifically capable of recognizing an epitope: the BCR receptor for B cells (this receptor is a membrane-bound immunoglobulin molecule), with the TCR receptor acting as an epitope recognition site for T cells. Unlike the B-lymphocyte receptor, the T-lymphocyte receptor only recognizes protein antigens which have been divided into epitopes. Proteins must be divided into peptides or epitopes which are then combined with MHC or major histocompatibility complex molecules. Cytotoxic cells recognize the antigen presented by an MHC class I molecule. The antigens presented are endogenous antigens produced by the cell.

Recognition is the first activation signal. A second co-stimulation signal permits the expression of the lymphocyte's cytotoxic power.

The therapeutic action of a specific immunotherapy is not direct. The product does not kill the tumor cell directly but activates the patient's immune system to recognize and kill the target cell. Adjuvants combine to generate an inflammatory reaction at the injection point and activate antigen-presenting cells leading to recognition of targeted antigens. Then, co-stimulation signals on the surface of antigen-presenting cells will be necessary to activate T lymphocytes.

ANTIGEN-SPECIFIC CANCER IMMUNOTHERAPIES

ASCI — antigen specific cancer immunotherapies

These antigen immunotherapies most often target a single tumor antigen such as, for example, MUC 1 or MAGE-3 or TERT.

They use a natural or recombinant macromolecule. They induce a cytotoxic T-cell response or a humoral B-cell response, producing antibodies against the tumor antigen.

They require the tumor antigen to have a detection threshold with definable detection limits.

Conclusion: Immunotherapy is currently center stage at US and European international oncology conferences and T-cell checkpoint inhibitors are now registered in several different cancers. Checkpoint inhibitor outcomes demonstrated a high level of effectiveness compared with chemotherapy in patients with advanced non-small cell lung cancer. Immunotherapies which are already indicated in lung cancer and melanoma seem to be just as effective in other types of cancer with cross-cutting action in different types of cancers. These treatments are not effective for all patients. The clinicians in question need to better identify patients likely to respond and better understand future combinations and the reasons for the failure of, or primary resistance to, these treatments.

5.6.3 Immuno-Inflammation

5.6.3.1 Targeted pathologies and treatments for autoimmune diseases

AUTOIMMUNE DISEASES

Autoimmune diseases are diseases in which the lesions observed are due to the activation of an immune response against part of the body.

Tolerance is a state of non-immune response to an antigen, specific to that antigen. It is an active phenomenon, caused by a prior contact with the antigen. Normally, an organism is tolerant of its own parts: it is self-tolerant or auto-tolerant. This latter involves T lymphocytes and, to a lesser degree, B lymphocytes.

Autoimmune diseases can be schematically divided into organ- or tissue-specific autoimmune diseases (such as autoimmune thyroiditis, myasthenia, pemphigus, etc.) and non-organ-specific autoimmune diseases also called systemic diseases (ASSIM D. Bernard, Marseille, autoimmune pathologies). Autoimmune diseases are of multifactorial origin (genetic, endocrinal and environmental factors).

Sexual hormones have an important role in the appearance of autoimmune diseases. This has been demonstrated in animal and human experimental models. The number of women affected is significantly greater. Genetic factors associated with autoimmune diseases initially concerned certain markers of major histocompatibility complex (MHC). For example, the DR1 and DR4 alleles are risk factors for rheumatoid arthritis, but in view of the number of genes involved, these are polygenic diseases.

The frequency of autoimmune diseases, even if some are very rare, makes this group of diseases a public health problem, the same as cardiovascular or cancerous diseases since these are chronic pathologies affecting young people with long treatment. Better understanding of their physiopathology allows considerable therapeutic progress of the most serious of them.

Table 1—Main Autoimmune Diseases

Non-organ-specific autoimmune diseases
- Systemic lupus erythematosus
- Scleroderma
- Dermatopolyositis
- Polymyositis
- Gougerot-Sjögren's dry syndrome
- Rheumatoid arthritis
- Antiphospholipid syndrome
Organ-specific autoimmune diseases
Endocrine glands
- Thyroiditis: Hashimoto's disease and Basedow's disease
- Addison's disease

	- Insulin-dependent diabetes
	- Polyendocrinopathies
Gastrointestinal tract	
	- Biermer's disease
	- Celiac disease
Kidney	
	- Goodpasture syndrome
Muscles and Nerves	
	- Myasthenia
	- Polyneuropathies
	- Guillain-Barré syndrome
	- Multiple sclerosis
Eyes	
	- Uveitis
	- Sympathetic ophthalmia
Skin	
	- Pemphigus, bullous pemphigoid, alopecia, vitiligo
Liver	
	- Autoimmune hepatitis
	- Primary biliary cirrhosis

According to D. Bernard, Marseille, autoimmune pathologies

EPIDEMIOLOGY

The epidemiology of autoimmune diseases shows great variations in frequency: autoimmune thyroid diseases are extremely frequent.

The prevalence of autoimmune diseases is greater among women, who are affected five to ten times more often than men.

Rheumatoid arthritis, Gougerot-Sjögren's syndrome and autoimmune diabetes (type 1, insulin dependent) are frequent systemic diseases. Their respective prevalence is from 1,000 to 4,000 patients affected per 100,000 inhabitants, 100 to 500 cases per 100,000 inhabitants and 200 to 300 per 100,000 inhabitants. The prevalence of celiac disease would be from 100 to 200 per 100,000 inhabitants. Systemic lupus erythematosus, scleroderma and dermatopolymyositis are much rarer diseases with respective prevalence of 15 to 50 per 100,000 inhabitants, 20 per 100,000 inhabitants and 5 to 10 cases per 100,000 inhabitants. In total, better diagnostic effectiveness, an increase in the life span of populations and a reduction of mortality for the most severe autoimmune diseases through better therapy give this group of pathologies an overall prevalence of 5% to 10%.

A CLINICAL EXAMPLE OF AUTOIMMUNE DISEASE (AID)

Chronic inflammatory bowel disease (CIBD)

Chronic inflammatory bowel disease (or CIBD) includes Crohn's disease and ulcerative colitis (UC). These are both characterized by inflammation of the wall of a portion of the digestive tract. In Crohn's disease, it may be located in the entire digestive system, from the mouth to the anus (most often in the intestine) whereas with ulcerative colitis is located in the rectum and the colon. These diseases progress by inflammatory flareups of extremely variable duration and frequency depending on the patient, alternating with remission phases. IBD is most often diagnosed in young people aged 20 to 30 but can occur at any age; 15% of cases are in children. Their frequency varies considerably from one country to another, but the most significant rates are found in the industrial countries and in particular in northwestern Europe and the United States. In France, approximately five new cases of Crohn's disease and as many cases of ulcerative colitis are diagnosed each year per 100,000 inhabitants.

During the flareups, the CIBDs are usually characterized by abdominal pain, frequent, sometimes bloody, diarrhea, or even attacks in the anal region (cracks, abscesses). The symptoms are often accompanied by fatigue, anorexia and fever, even non-intestinal manifestations, in the joints, skin, eyes and liver.

In approximately 20% of patients, the crises are severe. Their intensity may require hospitalization, suspension of food intake and infusion therapy for several days. Moreover, the progress of the disease may lead to narrowing of the affected intestinal segment and possibly occlusion or abscesses that could result in a fistula, which is a perforation and an abnormal path from the diseased intestine to another organ. These complications require surgical intervention. CIBDs are associated with increased risk of colorectal cancer, in particular when the lesions are present in the colon.

CURRENT TREATMENTS OF AUTOIMMUNE DISEASES

Treatment of autoimmune diseases has several objectives: to prevent disease flareups, to fight the progression of visceral attacks, to sustain employability and cure the disease while preventing the undesirable effects of treatments.

Immunological treatment of autoimmune diseases is based on three points: to eliminate pathogenic autoantibodies (plasmapheresis method), to modulate activation of lymphocytes and synthesis of cytokines (immunosuppressants such as corticosteroids, cyclosporin A, the molecules interfering with purine metabolism such as azathioprine (Imurel®) or mycophenolate mofetil (Cellcept®) and, in a more targeted fashion, to modify the immune response to make it non-pathogenic (principle of immunomodulation, for example by inhibiting the cytotoxic action of TNFα by anti-TNFα antibodies by blocking B lymphocytes by anti-CD20s).

The most commonly used therapies are the following:

CORTICOSTEROIDS

They have anti-inflammatory and immunosuppressive properties in strong doses, acting on the T lymphocytes, antibody production and the gene transcription of many cytokines. These are prednisone (Cortancyl®), prednisolone (Solupred®) or methylprednisolone (Solumedrol®) for intravenous administration. The corticosteroids exert their effect through intracytoplasmic receptors (glucocorticoid receptors). They inhibit synthesis of many proteins and transcription factors involved in the production of many cytokines.

IMMUNOSUPPRESSANTS

Cyclosporin A (Neoral®) CNI or calcineurin inhibitor. This substance, known as an antifungal, has shown excellent immunosuppressive properties. It works selectively and reversibly with respect to activated T lymphocytes, in particular CD4+ T lymphocytes. Cyclosporin A binds to intracytoplasmic receptors (cyclophilins, from the family of immunophilins) — the cyclosporin A/cyclophilin complex inhibits the activity of calcineurin that is a phosphatase that activates a transcription factor called NFATc. This results in the blocking of the gene transcription of interleukin 2 genes and other cytokine genes.

This molecule is very often used in preventing allogeneic graft rejection. It may be used in inflammatory myositis in cases of failure of corticosteroids, immunoglobins and methotrexate.

Azathioprine (Imurel®), mycophenolate mofetil (Cellcept®) and methotrexate (Methotrexate®):

These are immunosuppressive drugs with cytotoxic action acting as inhibitors of purine metabolism.

They also inhibit proliferation of T and B cells by blocking the DNA synthesis of the dividing molecules, formation of antibodies and glycosylation of adhesion molecules. These molecules are also toxic on hematopoietic cells.

Azathioprine (Imurel®) is inactive in vivo but deteriorates into active metabolites. Imurel® is indicated as a disease-modifying treatment for systemic lupus, or in some cases of Gougerot-Sjögren's syndrome or in some systemic vasculitides. It may be prescribed as a bridge of cyclophosphamide, as maintenance treatment. Its effectiveness is often delayed (approximately four weeks).

Mycophenolic acid (active metabolite of mycophenolate, mofetil-Cellcept®) has a more powerful immunosuppressant effect than azathioprine in preventing transplant rejection. It is used in systemic lupus (lupus nephritis).

Methotrexate is a tetrahydrofolate reductase inhibitor that blocks thymidylate synthesis, de novo purine synthesis and cell division. Methotrexate is indicated as a disease-modifying treatment for rheumatoid arthritis and inflammatory myositis. It becomes effective in one to two months. The decrease of certain bloodlines (dose-dependent cytopenia observed under methotrexate) is prevented by the administration of folic acid.

Cyclophosphamide (Endoxan®) is an alkylating agent forming covalent bonds with DNA leading to the death of dividing cells. It acts mainly on B lymphocytes (suppression of antibody production) and CD8+ T lymphocytes. It is indicated for treatment of some serious forms of systemic lupus and some systemic vasculitides. It quickly becomes effective by the second week.

Leflunomide (Arava®) is an immunosuppressant that inhibits de novo synthesis of pyrimidines by inhibiting dihydro-orotate dehydrogenase. It is indicated as a disease-modifying treatment for rheumatoid arthritis.

Rituximab (MabThera®) is an anti-CD20 monoclonal antibody, a membrane molecule of B lymphocyte. Its binding leads to destruction and rapid and prolonged decrease of B lymphocytes as well as their production of immunoglobulin. Rituximab is used in autoimmune hemolytic anemias, autoimmune thrombocytopenic purpura, serious refractory lupus, cryoglobulinemia and in some vasculitides. It is indicated in resistant rheumatoid arthritis with methotrexate.

IMMUNOMODULATORS

Intravenous immunoglobulins

Following the demonstration of their efficacy in the treatment of autoimmune thrombocytopenic purpura, their beneficial effect extends to other autoimmune diseases. They are used in the management of myasthenia, polymyositis, dermatopolymyositis, lupus and anemia or autoimmune thrombocytopenia. This treatment works in multiple ways and is not always well understood.

Anti-TFNα

Adalimumab (Humira®) acts by inhibiting a protein that is over-produced during Crohn's disease, TNFα. TNFα is produced by the cells of the organism and promotes inflammation, taking part in the fight against certain infections. Adalimumab is a monoclonal antibody, i.e. a very targeted molecule, produced using biotechnology to specifically neutralize TNFα. It is used for the synthesis of isolated cells of human origin and this antibody is 100% humanized. Several other molecules are available on the market:

Infliximab (Remicade®) is also a monoclonal antibody that neutralizes the activity of TNFα.

Etanercept (Enbrel®) is a chimeric molecule made of an antibody fragment called human IgG Fc associated with the soluble TNFα receptor. Certolizumab pegol (Cimzia®) is a monovalent fragment of a monoclonal antibody, modified by pegylation.

These molecules block the effect of TNFα by neutralizing the soluble TNF alpha and/or by preventing it from binding to a receptor. Anti-TNFα drugs are used for rheumatoid arthritis, severe cases of Crohn's disease, ankylosing spondylitis, juvenile idiopathic arthritis or psoriatic arthritis.

Prescription of anti-TNFα drugs must be systematically paired with immunosuppressant treatment in order to prevent the appearance of anti-TNFα antibodies.

The therapeutic schema of this autoimmune disease includes purely symptomatic anti-inflammatory, immunosuppressant treatment and/or substitutive treatment.

The limits of these treatments are linked to intolerances of these chronic treatments and to frequent escape. The use of long-term anti-TNFα-type biotherapies showed that approximately 20% of patients do not respond to these treatments and that they do not function after one year, in one out of two patients.

Associated risks:

Long course immunosuppressant treatment of the autoimmune disease itself increases the risk of developing cancer or a cancerous hematological disease. Thus, for celiac disease (Franks A. L. et al., 2012) associations with different cancers (hematological cancers such as non-Hodgkin's lymphoma or other organ tumors) appear over time in the development of that autoimmune enteropathy with a chronic inflammatory response and T-cell activation. These associations of autoimmune diseases with chronic inflammation and different cancers are also observed with a more elevated risk over time, for other pathologies such as Crohn's disease, lupus and rheumatoid arthritis.

OSE-127/S95011, designed for immuno-inflammatory diseases, including ulcerative colitis (UC) and Sjögren's Syndrome

Ulcerative colitis (UC), an inflammatory bowel disease, is a long-term inflammatory disease whose cause is unknown. It is characterized by persistent ulcers of the colon and the rectum. Digestive and non-digestive complications can also develop over

time, including inflammation of the megacolon, eyes or joints and colon cancer. Due to its prevalence in Western countries (60-280/100,000), its human, social and economic impact and its uncertain origin, UC is a disease with high unmet therapeutic need.

TREATMENT OF UC

To date, there is no cure for patients with UC. The main objective of medical treatment is to induce and maintain remission of the disease and prevent, in the long term, disability, colectomy and colorectal cancer. Patient care relies mainly on diet (still controversial) and on the administration of anti-inflammatories and/or immunomodulators, standard treatments for alleviating symptoms. In patients who do not respond to these treatments, biological drugs are used as second-line treatment (Harbord M. et al., J. Crohn's Colitis, 2017). Steroid-free endoscopic and clinical remission is currently the ultimate objective expected from maintenance treatment for UC (EMA 216, Guideline on the development of new medicinal products for the treatment of ulcerative colitis).

For patients with severe UC or during flareups, hospitalization may be necessary. When the disease cannot be controlled by drugs, surgery (including colectomy) is then the final option for patients with severe and unresponsive UC (approximately one third of patients), with potentially significant morbidity and often major consequences on the patient's quality of life.

COMPETITION AND PRODUCTS IN UC

The world market for UC is dominated by immunomodulator drugs (such as thiopurines, aminosalicylates and steroids) and by biological drugs (mainly anti-TNF monoclonal antibodies: Remicade® [infliximab], Humira® [adalimumab], Simponi® [golimumab] and more recently, an anti-α4β7 antibody, Entyvio® [vedolizumab]). The clinical data on anti-TNF treatments collected during the last 10 years has shown that primary resistance develops in approximately 30% of the native UC patients, whereas secondary resistance develops in more than 50% of primary responders in less than five years. Anti-TNF treatment is therefore unable to control the disease in approximately two thirds of all patients not presenting full remission (Sandborn W.J. et al., N. Engl. J. Med., 2016) and most of them resort to surgical intervention as a last recourse. There is thus still an unmet therapeutic need to induce and maintain control of the disease in primary patients unresponsive to standard treatments and maintain long-term remission and prevent consequences.

PRODUCTS IN DEVELOPMENT IN THE DIRECT FIELD OF OSE-127/S95011

OSE-127/S95011 (lustvertikimab): a humanized monoclonal antibody (IgG4), directed against the IL7 receptor alpha (CD127). The main characteristic of this antibody is that it recognizes an identified and patented epitope of the receptor giving it the specific property of not inducing internalization of the receptor while blocking the binding of the IL7 to its receptor. This allows it to block the proliferation of effector T cells without impacting the regulatory T cells. This non-internalization characteristic of the receptor is a very differentiating point compared with other competitors, in particular with respect to the two other products available in the domain of the IL7 described below.

GSK2618960 is a monoclonal antibody (IgG1) targeting the IL7 receptor alpha and internalizing the receptor. Phase 1 clinical trials have been developed by the company GSK. A trial was carried out among healthy volunteers (NCT02293161) and the results, in December 2018, demonstrated good product tolerance and blockage of IL-7 receptor signaling, consistent with the objectives that had been set. Moreover, it was demonstrated that even without discernible impact on a subgroup of peripheral T cells in healthy subjects, GSK2618960 effectively modulates the auto-inflammatory activity of the pathogenic T cells in the diseased tissue (Joanne Ellis et al., Br. J. Clin. Pharmacol., 2019 Feb).

The trial on multiple sclerosis (NCT01808482) was interrupted in June 2013 (after fraud was discovered concerning the data linked to a research team located in Shanghai).

PF-06342674 / ZB-168 is a monoclonal antibody (IgG1) targeting the IL7 receptor alpha and internalizing the PF-06342674 receptor. Pfizer conducted two Phase 1b trials with this product: one trial on diabetes (trial NCT02038764 terminated in September 2016) and a trial on multiple sclerosis (NCT02045732 terminated in April 2015). Following strategic company decisions, the company withdrew PF-06342674 from its product portfolio in July 2018.

In 2017, a Phase 2 trial (NCT03239600) conducted on primary Sjögren's syndrome was stopped.

In 2022, the company Zura Bio redeemed the rights of this antibody. Following its merger with the SPEC (Special Purpose Acquisition Company) JATT Acquisition Corp. the company is considering a Phase 2 in alopecia (alopecia areata).

ADX-914 is a monoclonal antibody (IgG1) targeting the alpha-IL7 receptor. It is developed jointly by Horizon Therapeutics ans Q32. A Phase 2 study has been completed and the drug candidate is evaluated in Phase 2 in atopic dermatitis. An additional Phase 2 study in another indication should be announced in 2023.

Several candidate drugs are in clinical development in UC to evaluate different ways of working including blocking of integrin or interleukin 12 and/or 23, modulation of sphingosine-1-phosphate receptors, inhibition of Janus kinases or antisense oligonucleotides. None of these therapeutically target the IL-7R (Sandborn W.J. et al., N. Engl. J. Med., 2016).

SJÖGREN'S SYNDROME

Sjögren's Syndrome occurs when a person's immune system attacks and destroys secretion-producing glands, in particular salivary and lacrimal glands. The lungs, intestines and other organs are less often affected by Sjögren's syndrome.

Sjögren's syndrome presents in two forms:

- primary Sjögren's syndrome (pSS): the disease itself, not associated with any other disease;
- secondary Sjögren's syndrome (sSS): a disease that develops in the presence of another autoimmune disease such as rheumatoid arthritis, systemic lupus erythematosus or vasculitis.

Sjögren's Syndrome is a rare disease affecting fewer than 1 out of 10,000 adults. Women are ten times more affected than men.

Primary Sjögren's syndrome (pSS) is characterized by lymphocytic infiltrates and progressive destruction of exocrine glands (saliva and tear glands) leading to xerostomia (dry mouth) and xerophthalmia (dryness and atrophy of the conjunctiva) associated with fatigue and pain. The inflammatory process may, however, affect any organ.

The pathological process implies both innate and adaptive immune systems. The precise physiopathological mechanisms of the disease are not completely understood. A complex interaction of types of immune cells, such as T cells, B cells, dendritic cells, monocytes/macrophages and NK cells and their effector molecules, would be the origin of the disease, eventually leading to hyperactivity of B cells, the production and formation of autoantibodies of germinal center type structures in the salivary glands.

COMPETITION AND PRODUCTS

Many therapeutic trials are currently in progress to evaluate the efficacy and the tolerance of new biotherapies in the treatment of primary Sjögren's syndrome. B lymphocyte dysfunction and hyperactivity are a hallmark of pSS. The activation factor of serum B cells (BAFF) is high in patients and is positively regulated in salivary glands.

A biological treatment, ianalumab (VAY736, Novartis) was successfully evaluated in a Phase 2b clinical trial (190 patients). This IgG1 anti-BAFF receptor monoclonal antibody aims at suppressing B lymphocytes with a double and targeted action in the treatment of pSS: a direct B depletion (antibody dependent cytotoxicity, ADCC) and a BAFF inhibition, increased after B depletion. The primary endpoint was achieved with a dose effect statistically significant on ESSDAI (Syndrome Disease Activity Index) in Sjögren. The largest reduction in the ESSDAI at week 24 is 1.92 point for VAY736 300mg compared to placebo (Bowman, SJ et al The Lancet Nov 2021).

In 2022, Horizon Therapeutics plc announced that its Phase 2 trial evaluating dazodalibep in the treatment of Sjögren syndrome was positive on the main assessment criteria in patients with a moderate to high systemic activity as defined by the European League against Rheumatisms (EULAR) (ESSDAI score ≥5). Patients treated with dazodalibep experienced improvement in their disease activity (6.3-point reduction) compared to those who received placebo (4.1-point reduction). This resulted in a statistically significant mean square difference of 2.2-point (p=0.017). Dazodalibep is a CD40 ligand antagonist that blocks T cell interaction with CD40-expressing B cells, disrupting the overactivation of the CD40 ligand co-stimulatory pathway.

References OSE-127/S95011

L. Belarif et al.; Full antagonist of the IL-7 receptor suppresses chronic inflammation in non-human primate models by controlling antigen-specific memory T cells; Cell Stress Micro Review (Dec. 2018)

L. Belarif et al.; IL-7 receptor blockade blunts antigen-specific memory T cell responses and chronic inflammation in primates; Nature Communication (Oct. 2018)

Lyssia Belarif et al.; Interleukin-7 receptor pathway controls human T cell homing to the gut and predicts response to anti-TNFα therapy in IBDLyssia; AAI 2018

L. Belarif et al.; "IL-7 pathway controls human T cell homing to the gut and culminates in inflammatory bowel disease mucosa"; FOCIS 2017

William J. Sandborn; The Present and Future of Inflammatory Bowel Disease Treatment; Gastroenterology & Hepatology Volume 12, Issue 7 July 2016

L. Belarif, et al.; IL-7 receptor blockade prevents intestinal human T cells infiltration by modulation of alpha4-beta7 integrin expression; FOCIS 2016

May, H.-L. et al.; IL-7 receptor blockade following T cell depletion promotes long-term allograft survival; J. Clin. Invest. 124, 1723–1733 (2014).

Dooms, H. Interleukin-7: Fuel for the autoimmune attack. J. Autoimmun. 45, 40–48 (2013).

Powell, N. et al.; The transcription factor T-bet regulates intestinal inflammation mediated by interleukin-7 receptor + innate lymphoid cells; Immunity 37, 674–684 (2012).

Willis, CR et al.; Interleukin-7 receptor blockade suppresses adaptive and innate inflammatory responses in experimental colitis; J Inflamm (Lond) 9, 39 (2012).

Lee, L.-F. et al.; Anti-IL-7 receptor-α reverses established type 1 diabetes in nonobese diabetic mice by modulating effector T-cell function; Proceedings of the National Academy of Sciences of the United States of America (2012).

Penaranda, C. et al.; IL-7 receptor blockade reverses autoimmune diabetes by promoting inhibition of effector / memory T cells; Proceedings of the National Academy of Sciences of the United States of America (2012).

Lee, L.-F. et al.; IL-7 promotes T (H) 1 development and serum IL-7 predicts clinical response to interferon-β in multiple sclerosis; Sci Transl Med 3, 93ra68 (2011).

Shinohara, T. et al.; Upregulated IL-7 receptor α expression on colitogenic memory CD4 + T cells may participate in the development and persistence of chronic colitis; J. Immunol. 186, 2623–2632 (2011).

Liu, X. et al.; Crucial role of interleukin-7 in T helper type 17 survival and expansion in autoimmune disease; Nat. Med. 16, 191–197 (2010).

Hartgring, S. A. Y. et al.; Blockade of the interleukin-7 receptor inhibits collagen-induced arthritis and is associated with reduction of T cell activity and proinflammatory mediators; Arthritis Rheum. 62, 2716–2725 (2010).

Hartgring, S. A. Y. et al.; Elevated expression of interleukin-7 receptor in inflamed joints mediates interleukin-7-induced immune activation in rheumatoid arthritis; Arthritis Rheum. 60, 2595–2605 (2009).

Hartgring, S. A. Y. et al; Interleukin-7 induced immunopathology in arthritis; Ann. Rheum. Dis. 65 Suppl 3, iii69–74 (2006).

Van Roon, J. AG et al.; Persistence of interleukin 7 activity and levels on tumor necrosis factor alpha blockade in patients with rheumatoid arthritis; Ann. Rheum. Dis. 66, 664–669 (2007).

Michel, L. et al.; Patients with relapsing-remitting multiple sclerosis have normal Treg function when cells expressing IL-7 receptor alpha-chain are excluded from the analysis; J. Clin. Invest. 118, 3411–3419 (2008).

Totsuka, T. et al.; IL-7 Is essential for the development and the persistence of chronic colitis; J. Immunol. 178, 4737–4748 (2007).

Liu, W. et al.; CD127 expression inversely correlates with FoxP3 and suppressive function of human CD4 + T reg cells; J. Exp. Med. 203, 1701–1711 (2006).

Seddiki, N. et al.; Expression of interleukin (IL) -2 and IL-7 receptors discriminates between human regulatory and activated T cells; J. Exp. Med. 203, 1693–1700 (2006).

Schluns, K. S. & Lefrancois, L.; Cytokine control of memory T-cell development and survival; Nat Rev Immunol 3, 269–279 (2003).

Yamazaki, M. et al. Mucosal T cells expressing high levels of IL-7 receptor are potential targets for treatment of chronic colitis. J. Immunol. 171, 1556–1563 (2003).

Watanabe, M. et al.; Interleukin 7 transgenic mice develop chronic colitis with decreased interleukin 7 protein accumulation in the colonic mucosa; J. Exp. Med. 187, 389–402 (1998).

Watanabe, M. et al.; The serum factor from patients with ulcerative colitis that induces T cell proliferation in the mouse thymus is interleukin-7; J. Clin. Immunol. 17, 282–292 (1997).

Watanabe, M. et al.; Interleukin 7 is produced by human intestinal epithelial cells and regulates the proliferation of intestinal mucosal lymphocytes; J. Clin. Invest. 95, 2945–2953 (1995).

FR104, designed for autoimmune diseases and transplantation

FR104 is a monovalent antagonist antibody in Fab format, directed against the co-stimulatory molecule CD28, for an effect that inhibits the responses of effector T cells and induces regulatory T cells (via CTLA-4) resulting in suppressive T activity for potential clinical applications in autoimmune pathologies and transplantation.

AUTOIMMUNE DISEASES: PRODUCTS UNDER DEVELOPMENT IN THE DIRECT FIELD OF FR104

Lulizumab pegol (BMS-931699) targets T cells and CD28. This product was evaluated by the company BMS as part of a Phase 2 study (NCT02265744 trial) evaluating the safety and efficacy of lulizumab versus placebo in the treatment of an autoimmune disease, systemic lupus erythematosus. The abstract presented to the 2018 ACR/ARHP conference ("An Anti-CD28 Domain Antibody, lulizumab, in Systemic Lupus Erythematosus: Results of a Phase II Study", Joan T. Merrill et al.) did not show any significant difference between lulizumab and the placebo in terms of primary and secondary criteria but a profile of favorable tolerance.

ALPN-101 is a first-in-class double inhibitor of the CD28 and ICOS costimulatory pathways expressed by cells. It is developed by AbbVie under a partnership agreement with Alpine Immune Sciences: after positive Phase 1 results in terms of safety, tolerance, pharmacokinetics and pharmacodynamics, the product entered Phase 2 in systemic lupus erythematosus in June 2021.

RENAL TRANSPLANTS: COMPETITION AND PRODUCTS IN RENAL TRANSPLANT

Renal transplant is the treatment of choice for end-stage renal disease and improves the quality of life and quantity of life of patients compared to dialysis thanks to the use of more effective immunosuppressive treatments. Knowledge of the mechanisms of lymphocytic activation and rejection phenomena has made it possible to define the use of these treatments and their combinations.

The principle of immunosuppression in renal transplants is a strong initial treatment, effective in the prevention of acute rejection, followed by effective maintenance immunosuppression to contain the immunological part of allograft nephropathy. Nevertheless, in the long term, these immunosuppression strategies have not yet shown significant long-term benefits, whether in the prevention of chronic allogeneic kidney disease or the occurrence of cardiovascular and/or oncological complications.

The therapeutic arsenal currently available comprises molecules mainly used at the time of transplantation and in the days following it. Used as an induction treatment, they cause a state of non-response to the transplant by depleting or blocking T lymphocyte proliferation, a key element of the allo-immune response. Other molecules, whose objective is to prevent acute rejection by blocking cellular signals between the lymphocytes and the antigen-presenting cells, will be used in the long term as maintenance treatment.

INDUCTION TREATMENTS

These are **antilymphocytic immunoglobulins** (ATG-Fresenius®, thymoglobulin) and **interleukin-2 antireceptor antibodies** (Anti-CD-25 Ab) (basiliximab, daclizumab).

TREATMENTS FOR INITIAL IMMUNOSUPPRESSION AND MAINTENANCE

Steroidal anti-inflammatory drugs have been used from the start for their immunomodulation potential. However, due to the many side effects, their use is currently limited.

Calcineurin inhibitors, which appeared in the '80s (ciclosporine/Neoral®, Sandimmune®; tacrolimus/Prograf®, Advagraf®), with comparable efficacy in preventing acute rejection, are chosen based on their metabolic side effects (hypercholesterolemia and hypertension blood pressure for cyclosporine and diabetes for tacrolimus).

Cell multiplication inhibitors (IMPDH): azathioprine (Imurel®), mycophenolate mofetil/CellCept®, unlike anticalcineurin, are devoid of nephrotoxicity and do not induce metabolic disorders (but still have side effects, particularly hematological and digestive effects).

Mammalian target of rapamycin (mTOR) inhibitors: sirolimus (Rapamune®) and everolimus (Certican®) are most often used as a maintenance immunosuppressive treatment, replacing anticalcineurin. Their main side effects are hyperlipidemia, thrombocytopenia and arthralgia.

Immunosuppressants blocking the second signal: the belatacept is used to prevent calcineurin inhibitors. In addition, it has been shown to improve long-term survival after transplantation.

RENAL TRANSPLANTS: PRODUCTS UNDER DEVELOPMENT IN THE DIRECT FIELD OF FR104

Lulizumab Pegol (BMS-931699) targets T cells and CD28. This product is currently undergoing a Phase 1/2 clinical trial in patients who have received a renal transplant. It assesses the safety of a combination of four products: lulizumab pegol, tocilizumab, belatacept and everolimus. Post-transplant follow-up is at least one year.

Other immunosuppressive therapies, acting at different levels of the immune response, are being evaluated.

FR104 references
Watkins et al., Journal of Clinical Investigation, (2018)
Masaaki et al.; JCI Insight. 2017 Zaitsu M. et al., Jounal of Clinical Investigation, (2017)

Dillinger et al., Frontiers in Immunology, (2017)
Poirier N. et al., Journal of Immunology, (2016)
Vierboom M. et al., Clin Exp Immunol, (2016)
Ville S. et al., J. Am. Soc. Nephrol., (2016)
Poirier N. et al., Am. J. Transplant. (2015)
Haanstra KG et al., J. Immunol, 194 (2015)
Poirier N. et al., Science Translational Medicine, (2010)
Dugast A. S. et al., J Immunol 180, (2008)
Jang, M. S. et al., Transplantation, 85, (2008)
Raychaudhuri S.P. et al., J Invest Dermatol 128, (2008)
Zhang T. et al., World Transplantation Congress, Boston, (2006)
Urakami H. et al., Transplant Proc 38, (2006)
Haspot F. et al., Am J Transplant 5, (2005)
Dong V. M. et al., Transplantation 73, (2002)
Laskowski IA et al., J Am SocNephrol 13 (2002)
Silver P. B, et al., J Immunol 165, (2000).
Perrin PJ et al., J Immunol 163, (1999)
Chapman AP et al., Nat Biotechnol 17, (1999)

5.6.3.2 Resolution of inflammation

Persistent inflammation is a hallmark of all chronic inflammatory and autoimmune diseases. If it is not controlled or resolved, it can lead to worsening tissue damage and cause tissue fibrosis, possibly associated with the loss of organ function. Most anti-inflammatory agents act using a mechanism that blocks pro-inflammation pathways. In contrast, OSE Immunotherapeutics is developing OSE-230 as a first-in-class therapeutic agent with the potential to resolve chronic inflammation by driving affected tissues to complete the inflammation program and restore tissue integrity.

Chronic inflammatory diseases are the most significant cause of death worldwide and their incidence is growing, highlighting the patients' need for disruptive innovations to manage such complex diseases. *(Chronic Inflammation; Roma Pahwa, Amandeep Goyal, Pankaj Bansal, Ishwarlal Jialal; In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2020 Jan.; 2020 Aug 10).*

Metformin is frequently used to treat type II diabetes patients with dyslipidemia and low-grade inflammation. The anti-inflammatory activity of metformin results in a reduction in circulating TNF-alpha, IL-1beta, CRP and fibrinogen in these patients.

Statins are anti-inflammatory as they reduce multiple circulating and cellular biomediators of inflammation. This pleiotropic effect appears to contribute in part to the reduction in cardiovascular events.

Non-steroidal anti-inflammatory drugs (NSAIDs) like naproxen, ibuprofen, and aspirin acts by inhibiting an enzyme cyclo-oxygenase (COX) that contributes to inflammation and are mostly used to alleviate the pain caused by inflammation in patients with arthritis.

Corticosteroids also prevent several mechanisms involved in inflammation. Glucocorticoids are prescribed for several inflammatory conditions including inflammatory arthritis, systemic lupus, sarcoidosis, and asthma.

5.7 Investments

The following financial information is derived from the Company's consolidated financial statements for fiscal year ended December 31, 2022, set out in paragraph 18.1 of this Universal Registration Document.

5.7.1 Key investments made by the Company

The Company invested in laboratory equipment in fiscal years 2018 and 2019, as well as the development of its laboratories for €945 thousand. They were financed out of equity as well as through subsidies received by the Company.

Early 2020, the Company has acquired a cytometer for nearly €300 thousand financed by leased from an historical bank partner.

In 2021, the Company invested €210 thousand in additional equipment for the Nantes laboratory and paid €65 thousand for work at the new Paris site. Other investments correspond to IT equipment.

5.7.2 Future key investments

Due to the economic context, the investments planned for 2023 will be minor.

5.7.3 Information on joint ventures or companies in which the Company holds a capital share likely to have a significant impact on the valuation of its assets and liabilities, its financial position or results

The information on the Company's subsidiaries is set out in paragraph 6.2 below.

5.7.4 Environmental impacts of investments made by the Company

Since industrial production and distribution are not included in research and development activities, the Company only invested in laboratory equipment as part of its property, plant and equipment assets. In this respect, the Company uses little raw materials and its activities neither release significant emissions in the environment nor greenhouse gases.

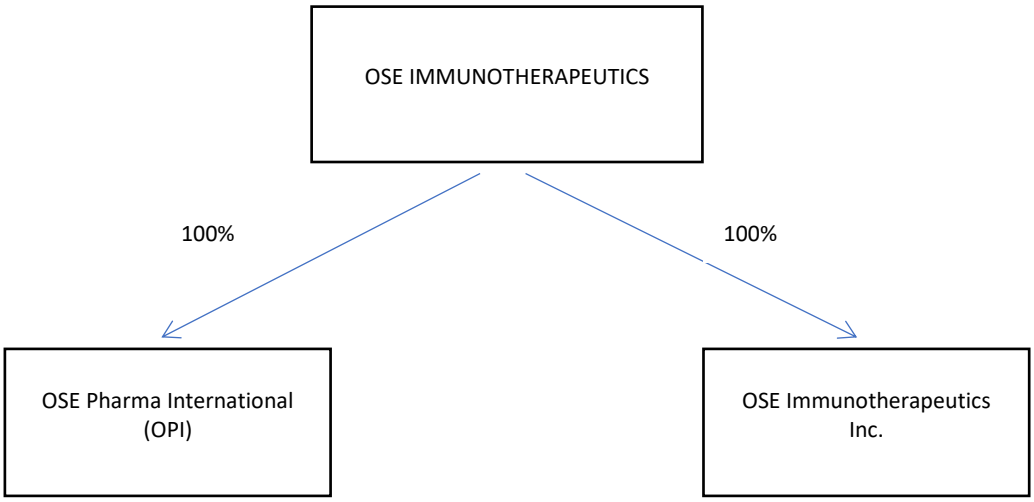
Furthermore, all the waste resulting from the tests conducted by employees are treated in accordance with existing regulations.

Please refer to the charter « Economic Social Governance" in Appendix D of this Universal Registration Document.

6 Organizational structure

6.1 Overview of the Company

At the date of this Universal Registration Document, the legal organizational chart of the Group is as follows:



6.2 Subsidiaries and investments

OPI

Since March 25, 2014, the Company holds all of the capital and voting rights of the Company OSE Pharma International, a public limited company whose registered office is located in Switzerland (called OPI SA).

OPI has share capital of 100,000 Swiss francs and was created in February 2012. Its corporate purpose is the acquisition, holding, operation, development and marketing of intellectual property rights in biotechnology; research and development of products and treatments resulting from such rights, the conduct of studies and clinical trials and the granting of licenses; the identification and the building of relationships involving partners and scientific, financial, manufacturing and governmental investors; investment in companies active in the same sector (in compliance with the Swiss Federal Law on Acquisition of Real Estate by Persons Resident Abroad - LFAIE).

Its main assets are world rights relating to the composition of peptides. It has no employees.

The existing agreements between OSE Immunotherapeutics and OPI are the European agreement for the OSE-2101 project signed in July 2012 and the agreement for the purchase of OPI by its shareholders on March 25, 2014.

The European license agreement is maintained since the intellectual property is owned by OPI. The Company expects, as part of its intragroup relations, to extend this licensing agreement to the other territories outside of Europe. The interest in maintaining the licensing agreement is to ensure the industrial property is financed through the OPI subsidiary and to finance, through these payments, the commitments made by OPI with respect to the pharmaceutical group Takeda. In fact, the Company made a commitment to pay an additional amount to Takeda when it registered its product in the United States and Europe, then royalties on future sales, limited to a single digit (see Section 20).

OSE IMMUNOTHERAPEUTICS INC.

On March 28, 2017, the Board of Directors authorized the creation of a subsidiary in the United States wholly owned by the company, in order to serve as a point of support for international scientific collaboration. Having an American presence is also justified given the current and future of Tedopi® in the United States (recruitment, partnership, licensing, etc.).

7 Review of the financial position and results

Chapter 7 presents the Company's results and financial position for fiscal years ended December 31, 2022, and 2021. The Company's financial statements are prepared in accordance with existing IFRS accounting standards.

Readers are invited to read this chapter in conjunction with the Universal Registration Document as a whole. In particular they should read the description of the Company's activities presented in Chapter 5 of this Universal Registration Document.

The following presentation and analysis should be read in conjunction with the Universal Registration Document as a whole, especially the Company's consolidated financial statements for fiscal years ended December 31, 2022, and 2021 set out in paragraph 18.1 of this Universal Registration Document.

7.1 Financial position

ASSETS IN K€	**Note**	**December 31, 2022**	**December 31, 2021**
Intangible assets	1.1	48,784	51,122
Tangible assets	1.2	743	926
Right-of-use assets	1.3	4,236	4,513
Financial assets	1.4	635	936
Differed tax assets	10.1	182	173
TOTAL NON-CURRENT ASSETS		***54,581***	***57,670***
Trade receivables	2.2	403	772
Other current assets	2.3	11,177	9,854
Cash and cash equivalents	2.1	25,620	33,579
TOTAL CURRENT ASSETS		***37,200***	***44,206***
TOTAL ASSETS		**91,781**	**101,876**

EQUITY & LIABILITIES IN K€	**Note**	**December 31, 2022**	**December 31, 2021**
SHAREHOLDERS' EQUITY			
Stated capital	4.1	3,705	3,705
Share premium	4.1	65,611	65,605
Treasury stock	4.4	(549)	(160)
Reserves and retained earnings		(18,349)	(4,411)
Consolidated result		(17,760)	(16,850)
TOTAL SHAREHOLDERS' EQUITY		***32,658***	***47,890***
NON-CURRENT DEBTS			
Non-current financial liabilities	5	37,231	30,801
Non-current lease liabilities	5	3,586	3,965
Non-current deferred tax liabilities	10.2	1,514	1,748
Non-current provisions	7	524	710
TOTAL NON-CURRENT DEBTS		***42,856***	***37,224***
CURRENT DEBTS			
Current financial liabilities	5	3,093	1,611
Current lease liabilities	5	883	756
Trade payables	6.1	8,539	9,607

Corporate income tax liabilities	6.2	21	14
Social and tax payables	6.2	2,916	3,724
Other debts and accruals	6.3	816	1,050
TOTAL CURRENT DEBTS		***16,268***	***16,761***
TOTAL LIABILITIES		**91,781**	**101,876**

7.2 Operating profit

7.2.1 Key factors affecting operating revenues

On April 3, 2018, the Company entered into a worldwide collaboration and exclusive licensing agreement with Boehringer Ingelheim International GmbH, an independent international pharmaceutical laboratory, to develop OSE-172. According to the terms of the agreement, OSE Immunotherapeutics granted Boehringer Ingelheim International GmbH the license for the worldwide exclusive rights for the development, registration and marketing of its OSE-172 product candidate. In return, OSE Immunotherapeutics will receive cash flows for a total amount up to €1.1 billion (exclusive of royalties), including an upfront payment of €15 million on signature of the agreement (the total amount was paid in 2018), a €15 million payment at the start of a Phase 1 trial (milestone reached in 2019), a payment of €8 million when the first patient is included in the expansion phase of the ongoing Phase 1 trial (milestone achieved in 2021) and milestone payments throughout the various clinical development steps and milestone payments related to sales targets. In addition, development costs incurred by the company are re-invoiced to BI.

In view of the accounting rules used for revenue recognition, the Company was able to recognize €12 million in revenue for the 2022 fiscal year.

In December 2016, the Company signed a worldwide licensing option agreement with Servier, an international independent pharmaceutical company, to develop and market OSE-127/S95011, an interleukin-7 receptor antagonist. According to the terms of the agreement, OSE Immunotherapeutics granted Servier a licensing option on the worldwide exclusive rights for the development and marketing of the product candidate. The agreement covers an amount up to €272 million, including a €10.25 million payment on signature of this option and a payment of €30 million on exercise of a two-step licensing option. Since the first step was achieved with the start of Phase 1, the Company received €10 million in 2019. In March 2020, OSE Immunotherapeutics and Servier signed an amendment covering the terms of the potential exercise of the licensing option by modifying Step-2 of this option.

Thus, OSE Immunotherapeutics has received from Servier a milestone payment of €5 million on the recruitment of the first patient in the Phase 2 clinical trial in Sjögren's Syndrome in 2021, and could receive an additional payment of €15 million on exercise of the option at the end of the two scheduled Phase 2 clinical trials, and in priority upon completion of the study in Sjögren's Syndrome sponsored by Servier, the other study being conducted since December 2020 in ulcerative colitis sponsored by OSE Immunotherapeutics (the initial agreement providing for a total payment of €20 million upon completion of a Phase 2 clinical trial).

Subsequent payments will be linked to clinical development milestones, registration in multiple indications, then sales-related milestones with double-digit royalties.

In view of the accounting rules used for revenue recognition, the Company was able to recognize €1 million in revenue for the 2022 fiscal year.

In April 2021, the Company signed a global licensing agreement with Veloxis Pharmaceuticals Inc., a subsidiary of Asahi Kasei, which grants Veloxis Pharmaceuticals Inc. the worldwide rights to develop, manufacture, register and market FR104, a monoclonal antibody fragment antagonist of CD28, in all indications for transplantation. Under this agreement, the Company will receive up to €315 million in potential milestone payments from Veloxis, including a €7 million due on signature, development, registration and marketing milestones, and tiered royalties on potential future sales. Veloxis will assume all production, development and marketing costs of FR104 in transplantation indications. In addition, the Company sold the product to Veloxis Pharmaceuticals to enable them to conduct their clinical study.

In view of the accounting rules used for revenue recognition, the Company was able to recognize €5 million in revenue for the 2022 fiscal year.

The development of OSE-127/S95011 and BI 765063 (OSE-172) products continued at the clinical stage, in particular with the and completion of Phase 1 clinical trials, and the continuation of Phase 2 clinical trials for OSE 127/S95011.

7.2.2 Explanation of material changes in revenue or net income in the comparative annual financial statements

7.2.2.1 Comparative figures from the consolidated statement of operations at December 31, 2021 and 2022

Annual financial statements (in €K)	2022 12 months	2021 12 months
Operating income	**18,302**	**26,306**
of which Revenue	**18,302**	**26,306**
of which Other operating income	**0**	**0**
R&D expenses	**(26,893)**	**(30,550)**
Overhead expenses	**(6,672)**	**(8,608)**
Expenses related to share-based payments	**(3,130)**	**(3,773)**
Operating profit/(loss)	**(18,476)**	**(16,625)**
Financial income	**2,079**	**267**
Other financial expenses	**(1,624)**	**(856)**
Profit/(Loss) before tax	**(18,022)**	**(17,213)**
Income tax	**263**	**364**
Consolidated result	**(17,760)**	**(16,850)**

Operating income

Revenue stood at €18,302 thousand and comprised:

- €2,396 thousand related to the re-invoicing of fees under the agreement signed with Boehringer Ingelheim (BI) and €10,000 thousand related to the staggering of milestones received.
- €831 thousand related to the re-invoicing of a portion of intellectual property costs and CMC costs.
- €5,000 thousand of milestone payment following the signature of the licensing agreement with Veloxis on April 24, 2021 and €72 thousand related to the sale of reagents and to the re-invoicing of intellectual property costs.

The Company's revenue is directly correlated with the signing of licensing agreements and achieving key milestones.

As a result, the partnership agreements signed with Boehringer Ingelheim and Veloxis mainly accounted for 2022 revenue.

8 Capital resources

8.1 Information on the Issuer's capital

Since 2012, the Company has been financed by capital increases, loans and repayable advances. The following table summarizes all various sources of financing.

Financing sources – in €K	
2012 capital increase	527
2013 capital increase	0
2014 capital increase	3,148
2015 capital increase	19,304
2016 capital increase	852
2017 capital increase	17
2018 capital increase	23
2019 capital increase	0
2020 capital increase (1)	17,427
2021 capital increase (2)	265
Subtotal capital raised*	**41,563**
P2RI loan	1,500
French Government-Guaranteed loan (PGE)	7,008
EIB	20,000
Subtotal loans	**28,460**
OSEO repayable advances	330
Bpifrance repayable advance	100
Bpifrance EFFI-CLIN repayable advance	6,044
Bpifrance EFFiMab repayable advance	4,474
BPI PSPC repayable advance	908
BPI Capacity Building repayable advance	2,999
Subtotal repayable advances	**14,855**
Total financing sources	**84,878**

* These amounts have been restated for capital increase costs.

(1) In 2020, the Company completed a capital increase with cancellation of preferential subscription rights through a private placement with 25 qualified French and international investors, a large majority of them new shareholders, and by the accelerated construction of an order book, for €18.6 million.

(2) In 2021, the Company received a request to exercise 42,000 of the 2017 share subscription warrants, resulting in a capital increase of a total nominal amount of €8,400, as well as a request for the exercise of 10,000 founders' share warrants giving right to 10,000 shares, resulting in a capital increase of a total nominal amount of €2,000. Readers are invited to refer to Section 18.1.4.3.1 of this Universal Registration Document for more information on these warrant exercises.

The data included in the table below are from the consolidated financial statements for fiscal years ended December 31, 2021, and 2020 under IFRS standards.

In €K	**12/31/2022**	**12/31/2021**

Consolidated equity	**32,658**	**47,890**
Loans and financial liabilities	40,324	32,412
Cash and cash equivalents	25,620	33,579
In debt (Net cash) – Net position	**14,704**	**(1,167)**

Cash stands at €25,620 thousand and €7,108 thousand is held in term deposit accounts.

8.2 Cash flows

8.2.1 Statement of cash flows

In K€		Note	2022	2021
	CONSOLIDATED RESULT		**(17,760)**	**(16,850)**
+/-	Depreciation, amortization & provision expenses	1.2	2,795	1,970
+/-	Provision for pensions and retirement	7	147	78
+/-	Provision for litigations		(198)	289
+	Amortization on "right-of-use"	1.3	742	687
+/-	Shares based payments (1)	8.4	2,728	2,944
	CASH FLOW BEFORE TAX		**(11,545)**	**(10,881)**
+	Financial charges	5	(3,066)	634
-	Income tax expenses	10.3	(263)	(364)
	CASH FLOW FROM OPERATIONS BEFORE NET BORROWING COST AND TAXES (A)		**(14,874)**	**(10,612)**
-	Tax paid		0	0
-	Receivable/Tax debt variation		(236)	(332)
+/-	Working capital variation (2)		(3,142)	1,025
	CASH FLOW FROM OPERATING ACTIVITIES (D)		**(18,252)**	**(9,919)**
-	Tangible assets increase	1.2	(274)	(472)
+/-	Financial assets variation		0	0
+/-	Mutual finds units accounted in current financial assets		300	(355)
	CASH FLOW FROM INVESTING ACTIVITIES (E)		**26**	**(827)**
+	Capital increase	4.1	0	265
+/-	Capital increase costs	4.1	6	0
+	Loan subscription	5	12,056	15,281
-	Loan repayment	5	(1,010)	(40)
-	Lease debt repayment (3)	5	(785)	(549)
	CASH FLOW FROM FINANCING ACTIVITIES (F)		**10,267**	**14,957**
+/-	Currency translation transactions (G)		0	0
	CASH VARIATION H = (D + E + F + G)		**(7,959)**	**4 211**
	CASH OPENING BALANCE (I)	2.1	33,579	29,368
	CASH CLOSING BALANCE (J)	2.1	25,620	33,579

(1) €2,728 thousand in valuation costs for free shares and founders' share warrants allocated as of December 31, 2022.

(2) The change in working capital requirement was primarily due to the following:
- decrease in trade receivables of €369 thousand
- increase in other current assets of €1,323 thousand
- decrease in trade payables for €1,067 thousand
- increase in tax and social security payables amounting of €808 thousand
- decrease in other payables amounting to €234 thousand

(3) This line relates to the application of IFRS 16 and corresponds to the repayment of lease liabilities of €785 thousand.
(4) *Of which €2 thousand of CCB*

8.3 Financing requirements and structure

8.3.1 Financing requirements

Due to the war between Russia and Ukraine and to the difficult economic context, the Company has updated its working capital requirement projections.

Despite a strong cash position that will help the Company through the current crisis, it needs to anticipate any delay in product development that could delay expected cash inflows.

As a result, the Company is assessing various options for potentially strengthening its financing structure in the coming months. The reader is invited to refer to Section 3.5.1 of this Universal Registration Document.

8.3.2 Financing structure

In €k	12/31/2021	Increase	Decrease	Other transactions*	12/31/2022	Interest at 12/31/2022
BPI EFFIMAB advance	4,688	75			4,763	(75)
BPI EFFICLIN Advance	6,464	92			6,556	(92)
Loan guaranteed by the French State	5,932			(1,695)	4,237	
BPI CoVepiT Advance	911	6			916	(6)
BPI Capacity/CoVepiT2 Advance	3,008	16		(247)	2,777	(16)
BEI Loan	5,810	10,000	(2,056)		13,754	
BEI Loan - Warrants	3,989	2,056	(1,816)		4,229	
Non-current financial liabilities	**30,801**	**12,244**	**(3,872)**	**(1,942)**	**37,231**	**(188)**
Nantes Lot 1 Lease	124			(111)	13	
Nantes Lot 2 Lease	78			(35)	43	
Nantes Lot 3 Lease	69			(31)	38	
Paris Suffren Lease 1	(0)				(0)	
Pl. de Catalogne Lease 3	3,595			(491)	3,104	
Leasing Cytometre	98			(68)	30	
La Chapelle Sur Erdre		466		(108)	358	
Non-current lease liabilities	**3,965**	**466**		**(844)**	**3 586**	

BPI EFFIMAB Advance						
BPI EFFICLIN Advance						
Loan guaranteed by the French State	1,093		(1,034)	1,695	1,753	(43)
BPI COVEPIT Advance						
BPI Capacity/COVEPIT 2 Advance				247	247	
BEI Loan	517	1,073	(500)		1,090	(1,073)
Bank overdrafts	1	1			2	
Current financial liabilities	**1,611**	**1,074**	**(1,534)**	**1,942**	**3,093**	**(1,117)**
Nantes Lot 1 Lease	117		(107)	111	122	(4)
Nantes Lot 2 Lease	42		(36)	35	41	(2)
Nantes Lot 3 Lease	32		(29)	31	34	(2)
Paris Suffren 1 Lease	10		(10)		0	
Place de Catalogne Lease	476		(414)	491	553	(54)
Leasing Cytometre	79		(69)	68	78	(3)
La Chapelle Sur Erdre			(52)	108	56	(3)
Current lease liabilities	**756**		**(717)**	**844**	**883**	**(68)**
Total financial liabilities	**37,133**	**13,784**	**(6,123)**		**44,794**	**(1,372)**

*This column includes the recurring and non-recurring breakdown as well as IFRS 9, IAS 20 and IFRS 16 restatements for the year.

8.3.2.1 Non-current financial liabilities

Non-current financial liabilities are:

REPAYABLE ADVANCE FROM BPIFRANCE FOR THE EFFIMAB PROJECT

On June 19, 2017, the Company received from Bpifrance the first payment of €2,328 thousand as part of a repayable advance for the EFFIMab project.

This interest-bearing advance (interest rate of 1.66% under the contract) was initially for an amount up to €3,609 thousand paid on achievement of three key milestones within a completion period of 72 months.

If all milestones are achieved, a notional repayment in annual installments was to be put in place from June 30, 2021, based on a notional amount of €3,609 thousand at the applicable contractual discount rate of 1.66%, i.e. a fixed amount of €4,100 thousand, including interest of €490,595. Repayments, amounting to €4,100 thousand, were spread between June 30, 2021, and June 30, 2025.

Following amendment no. 2, signed on December 28, 2018, this interest-bearing advance was then a maximum amount of €3,991 thousand paid if 4 milestones were reached within a completion period of 115 months, with the repayment schedule spread over a period between December 31, 2024 and December 31, 2028.

As part of the achievement of the EC3 milestone, the Company obtained the payment of a repayable advance for €2,328 thousand in accordance with the initial contract.

As part of the achievement of the EC4 milestone, the Company obtained the payment of a repayable advance for €820 thousand on April 10, 2019.

Following amendment no. 3, signed in October 2020, this interest-bearing advance was modified and increased to a maximum amount of €5,264 thousand paid in the event of the achievement of six milestones within a 122-month period.

As part of the achievement of the EC5 milestone, the Company obtained payment of a repayable advance of €1,325 thousand for the first quarter of 2021.

If all milestones are achieved, the theoretical repayment is now a fixed amount of €6,198 thousand, which will be paid in annual installments from September 30, 2025, and which has been calculated on the basis of the theoretical €5,264 thousand receivable.

Repayments will be spread between September 30, 2025, and September 30, 2030.

REPAYABLE ADVANCE FROM BPIFRANCE FOR THE EFFICLIN PROJECT

On December 18, 2017, the Company received from BPI France a first payment of €1,236 thousand as part of a repayable advance for the EFFI-CLIN project. This interest-bearing advance (discount rate of 0.90% according to the agreement) is for up to €8,106 thousand paid on achievement of four key milestones within a completion period of 60 months.

If all milestones are achieved, a notional repayment in annual installments from June 30, 2024, based on the notional amount of €8,106 thousand at the applicable contractual discount rate of 0.90%, will be a fixed amount of €8,593 thousand, including interest of €487 thousand.

The Company received a portion of the advance, i.e. €1,236 thousand at the start of the trial.

On September 18, 2019, the Company received the second payment of the repayable advance, i.e. €4,808 thousand on achievement of the first key milestone.

If the Company's program is successful, the first payment will be repaid between June 30, 2024, and March 31, 2028.

FRENCH GOVERNMENT-GUARANTEED LOAN

To address the financial consequences of the COVID-19 pandemic, on May 5, 2020, a French Government-guaranteed loan of €6,960 thousand was granted, split between three banks (CIC, CM and BNP).

These loans meet the conditions of the Rectifying Finance Law for 2020, n°2020-289, of March 23, 2020, and the specifications defined in the decree dated March 23, 2020, providing the French Government guarantee to credit and financial institutions under that law.

This funding is one-year cash loan immediately made available to the borrower for the full amount on the date that the funds are transferred into their current account. Capital will be repaid and interest and ancillary costs paid in a single installment on the annual repayment date, with the option for the borrower to apply to spread the outstanding amount due on the repayment date over a further 4 years. Management has already decided to exercise the option and repay this loan at the end of 5 years.

The optional amortization amendments to French Government-guaranteed loans corresponding to the exercise of options spreading the repayment over five years were signed at the end of March 2021.

The funds received and conditions are as follows:

- Crédit Mutuel = €2,300,000 received May 6, 2020, repayable on May 6, 2026. 48 monthly payments with a first du on 06/05/2022 and a final due date on 05/05/2026. (Fixed rate: 0,70% / TEG: 1,39% per year).
- BNP = €2,300,000 received on May 6, 2020, repayable on May 6, 2026. 48 monthly payments with a first due date on 06/05/2022 and a final due date on 05/05/2026. (Fixed rate: 0.75% / TEG: 1.44% per year). An additional commission was recognized on 07/30/2021 for 48,489 euros. The total amount due at closing therefore amounts to 2,348,489 euros.
- CIC = €2,360,000 received on May 18, 2020, repayable on May 18, 2026. 48 monthly payments with a first due date on 06/15/2022 and a finale due date on 05/15/2026 (Fixed rate: 0.70% / TEG: 1.39% per year).

EIB LOAN

The overall financing agreement signed with the EIB includes two tranches of respectively €10 million and €5 million.

Tranche 1

In early July 2021, the Company received the payment of €10 million for the first tranche of the loan granted by the European Investment Bank (EIB) on February 12, 2021.

This type of financing, granted by the EIB, and benefiting from a guarantee from the European Commission under the European Fund for Strategic Investments (known as the "Juncker Plan"), aims to support developed research and innovation projects by companies with high growth potential.

This first tranche bears a fixed annual interest of 5% paid annually, over a five-year maturity (each drawdown is treated separately in terms of maturity). The repayment of each tranche will therefore be made at the end of a period of five years after the date of disbursement of said tranche.

As collateral for this financing, OSE Immunotherapeutics granted the EIB an assignment of trade receivables relating to existing receivables and future receivables from the development or marketing of its pipeline of drug candidates to be collected from its pharmaceutical partners (Servier and Boerhinger Ingelheim).
Other than the usual restrictions in such cases (restrictions on the sale of assets, clause maintaining key executives), the contract does not contain any financial covenants or restrictions in terms of management and development.

The first tranche is accompanied by the issue of share subscription warrants (BSA T1) entitling EIB in the event of exercise, to subscribe to 850,000 shares of the Company (i.e. 4.44% of the share capital on an undiluted basis). The share subscription warrants are not subject to a request for admission to trading on any market.

Given the characteristics of the loan contract, this financial instrument is considered a hybrid instrument consisting of debt and embedded derivatives (call and put share subscription warrants).

Debt is measured using the amortized cost method, including issue costs corresponding to the fair value of the share subscription warrants T1 (on the issue date) in the amount of €4.19 million.

The share subscription warrants are derivative liabilities to be measured at fair value through profit or loss at each closing date (i.e. €2.45 million at 12/31/2022).

Tranche 2

The second tranche (€10 million) is subject to the issuance of an additional 550,000 share subscription warrants by the Company. The tranche may be exercised by the Company and subject to the achievement of scientific milestones related to several of its clinical research programs.

The subscription price of these 550,000 share subscription warrants linked to the second tranche (if exercised) will be €0.01 per share subscription warrant. Each share subscription warrant will entitle the holder to subscribe to one new share with a nominal value of €0.20 each, with dividend rights from the date of delivery, at a price equal to the volume-weighted average price of the last three (3) trading sessions preceding the setting of the issue price, less a discount of 2.5%.

The second tranche has been drawned in December 2022 according to the above conditions.

The debt is valued using the amortized cost method including issue costs corresponding to the fair value of the warrants T2 (on the date of issue) for €2.05 million.

The warrants T2 are liability derivatives to be measured at fair value through profit or loss at each closing (i.e. €1.78 million at 12/31/2022.

The reader is invited to refer to Note 5 to Section 18 of the Consolidated Financial Statements.

8.3.2.2 Lease liabilities and leases

OSE recognizes in the balance sheet a liability for future lease payments and an asset for the right of use for operating leases.

The Company identified one new lease (falling within the scope of the standard) for the 2022 fiscal year, with the following characteristics:

- A lease for real estates in France. The incremental borrowing rate used was 1.15%.

8.4 Restrictions on the use of capital resources that have materially affected, or could materially affect, directly or indirectly, the issuer's operations

None

8.5 Expected financing sources

The Company is primarily aiming for partnering and licensing agreements for some of its products and further public funding for its programs.

With €25.6 million in cash and cash equivalents at December 31, 2022 (excluding €5.4 million in 2022 research tax credits), the Company believes it has the financing resources necessary to continue its clinical and preclinical programs at least for the twelve months following its published financial statements for the fiscal year ended December 31, 2022.

9 Regulatory environment

The description of the risks linked to the Company's regulatory environment is available in paragraphs 3.1 "preclinical and clinical development of drug candidates") and 3.3 "drug marketing".

9.1 Introduction

The research and development work, preclinical studies, clinical studies, facilities, as well as the manufacturing and marketing of our drug candidates are and will be subject to complex legislative and regulatory requirements defined by various public authorities in France, Europe, the United States and other countries of the world.

The European Medicines Agency (EMEA), the US Food and Drug Administration (FDA), the French National Agency for the Safety of Medicines and Health Products (ANSM) and the equivalent regulatory agencies in the other countries impose significant restrictions concerning development (including clinical) trials), manufacturing and sales of products such as those developed by the Company. Failure to comply with these regulations can lead to the imposition of fines, the seizure or withdrawal of the products from the market or even the partial or total suspension of their production by the regulatory authorities. They may also withdraw marketing authorizations granted previously or refuse applications for authorizations that the Company has filed or even pursue legal remedies. Regulatory constraints are important for assessing whether a main asset can eventually become a drug and evaluating the time and the investments necessary for such development.

Although there are differences from one country to another, the development of therapeutic products for human usage must comply with certain common regulatory prerequisites in all developed countries.

To obtain marketing authorization for a product, proof of its efficacy and safety, as well as detailed information on its composition and its process of manufacturing, must generally be provided. Laboratory tests, pharmaceutical development, preclinical studies and clinical trials are conducted in this framework.

The development of new drugs, from basic research to product marketing includes five stages:

- Research
- Preclinical studies, pharmaceutical development, manufacturing
- Clinical trials in humans
- Marketing authorization (MA)
- Sales

Regulatory authorities require follow-up after marketing authorization is granted in order to continue monitoring the effects and the safety of the authorized products (pharmacovigilance). After obtaining marketing authorization, authorities may also ask for additional trials to evaluate tolerance and efficacy on special populations of patients or impose conditions that could limit the commercial development of some products.

9.2 Preclinical studies

Preclinical studies include pharmacological studies establishing the mechanism of action *in vitro* and *in vivo*, laboratory evaluation of the quality, purity and stability of the pharmaceutical drug substance and the formulated product, as well as studies to evaluate tolerance (toxicological studies) before initiating clinical trials in human. The conduct of toxicological studies is submitted to regulatory and legislative requirements, as well as to Good Laboratory Practices (GLP). Manufacturing studies are conducted according to Good Manufacturing Practices (GMP). All results of preclinical trials and of manufacturing and product stability are submitted to the regulatory authorities jointly when applying to start medical trials.

9.3 Conduct and regulation of clinical trials

- **PHASE 1:** the product is administered in order to determine its initial tolerance profile, identify the side effects and evaluate the tolerance to the doses administered, as well as its distribution in the organism and impact on metabolism. Developers sometimes name their trials Phase 1a or Phase 1b. Phase 1b trials generally aim to confirm dosage, pharmacokinetics and tolerance in a greater number of patients than Phase 1a. In oncology, accelerated development is sometimes pursued, based on Phase 1 trials including cohort extensions potentially leading to accelerated marketing authorization for the drug. This is for example the case of molecules developed for rare diseases.
- **PHASE 2:** the product is studied in a limited population of patients in order to obtain signs of preliminary efficacy and determine the level of optimal administration as well as any side effects and risks linked to tolerance.
- **PHASE 3:** Phase 3 trials are carried out on a large number of patients carrying the targeted disease to compare the study treatment to a reference treatment in order to produce the data demonstrating its relative efficacy and tolerance.
- **PHASE 4:** trials, sometimes referred to as Phase 4 trials, may also be conducted following the initial marketing authorization. These trials aim to obtain more information on the treatment of patients in the targeted therapeutic indication. In some cases, the competent regulatory agency may require a Phase 4 clinical trial as a condition of approval.

Clinical trials may be carried out in Europe, the United States or the rest of the world when authorized by the regulatory authorities and the independent ethics committee of each country in question. In fact, regulatory authorities may oppose clinical trial protocols proposed by the companies that seek to test the products, suspend them or require major modifications.

The purpose of the clinical trials is to administer the drug candidate to human subjects under the supervision of qualified investigators, in compliance with good clinical practices defined by the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). These latter require that all research subjects give their informed consent in writing in order to participate in any clinical trial. Clinical trials are conducted according to protocols that describe in detail, among others, the objectives of the trials, the parameters used to control the safety of use and the criteria for evaluating efficacy.

In addition, EU Regulation 2016/679 of the European Parliament and of the Council of April 27, 2016, on the protection of physical persons with respect to the processing of personal data and the free circulation of data (GDPR), that became effective on May 25, 2018, significantly increases the rights of citizens, giving them more control over their personal data. French national law was brought into compliance with the GDPR through the updating of French Law no. 78–17 of January 6, 1978, on computer processing, data files and freedom (Law no. 2018-493 of June 20, 2018, and re-drafting Order no. 2018-1125 of December 12, 2018).

In compliance with the data protection law, personal data collected as part of clinical trials is subject to a declaration with the French data protection authority (CNIL). Patients have a right to access and correct this data. Finally, patients must be regularly informed of the conduct of clinical trials and the overall results of the research.

The conduct of clinical trials must therefore comply with complex regulations throughout the different phases of the process that rely on the principle of the informed consent of the patient to whom the product (s) will be administered. The information relating to the objective, the methodology and the duration of the research, as well as the expected benefits, the constraints and the foreseeable risks due to the administration of the products provided are summarized in a written document provided to the patients prior to their participation in the research.

9.3.1 Clinical trial authorization in the European Union

In the European Union, the texts governing clinical trials are currently based on Directive n°2001/20/EC of April 4, 2001, relating to the application of good clinical practices in the conduct of clinical trials of drugs for human use, while waiting for the application of Regulation (EU) No. 536/2014 of the European Parliament and of the Council of April 16, 2014 repealing Directive 2001/20/EC. Each Member State had to transpose this directive into its national law.

In France, this is Law no. 2004-806 of August 9, 2004, relating to public health policy and Decree no. 2006-477 of April 26, 2006, amending the title of the Public Health Code dedicated to biomedical research, supplemented by several Ministerial Decrees of May 24, 2006. An interventional clinical trial bearing on a drug must first receive a favorable opinion from a French Institutional Review Board (IRB) and authorization from the ANSM.

Opinion of the Central Ethics Committee: the three types of research (i) interventional research which includes an intervention on the person not justified by his usual care; (ii) intervention research which involves only minimal risks and constraints; (iii) non-interventional research) can only be implemented after a favorable opinion from the competent CPP.

Pursuant to article L.1123-7 of the public health code, the competent CPP - now selected randomly under article L.1123-6 of the public health code - must in particular give its opinion on the conditions of validity of the research, in particular as regards the protection of participants, the information communicated to them and the procedure followed to obtain their informed consent, as well as the relevance of the research, the satisfactory character of the evaluation of the expected benefits and risks, the adequacy between the objectives pursued and the means implemented, the qualifications of the investigator (s), the amounts and terms of compensation for participants and the terms of recruitment of participants.

Authorization from the French National Agency for Medicines and Health Products Safety (ANSM): after submission of the complete trial authorization application file, containing an administrative file, a research file including in particular the protocol and the investigator brochure and, where applicable, a technical file relating to the product, the acts performed and methods used, as well as the opinion of the ethics committee, the ANSM can inform the sponsor that it is opposed to the implementation of the research or ask it for any additional information to decide on its request. The latter can then modify the content of his research project and submit his modified or completed request to ANSM; procedure which, however, cannot be followed more than once. If the sponsor does not modify the content of his request or does not produce the requested elements within the allotted time, he is deemed to have waived his request.

Generally speaking, the Agency evaluates the efficacy and the quality of the products used during the research, with the goal to guarantee the safety of the persons involved in biomedical research. The French Institutional Review Board (IRB) gives its opinion on the validity conditions of the research, in particular on the protection of the participants, their information and the methods of collecting their informed consent, as well as the general relevance of the project, whether the evaluation of benefits and risks is satisfactory, and the adequacy of the resources implemented for the objectives pursued. Since the application of the Jardé Law no. 2012-300 of March 5, 2012, relating to research involving humans, amended by Order no. 2016-800 of June 16, 2016, and by the publication of Decree no. 2016-1537 of November 16, 2016, the previous regional authority of the IRBs is now national. The time for approval of applications for authorization from the authorities cannot exceed 60 days starting from the receipt of the full dossier.

In accordance with Article L. 1123-11 of the public health code, in the event of a risk to public health or of a lack of response from the sponsor or if the ANSM considers that the conditions under which the research is conducted no longer corresponds to those indicated in the authorization request or do not comply with the provisions of the CSP, it may, at any time, request that modifications be made to the methods of carrying out the research, to any document relating to the research, as well as suspend or ban this search.

The ANSM decision of November 24, 2006 sets the rules of good clinical practice ("GCP") in the conduct of clinical trials on medicinal products for human use, provided for in Article L. 1121-3 of the public health code. The purpose of the public health code is to ensure the reliability of data from clinical trials and the protection of trial participants. GCPs should be applied in all clinical trials, including pharmacokinetic, bioavailability and bioequivalence studies conducted in healthy volunteers

Current European regulations on clinical trials of drugs for human use is governed by EU Regulation no. 536/2014 of April 16, 2014. The major points of this regulation are the following:

- Applications for single authorization must be filed through the portal associated with the European Union database, including a common portion evaluated jointly by all participating members of the European Union and a national portion covering the ethical and operational aspects of the trial evaluated by each member of the European Union independently. A single decision covering all aspects of the application is delivered by each of the Member States concerned;
- Increased transparency regarding clinical trials authorized in the EU: the European Union database is a source of public information, notwithstanding the protection of personal data, the protection of confidential commercial data and the protection of confidential communication between Member States and the supervision of trials between Member States. For drugs in development, the public information includes the authorization of the clinical trial, general information on the trial and the summary of the final results.

Depending on the processing of personal data carried out during clinical trials and the nature of these trials, it may be necessary to carry out formalities with the National Commission for Informatics and Freedoms (“CNIL”). The sponsor of the clinical trial may be

required to make a commitment to comply with one of the CNIL's reference methodologies through a simplified notification procedure or to submit an authorization request if necessary. Patients then have in all cases the right to access and rectify their personal data as well as the right to oppose their collection / withdraw their consent in accordance with Law No. 78-17 of 6 January 1978, as amended and the General Data Protection Regulation (GDPR). The European Commission published on April 10, 2019 questions / answers on the interaction between Regulation (EU) No 536/2014 of the European Parliament and of the Council of April 16, 2014 on clinical trials of medicinal products for human use (the "Regulation on clinical trials") and the GDPR, carried out after consultation of the European Data Protection Council. They relate to the general obligations put in place by the Regulation on clinical trials in relation to those of the GDPR, the responsibility for determining the legal basis for the processing of personal data in the context of a clinical trial, the legal basis for the processing of personal data of subjects of a clinical trial in the context of these trials (primary use), the difference between informed consent (Regulation on clinical trials) and consent within the meaning of the GDPR, or the meaning of the GDPR requirements regarding the information to be provided to clinical trial subjects.

9.3.2 Authorization of clinical trials in the United States

In the United States, a clinical trial can only begin after it obtains authorization from the Food & Drug Administration (FDA) and from an ethics committee, the Institutional Review Board (IRB). An Investigational New Drug (IND) application must be filed with the FDA and must be approved before a clinical trial can be started in humans. This application includes the early scientific data of the product being studied, the manufacturing data, the preclinical and clinical data (including the clinical trial protocol). Unless the FDA objects, the application for an IND is approved 30 days after receipt. The FDA may, at any time, request that a clinical trial that is planned or in progress be interrupted. This temporary interruption is maintained as long as the FDA has not obtained the information that it requires. Moreover, each ethics committee (IRB) having authority over an investigating site, can delay, even temporarily or permanently interrupt, a clinical trial if it believes that the safety of patients is not ensured or in the case of noncompliance with regulatory requirements.

9.3.3 Publication of information on clinical trials

In the United States, sponsors of clinical drug trials regulated by the FDA must register and publish a certain amount of information related to the clinical trial and its results, available publicly on the website www.clinicaltrials.gov.

In Europe, the information on the clinical trial as well as the results at the end of study are made public for Phase 2 to 4 trials, as well as for any pediatric study on the website www.clinicaltrialsregister.eu.

9.4 Regulation of marketing authorizations

In order to be marketed, all drugs must obtain a marketing authorization (MA) delivered by the competent European or national authorities (the ANSM in France, the EMA in Europe, the FDA in the US, etc.) and after filing an application for an MA or NDA (New Drug Application). This application will be evaluated according to scientific criteria of quality, safety and efficacy.

The MA application is drafted in the standardized CTD (Common Technical Document) format, used in Europe, the United States and Japan. This application includes detailed and precise information on the product, in particular its composition, the way it works, the associated quality elements, its toxicity, efficacy and safety. It also describes the manufacturing process of the active substance, the finished product manufacturing process and the preclinical and clinical studies.

In Europe, applications for marketing authorization (MA) can be made via two types of procedures: Community procedures used when the drug is innovative or intended for several member states of the European Community and the national procedure for drugs that are not marketed in more than one Member State. According to the Community procedure used, the EMA or the company chooses, respectively, the reporting State or the referring State.

A drug may be withdrawn from the market, either directly by the company or at the request of health authorities, when a serious problem arises, in particular concerning safety or noncompliance with manufacturing rules.

9.4.1 Community procedures

Access to the Community market has been, since January 1, 1998, subject either to the centralized procedure (defined in Regulation no. 2309/93/EEC amended by Regulation no. 726/2004/EEC), or to the mutual recognition procedure (specified in Directive 2001/83/EC amended by Directive 2004/27/EC) and, since October 2005, to the decentralized procedure (specified in Directive 2004/27/EC).

- **THE CENTRALIZED PROCEDURE** (mandatory for products from biotechnology, new products developed in the field of cancer and drugs with orphan drug status): a single registration application file must be submitted to the EMA. The Committee for Medicinal Products for Human Use (CHMP) of the (composed of one member appointed by each Member State of the European Union and country of the European Economic Area, and of five scientific experts) issues its recommendation with respect to the approval of the drug with the European Commission. The European Commission then makes the final decision to deliver the marketing authorization (MA), valid throughout the European Union. The drug can then be marketed in all member states of the European Union.

  - If granted, the MA is valid for five years, without prejudice to paragraphs 4, 5 and 7 of Article 14 of the Regulation (Article 14). The MA may be renewed after five years, based on a reassessment of the benefit/risk ratio carried out by the competent authority. Once renewed, the MA is in principle valid for an unlimited period, unless the Commission decides otherwise in relation to pharmacovigilance (Article 14).
  - Pursuant to article 10 bis of Regulation 726/2004, after having issued the MA, the EMA can thus require its holder to carry out (i) post-authorization safety studies if there are concerns regarding the safety risks posed by an authorized medicinal product and / or (ii) post-authorization efficacy studies when the understanding of the disease or clinical methodologies indicate that previous efficacy evaluations may need to be significantly revised (Article 10 bis)

- **MUTUAL RECOGNITION PROCEDURE AND THE DECENTRALIZED PROCEDURE:** these enable harmonized national marketing authorizations to be more easily obtained in several Member States. These two procedures are founded on the recognition, by the competent national authorities, of the first evaluation made by the regulatory authorities of one of the Member States (Reference Member State).

  The decentralized procedure is provided for by Directive 2001/83/EC of the European Parliament and of the Council of November 6, 2001, as amended. It can be used when the applicant wishes to authorize a medicine in more than one Member State, provided that this medicine is not already authorized in a Member State. Under this procedure, the applicant submits an application based on an identical dossier to the competent authorities of each of the Member States, one of which is selected by the applicant to act as Reference Member State ("RMS"). The competent authorities of the RMS prepare a draft assessment report for the medicinal product, a draft summary of product characteristics ("SPC") and a draft labeling and package leaflet, which are sent to the other Member States, referred to as the Member States concerned ("MS") for approval and to the applicant.
  - The mutual recognition procedure is for its part provided for by Directive 2001/83/EC of the European Parliament and of the Council of November 6, 2001, as amended. It can be used when the applicant wishes to authorize a medicinal product in more than one Member State and this medicinal product has already received a Marketing Authorization at the time of the request in a Member State.

- **NATIONAL PROCEDURE**: The MA, issued at national level by the competent authorities of the EEA Member States, covers only its respective territory. It can be requested when the medicinal product concerned is not within the scope of the centralized procedure

- Registration of an international drug (in more than one country of the European Union) must use one or the other of these procedures.
- Products developed by the Company in immuno-oncology or in transplantation, all derived from biotechnology, are therefore subject to the centralized procedure for their application for marketing authorization.

9.4.2 Registration procedures outside the EU

Companies that wish to market their products outside of the European Union must again file applications to register the drugs with the national authorities of the countries concerned, for example with the FDA in the United States, the Kosheisho (Pharmaceutical and Medical Device Agency, PMDA) for Japan.

In the United States, the application for drug approval must be submitted to the FDA that has regulatory powers over all pharmaceutical and biological products intended to be marketed in American territory.
Applications for marketing authorization must be submitted to the FDA, depending on whether it is a request for the approval of a new drug (NDA, New Drug Application) or a request for a biological product license (BLA, Biological License Application). The application must provide all information enabling the FDA to determine whether the drug is safe and effective for the targeted

indication, whether the benefits are greater than its risks, whether the summary of the product characteristics is adequate and whether its manufacturing process and the controls intended to ensure quality enable the identity, dosage, quality and purity to be guaranteed.

9.4.3 Exceptions to the usual registration procedures

Exceptions to the traditional procedure for granting a marketing authorization (MA) as described above exist to enable quicker marketing of drugs.

In Europe, the following exists:

- **CONDITIONAL MA:** this is valid for one year instead of five. It is only granted when the drug meets unmet medical needs and if the benefits for public health are greater than the risk linked to an uncertainty due to an incomplete evaluation of the drug. The delivery of a conditional marketing authorization is subject to the finalization of clinical trials and / or the completion of new trials, in order to confirm the benefit / risk of the drug.

- **ACCELERATED ASSESSMENT:** the evaluation procedure is accelerated (150 days instead of 210 days) when a drug presents a major interest from a public health standpoint or represents a therapeutic innovation. The PRIME project (priority drugs), an EMA initiative launched in 2015, allows the early identification (from Phase 2/3) of drugs eligible for the accelerated procedure and enhanced assistance by scientific advice and dialogues throughout development.

- **MA FOR EXCEPTIONAL CIRCUMSTANCES:** a MA may be authorized on an exceptional basis, and may be reevaluated each year, when the drug's evaluation file cannot initially be submitted completely, for example, when a therapeutic indication applies to too few patients, or the collection of necessary data would be unethical.

- **TEMPORARY AUTHORIZATION FOR USE (TAU) :** A Member State may use a drug that does not yet have marketing authorization in the country, in order to treat serious or rare diseases that do not have adequate treatment. In France, a Temporary Authorization for Use may be given by the ANSM for a particular patient (nominative TAU) or for a group of patients (cohort TAU).

  EARLY ACCESS AUTHORIZATION (EAA): Early access authorization scheme enables to accelerate the access to innovation for drugs without any alternative and used in rare, severe or incapaciting diseases, to verify as early as possible if the expected benefits are relevant thanks to the data collection in real life and to their analysis. It applies to innovative drugs and is focused on authorizing drugs at early stage of their development (pre-Market Authorization, MA) or awaiting their eligibility to reimbursement (post-MA) until they are included within the common law framework of health product authorization and reimbursement. The early access is now authorized by the HAS (Haute Autorité de Santé), upon notice from the ANSM (Agence Nationale de Sécurité du Médicament) for drugs without MA in the considered indication.

- **COMPASSIONATE USE** is a treatment option that allows for the use of an unauthorized medicine. Under strict conditions, products in development can be made available to nominative patients who have a disease with no satisfactory authorized therapies and who cannot enter clinical trials (https://www.ema.europa.eu/en/human-regulatory/research-development/compassionate-use).

In the United States, procedures allow more rapid development and market access for drugs for serious pathologies for which there is not yet any appropriate treatment or if there is a high medical need (cancer, AIDS, Alzheimer's disease, etc.):

- **"ACCELERATED APPROVAL":** this procedure is intended to allow marketing of promising products to treat serious pathologies on the basis of initial evidence prior to the formal demonstration of patient benefits. The FDA may in fact rely on an effect, an alternative result or any other result that has reasonable chances of being predictive of a clinical benefit and not on a well-defined clinical criterion. As such, a substitute result or marker (surrogate endpoint) is a result obtained in the laboratory or a physical sign that does not constitute, in itself, a direct measure of how the patients feel, their organ functions or their survival, but enables a therapeutic benefit to be expected. The MA granted may be considered as a provisional approval with written commitment to complete the clinical studies that demonstrate true benefit for the patient. This procedure corresponds to the "Conditional MA" procedure in Europe.

- **"PRIORITY REVIEW":** this procedure is used for drugs treating serious diseases that present a major therapeutic advance or provide treatment for a disease for which there is no suitable therapy. This procedure means that the time for evaluation

of the application by the FDA is reduced from ten months to six months. This procedure corresponds to the "Accelerated Assessment" in Europe.

- **"FAST TRACK DESIGNATION":** a program of interactions with the FDA to facilitate the development and accelerate the review of new drugs that are used in the treatment of serious or potentially fatal diseases that are likely to respond to an unmet therapeutic need. The advantage of this process is that the company may benefit from more frequent meetings with the FDA in order to discuss the product development plan and ensure the appropriate data are collected for the MA. Fast Track designation does not necessarily lead to the Priority Review procedure nor to Accelerated Approval.

- **"BREAKTHROUGH THERAPY DESIGNATION":** this procedure, put in place in 2012, aims to accelerate the development and review of drugs for treating serious diseases or potentially fatal diseases, and for which the preliminary clinical proof demonstrates substantial improvement from the drug with respect to treatments available on a clinically significant criterion. A drug that is designated "Breakthrough Therapy" may receive the following:
  - all the special characteristics of the Fast Track designation;
  - starting at the Phase 1 clinical trial, intensive support in a development program for effective drugs;
  - an organizational commitment involving senior managers.

If additional research or experiments demonstrate that a product presents risks while being marketed, the FDA can require it to be withdrawn immediately. In addition, the FDA can withdraw a marketing authorization for other reasons, in particular if studies after authorization are not conducted with the necessary diligence.

9.4.4 Orphan drugs

There is a specific procedure for the authorization for orphan drugs.

Orphan drugs are drugs used for the diagnosis, prevention and treatment of fatal or very serious and rare diseases. To be qualified as rare or orphan within the European Union, a disease must affect fewer than 1 person out of 2,000, and in the United States the disease must affect fewer than 200,000 persons.

These drugs are called "orphan" because the pharmaceutical industry has little interest in the usual market conditions to develop and market products intended only for a limited number of patients (so-called orphan diseases). For the pharmaceutical companies, the cost of marketing a product recommended for a rare disease might not be covered by the expected sales in this market.

In Europe, legislation was adopted to promote treatments for rare diseases. By virtue of Regulation no. 847/2000/EC of December 16, 1999, as amended by Regulation no. 847/2000/EC of April 27, 2000, a drug is considered an orphan drug if its developer demonstrates, in an application filed with the EMA, that it is used for the treatment of a so-called orphan disease in the European Union, or when it is used for the treatment of a disabling or serious and chronic disease for which there is yet no treatment or satisfactory treatment, and that in the absence of incentive measures, the costs incurred in the development cannot be covered by the profits from sales with a ten-year exclusivity in Europe.

In the United States, the 1983 American law on orphan drugs (Orphan Drug Act) combines several laws encouraging the development of treatments for rare diseases. The Orphan Drug Act also provides for the chance to obtain subsidies from the American Government to cover clinical trials, tax credits for covering research expenses, possible waiver of filing costs when applying for registration with the FDA and seven years of exclusivity of the active ingredient for the given indication in the case of a marketing authorization.

If the orphan drug status is obtained, the product then receives an exclusive marketing period, during which no similar product can be marketed for the same indication, as well as a waiver of regulatory fees and other advantages.

9.5 French Sunshine Act - Transparency of interests

Decrees no. 2013-414 of May 21, 2013 "on the transparency of benefits granted by companies manufacturing or marketing health and cosmetic products intended for human use" and no. 2016-1939 of December 28, 2016, on the public declaration of interests and transparency of benefits, specify the conditions of public "transparency" concerning relations (benefits procured or agreements made) between the companies that introduce or sell health and cosmetic products and some healthcare providers. As soon as the Company markets drugs, it must then make public:

- the information relating to agreements existing with healthcare professionals and other similar persons (except for agreements governed by Articles L.441-3 and L.441-7 of the French Commercial Code);
- all compensation, benefits in kind or cash given in an amount greater than or equal to € 10;
- The information is centralized on a single website (www.transparence.sante.gouv.fr) under the responsibility of the French Ministry of Health.

These requirements took effect on July 1, 2017. Similar resources exist in other countries, especially the United States (US Sunshine Act).

The Public Health Code also contains "anti-gift" provisions which provide for a general ban on companies that manufacture or market health products from making payments and benefits to health professionals, with limited exceptions, and strictly defines the conditions under which these payments or benefits can legally be granted. The provisions arising from Law No. 2011-2012 were amended by Ordinance No. 2017-49 of January 19, 2017, which notably extended their application to a wider range of legal and physical persons, clarified the scope of operations excluded from the ban and those authorized under certain conditions, and provided for a new authorization process. The decree of August 7, 2020 set the amounts for which the service, depending on the service provided, is considered negligible and does not require any declarative action. A second decree of August 7, 2020 defined the amounts beyond which the agreement is subject to an authorization regime, the amounts less than or equal to these amounts requiring a simple declaration. The decree also provides the reporting schedule to the competent authority.

10 Information on trends

10.1 Main trends since the end of the last fiscal year

With five of its product candidates in clinical development, including three with leading pharmaceutical partners, and the progress of new preclinical programs towards the clinical phase, the Company is entering the next stages of its growth, financially supported, in particular, by partnerships with international pharmaceutical groups and grants from Bpifrance:

PROPRIETARY PRODUCTS IN CLINICAL DEVELOPMENT

TEDOPI® (COMBINATION OF NEOEPITOPES FROM TUMOR ANTIGENES)

- **Confirmatory Phase 3 clinical trial of Tedopi® in preparation in advanced non-small cell lung cancer** based on the positive results from Atalante-1 trial in third line therapy after secondary resistance.

  Following the positive recommendations from the FDA "Type C" meeting and to the scientific advice from the EMA, OSE Immunotherapeutics is preparing a new confirmatory Phase 3 trial to support the regulatory registration of Tedopi® in second line trial. This confirmatory phase 3 clinical trial will evaluate Tedopi® versus chemotherapy standard of care, after failure and secondary resistance to checkpoint inhibitors. Tedopi® will be administered in second line treatment, after a platinum-based chemotherapy followed by a checkpoint inhibitor maintenance treatment of at least 12 weeks. Only HLA-A2 positive patients with NSCLC will be eligible to this trial.

  Moreover, patients can benefit from Tedopi® through compassionate use programs in third or further lines of treatment (post chemotherapy and immunotherapy) currently approved in France, Italy and Spain, confirming thereby the significant medical need for new therapeutic alternatives.

  At the same time, given the significantly strengthened value of Tedopi® due to positive phase 3 results, the Company is continuing to explore any potential partnering opportunities for the product.

- **The Phase 2 clinical trial, TEDOPaM:** Tedopi® is being evaluated in the Phase 2 clinical trial, TEDOPaM, sponsored by the GERCOR cooperative oncology group in HLA-A2 positive patients with locally advanced pancreatic cancer.

  The first interim results from this Phase 2 clinical trial of Tedopi® versus FOLFIRINOX in advanced or metastatic pancreatic cancer have been presented at the 2022 ASCO (American Society of Clinical Oncology) meeting. The primary endpoint of the trial is the one-year survival rate (Fleming- futility analysis; null hypothesis <25%), and the key secondary endpoint was the Time to maintenance Strategy Failure (TSF= time maintenance + FOLFIRI reintroduction).

  The interim results refer to the 29 randomized HLA-2 positive patients with no progression after 8 cycles of FOLFIRINOX: 9 patients included in standard arm A (FOLFIRI) with 44% of 1-year Overall Survival (OS) rate and one partial response (11%); 10 patients in experimental arm B (Tedopi® monotherapy) with 40% of 1-year OS rate and one partial response (10%); 10 patients in arm C (nivolumab + Tedopi®) with 30% of 1-year OS rate and no partial response.

  Tedopi® as maintenance monotherapy showed a favorable safety profile and encouraging time to strategy failure warranting further evaluation. Nivolumab + Tedopi® was associated with poorer outcomes leading to the closing of this arm.

  Following an Independent Data Monitoring Committee (IDMC) recommendation, the study is ongoing with an amended protocol comparing a maintenance treatment Tedopi® in combination with FOLFIRI versus FOLFIRI chemotherapy after treatment with FOLFIRINOX.

  **FOLFIRINOX: a chemotherapy regimen combining folinic acid, fluorouracil, irinotecan and oxaliplatin*
  ***FOLFIRI: a chemotherapy regimen combining folinic acid, fluorouracil and irinotecan*

OSE-279 (MONOCLONAL ANTI-PD1 ANTIBODY)

- OSE-279, the backbone of the BiCKI® bispecific fusion protein platform, is a humanized anti-PD1 monoclonal antibody. It is under Phase 1/2 clinical trial since December 2022 in advanced solid tumors and lymphomas. Thus the Company owns a patented anti-PD1. This first clinical study will also allow the Company, at a later stage, to explore OSE-279, the backbone of OSE's BiCKI® platform, in combination with other OSE drug candidates or with external assets accessed through potential new partnerships with biotech or pharmaceutical companies.

COVEPIT (COMBINATION OF EPITOPES FROM VIRAL PROTEINS)

- On March 16, 2022, the Company announced the positive analysis of the long-term immune T response of CoVepiT with positive immunological results at 6 months on the memory T response in vaccinated subjects. At the same time, the resolution of local indurations related to the T cells' mechanism of action and a good tolerability profile were confirmed.
- OSE Immunotherapeutics has thus validated the concept and reference model according to which long-term immunity against coronavirus can be achieved in humans with its T cell-based vaccine platform inducing long-lasting memory T cells.
- For immunocompromised patients, new treatments such as monoclonal antibodies or antiviral treatments are available. Regular booster shots of registered vaccines are also recommended for this fragile population with a deficient antibody response. With these new treatments available and multiple vaccine boosters recommended for these patients, further clinical development of CoVepiT is currently difficult.

PRODUCTS IN PARTNERSHIP IN CLINICAL DEVELOPMENT

OSE-127/S95011, IL-7 RECEPTOR ANTAGONIST

- OSE-127/S95011 is being developed in partnership with Servier as part of a license option agreement. Two clinical trials evaluating the product are ongoing: a phase 2a in primary Sjögren syndrome conducted by Servier and a phase 2 in ulcerative colitis conducted by OSE Immunotherapeutics.
- The article published in 'The journal of Immunology' in 2023 reported OSE-127 phase 1 results showing the product's safety and efficacy and the interest of a differentiated and novel mechanism of action of the only monoclonal antibody with purely IL-7R antagonist properties in the treatment of chronic autoimmune diseases.
- Both clinical trials are ongoing: in the Sjögren syndrome (sponsor Servier) with a trial's completion expected in the first semester 2023, and in ulcerative colitis (sponsor OSE). The product's good safety profile is confirmed.
- Besides immuno-inflammation, OSE-127 has also demonstrated great therapeutic potential in Acute Lymphoblastic Leukemia (ALL), a very aggressive tumor arising from B or T cell precursors. This preclinical program (B and T-ALL) was presented in December 2022 at the 'American Society of Hematology' (ASH) annual meeting. This oral presentation has received the merit-based "Abstract Achievement Award" from the ASH peer-review committee. This research program, being conducted through a collaborative research program between OSE Immunotherapeutics and the University Medical Center Schleswig-Holstein in Kiel (Germany), aims at evaluating OSE-127's therapeutic potential aims at targeting and blocking the high and dysregulated IL-7R-expression observed in more than 80% of B- or T-ALL patients. Relapse remains a clinical challenge in B-ALL in high-risk patients and treatment options for T-ALL remain very limited. Novel targeted immunotherapy approaches are urgently needed to prevent relapse and to treat refractory diseases in ALL patients.

FR104 (CD28 ANTAGONIST)

- The positive results of the Phase 1 clinical proof-of-concept trial of FR104, combined with the preclinical tolerability profile and the efficacy data for a large number of preclinical models of inflammatory and autoimmune diseases support the continuation of the product's clinical development in immuno-inflammatory diseases and transplants.
- Since December 2020, FR104 is currently undergoing a Phase 1/2 clinical trial in patients who have received a renal transplant. This study aims to assess the safety, tolerability, pharmacokinetics, pharmacodynamics and efficacy of FR104 in patients who have received a renal transplant. It is carried out under a clinical collaboration agreement between OSE Immunotherapeutics and the Centre Hospitalier Universitaire de Nantes, which is the sponsor (the product and the pharmacological development costs being supported by the Company).
- In parallel, FR104 is being developed as part of a worldwide licensing agreement with Veloxis Pharmaceuticals Inc., (April 2021) for the development in the prophylaxis of organ rejection in solid organ transplant patients.
- At the end of January 2022, Veloxis Pharmaceuticals, Inc. received acceptance of the New Investigational Drug (IND) application in the United States to set up a Phase 1 clinical trial of VEL-101/FR104, sponsored and conducted by Veloxis. As part of the global licensing agreement signed in April 2021, this first step triggered a €5 million payment from Veloxis Pharmaceuticals, Inc. to OSE Immunotherapeutics.

- Moreover, Veloxis Pharmaceuticals has obtained fast track designation from the U.S. Food & Drug Administration (FDA) for VEL-101/FR104. This product is an immunosuppressive agent being developed for prophylaxis of renal allograft rejection in recipients of kidney transplants. Fast track designation, granted to therapies having the potential to fill an unmet medical need, opens the pathway to an accelerated registration process.
- The first participant in this US trial has been included in May 2022.

BI 765063 (OSE-172) (ANTI-SIRP α MONOCLONAL ANTIBODY)

- BI 765063 is developed as part of a collaboration and license agreement with Boehringer Ingelheim (April 2018) for the development, registration and marketing of the product in immuno-oncology. The product candidate is in a Phase 1 clinical trial in patients with advanced solid tumors.
- The results of Phase 1 dose escalation of BI 765063 in monotherapy and in combination showed a good tolerability, without haematological toxicity and without reaching the maximum tolerated dose (MTD). In addition, promising early efficacy of BI 765063 was observed both alone and in combination, especially in advanced hepatocellular carcinoma, endometrium and colorectal cancer, including microsatellite stable (MSS) tumors.
- Based on the promising first results from Phase 1 clinical trial of BI 765063 in monotherapy and in combination, the Company is progressing in 2023 on the expansion Phase 1 in cohorts in several cancers: colorectal and endometrium cancer (sponsor OSE Immunotherapeutics) and a new cohort in hepatocellular carcinoma and head and neck cancer (sponsor Boehringer Ingelheim) to explore the potential on a combination approach of BI 765063 and ezabenlimab as a relevant therapeutic strategy in solid tumors.

MYELOID PLATFORM

OSE-230 (CHEMR23 AGONIST ANTIBODY)

- Resolution of inflammation is triggered by pro-resolving lipids activating GPCRs (G-Protein Coupled Receptor) targets. The ChemR23 GPCR is expressed on inflammatory myeloid immune cells, such as macrophages and neutrophils, and is over-expressed in tissues affected by chronic inflammatory diseases, such as lung inflammatory diseases or severe IBD (Inflammatory Bowel Disease) unresponsive to anti-TNF or anti-integrin therapies. ChemR23's over-expression is associated with chronic neutrophil accumulation in damaged tissues. OSE-230 is the first monoclonal antibody (mAb) to activate a pro-resolutive GPCR target (ChemR23). Its innovative mechanism of action drives inflammatory neutrophil tissue clearance through apoptosis and inhibition of the pathogenic NETosis* process (new preclinical advances presented at the 2022 PEGS (*Protein & Antibody Engineering Summit*) Europe. This mAb triggered resolution demonstrated positive preclinical efficacy in chronic colitis or chronic arthritis models with significant decrease in tissue fibrosis and restoration of tissue healing.

  ** NETosis is a program for formation of neutrophil extracellular traps (NETs), which consists of modified chromatin decorated with bactericidal proteins from granules and cytoplasm. Recent research has highlighted that neutrophils, and in particular NETs that can be released upon activation, have central roles in the initiation and perpetuation of systemic autoimmune disorders and trigger complex and chronic inflammatory responses that lead to organ damage and fibrosis.*

This breakthrough discovery opens the development pathway of OSE-230 in various chronic inflammations such as inflammatory bowel diseases, arthritis, type 1 diabetes, lung or kidney inflammatory diseases.

CLEC-1 (IMMUNE MYELOID CHECKPOINT)

- The OSE Immunotherapeutics teams have succeeded in characterizing the CLEC-1 myeloid checkpoint as a new therapeutic target in immuno-oncology and have identified monoclonal antibody antagonists that block this novel "Don't Eat Me" signal. They increase both the phagocytosis of tumor cells by macrophages and the uptake of antigens by dendritic cells. The identification of CLEC-1 and its antagonists constitute an exciting innovative step in cancer immunotherapy.
- A scientific article (*CLEC-1 is a death sensor that limits antigen cross-presentation by dendritic cells and represents a target for cancer immunotherapy*) published in the peer-reviewed journal "Science Advances" in November 2022 describes the latest data of the preclinical program conducted with CLEC-1:
  - Overall, CLEC-1 genetic deletion leads to a profound reinvigoration of the tumor immune microenvironment by enhancing infiltrates of dendritic cell (antigen presenting cells), increasing memory and activated T lymphocyte infiltrates,

decreasing infiltrates of exhaustion marker PD1-expressing T lymphocytes and limiting the recruitment of immunosuppressive cells such as myeloid derived suppressor cells (MDSCs).

. Importantly, CLEC-1 blockade using monoclonal antibody treatment demonstrates robust anti-tumor activity, also by reinvigorating the tumor immune microenvironment in several preclinical oncology models, thereby faithfully recapitulating the effect of CLEC-1 genetic deletion in the context of human CLEC-1-expressing mice. Proprietary anti-CLEC-1 mAbs increase survival in monotherapy in orthotopic model of hepatocellular carcinoma while combination with chemotherapy increases preclinical tumor eradication in colon carcinoma model.

These fundamental discoveries and preclinical results showing that CLEC-1 is a novel myeloid checkpoint interacting with a new ligand TRIM-21 and highlighting the therapeutic potential of CLEC-1 antagonist antibodies (Abs) as innovative cancer immunotherapy.

(1) *Collaborative academic program between OSE Immunotherapeutics and Dr Elise Chiffoleau's research teams (Center for Research in Transplantation and Translational Immunology (CR2TI), UMR1064, INSERM, Nantes University at Nantes University Hospital.*

BICKI® PLATFORM

BiCKI®-IL-7

BiCKI®-IL-7 is a bifunctional therapy which targets PD1 and at the same times provides selectively the IL-7 pro-survival cytokine to restore exhausted T-cell function, disarms Treg suppressive activity and extends stem-like memory T-cells, the key T-cell subpopulation associated with anti-PD(L)1 clinical responses. In addition, the BiCKI®-IL-7v immunocytokine significantly improves the quality and durability of memory T lymphocytes in the tumor microenvironment (with T lymphocyte stem cells without immune exhaustion).

This immunotherapy has potential to address the high medical need of patients with cancers with primary or secondary resistance or that are refractory to immune checkpoint inhibitor treatments.

The Company has been invited to present the latest progress on BiCKI®-IL-7: *« Anti-PD1/IL7v immunocytokine promotes durable T-cell responses and overcomes anti-PD1 resistance »* at the American Association Cancer for Research (AACR) 2022 annual meeting

The monoclonal antibody OSE-279, the anti-PD1 backbone of the BiCKI® platform, is in Phase 1/2 clinical phase since end of 2022 in advanced solid tumors and lymphomas.

Given the Company's current activities, it has not provided any specific comments on the trends that may affect its recurring revenues and general operating conditions from the date of the last fiscal year ended December 31, 2021, until the publication date of this Universal Registration Document.

With a cash position as of March 31, 2023, of €15.6 million (not including the 2022 research tax credit (CIR) for a total amount of €5.4 million, nor the new equity or debt financing lines, nor the milestones expected in 2023 under the licensing agreements, the Company has the necessary cash to continue its activities for the next 12 months following the date of this Universal Registration Document.

This capital will enable the Company to accelerate and expand its portfolio of products in the clinical phase with the launch of three programs:

- The preparation of an international confirmatory phase 3 clinical trial of Tedopi®;
- The preparation of the preclinical steps of OSE-230, a new monoclonal antibody developed for the resolution of chronic inflammation and;
- The preparation of the preclinical steps for BiCKI®-IL7, a bifunctional therapy targeting PD1 while delivering the IL-7 cytokine to restore the functions of exhausted T cells and to rejuvenate effector memory T cells.

This capital will also finance its development costs for ongoing clinical studies on:

- Tedopi® with the various exploratory Phase 2 clinical studies in pancreatic cancer, ovarian cancer and NSCLC;
- OSE-127/S95011 in the continuation of its Phase 2 clinical step;
- BI 765063/OSE-172 in its Phase 1 clinical step and cohort expansion, mainly funded by its partner;

As well as research on earlier products.

The reader is invited to refer to Section 3.5 of this Universal Registration Document covering financing needs.

10.2 Trends, uncertainties, demands, commitments or events that are reasonably likely to have a material effect on the Company's prospects

The Russia-Ukrainian conflict since February 2022 has affected the global economic environment.

At this point, Management cannot reliably assess the impacts that this crisis may have on the Group's business should it continue. However, Management considers that the medium-term impact should be moderate and should not hinder its ability to continue as a going concern.

If the crisis were to continue, the impacts could be the following:

- The pace of recruitment in international clinical trials may be reduced due to hospital closures or the inability of patients to go to hospitals;
- The rate of patient inclusion could be reduced due to the impossibility of supplying the product to hospitals;
- The Company may also be subject to subcontractor prioritization policies, particularly for clinical batch production of its products or for regulatory toxicology studies.

The Company's management observes that the life sciences and biopharmaceutical sectors are more volatile, some difficulties have been observed on the financial markets. Moreover, the outlook might be impacted by the global economic and geopolitical situation, supply chains, inflation and energy supply might be impacted by new major restrictions. The current outlook therefore reflects a greater degree of uncertainty than usual.

For example, the price of certain primary products, research services and raw materials used by OSE Immunotherapeutics has increased, sometimes very sharply.

11 Profit/(loss) forecasts or estimates

The Company does not make any profit forecast or estimate.

12 Administrative, management and supervisory bodies, and senior management

12.1 Management and directors

12.1.1 Composition of the Board of Directors

As of the date of this Universal Registration Document, the Board of Directors is comprised of 9 members:

First name – Last name or corporate name of the member	Main position in the Company	Main position(s) outside the Company
Dominique Costantini	- Director of Development - Chairwoman - Director	- Director of Smart Immune
Maryvonne Hiance	- Vice-Chairman of the Board of Directors - Director	- Vice Chairman of the Atlanpole Biotherapies - Chairman of HealthTech For Care - Chairman of Olgram - Director of Pherecydes Pharma
Elsy Boglioli	- Director	- Founder and Chief Executive Officer of Bio Up - Independent Director of Gensight - Independent Diroctor of Laverock Therapeutics - Member of the Supervisory Board of Inova Software, Metafora Biosystems, Womed
Jean-Patrick Demonsang	- Director	- Chairman of Demonsang Consulting SAS - President of the Strategic committee of Medjeduse SAS
Brigitte Dréno	- Director	- Consulting activities: BMS, Fabre Oncology, Almirall, Biofortis, Galderma, Sun Pharma - Vice-president, Sciences -Nantes University - Coordinator RHU SUccESS Elected member of the « Académie de Médecine »
Didier Hoch	- Director	- Chairman of Pherecydes Pharma - Director of the University of the Underground Charity Foundation - Strategic Advisor for Goliver Therapeutics
Alexandre Lebeaut	- Director	- Immunorx Pharma Inc., Director - Object Pharma Inc., Director - Calypso Biotech, Director
Nicolas Poirier	- Chief Executive Officer and Chief Scientific Officer - Director	- Member of the Scientific Board of MabDesign and MAbSillico
Gérard Tobelem	- Director	- Director of Dendrogenix

BIOGRAPHIES OF THE MEMBERS OF THE BOARD OF DIRECTORS

The 9 members of the Board of Directors combine international expertise in drug development, marketing, industry and finance with experience working with listed biotechnology companies.

Dominique Costantini — Chairwoman of the Board of Directors

Since co-founding OSE in 2012, Dominique Costantini has raised private equity funds in 2014, completed the Company's IPO in 2015, acquired Effimune in 2016 to lead the Company's development programs and contributed to the partnership agreements implemented in 2016 and 2018. She is the founder and former Chief Executive Officer of BioAlliance Pharma (1997–2011), listed on Euronext Paris end of 2005 and which was renamed Onxeo in 2014. Dominique has designed, developed and secured approval for innovative cancer therapies. Three successful stock market fundraisings were then based on product development benchmarks: two innovative products were approved in Europe and the United States. She has established international industrial partnerships, signing contracts worth more than €130 million. Dominique gained more than 15 years of operational management experience in the pharmaceutical industry while working at HMR (now Sanofi). She led R&D and drug marketing activities from research to market in fields including immunology, endocrinology, inflammation, infection and oncology. Medical Doctor, Immunology – René Descartes University – Paris V.

Maryvonne Hiance — Vice Chairwoman of the Board of Directors, Director

Maryvonne, who was previously the Chairman and co-founder of Effimune, is an engineer who specializes in nuclear science. For 14 years she managed a neutron studies program at Framatome (Areva). Over the past 20 years, she has also led various innovation biotechnology companies: SangStat Atlantic (the parent company SangStat medical corporation was acquired by Genzyme in 2003 for its product portfolio in immunosuppression and transplantation); she also led the innovation companies DrugAbuse Sciences and the company TcLand. Maryvonne founded and managed Strategic Ventures, a consulting firm that works with technology companies. Maryvonne Hiance has been a member of the French Strategic Council for Innovation and has served as advisor to the French SMEs and Industry Ministry. From 2016 to 2021, she was successively Chairman and then Vice-Chairman of France Biotech.

Elsy Boglioli - Director

Elsy Boglioli is the founder and Chief Executive Officer of Bio-Up, a healthcare consulting company that supports companies in their high growth or transformation phases, mainly in the field of cellular and gene therapies. She has extensive expertise and a large network in pharma and medtech companies.

Elsy is a graduate of the École Polytechnique de Paris and holds a master's degree in economics and management from the Pompeu Fabra University in Barcelona (Spain). She also holds a degree in immuno-oncology from the Institut Gustave Roussy in Paris.

Jean-Patrick Demonsang — Director

Jean-Patrick Demonsang joined the Board of Directors of OSE Pharma in 2014. During his tenure as Chairman and Chief Executive Officer of Seventure Partners until 2013, he supported the activities of more than 150 companies. Seventure is now a leading venture capital firm in France, managing more than €500 million with a team of 12 experts in two investment sectors: information technologies and life sciences, in France and Europe.

Jean-Patrick Demonsang is also an entrepreneur who has created and led several SMEs, and he is currently leading an entrepreneurial project involving a theme park in the south of France. Jean-Patrick holds an MBA from HEC and a degree in physics.

Brigitte Dréno — Director

Professor Brigitte Dréno is head of the Dermatology Department at the Nantes University Hospital Center, which develops research expertise and groundbreaking treatments in skin oncology. Brigitte Dréno is also the Director of the Biotherapy Clinical Investigation Center and Director of the Unit of Cell and Gene Therapy, and as such closely oversees all immuno-oncology advances. She is Vice Dean of the Medical School. In collaboration with the academic leadership, she supports OSE Immunotherapeutics' R&D initiatives on the Nantes University campus.

Didier Hoch — Director

Didier Hoch is a medical doctor and Chairman of the Biovision Forum and of Big Booster, a start-up accelerator. He also serves as a director for listed companies, including Genticel and, previously, DBV Technologies. From 2000 to 2010, he was Chairman of Sanofi-Pasteur-MSD, a joint venture between Sanofi and Merck dedicated to vaccines. He also held a variety of managerial positions at

Rhône Poulenc Rorer and then Aventis where he was Vice Chairman for Middle East & Africa. He previously served as Chairman of the European Vaccine Manufacturers' Association and Chairman of the LEEM Biotechnology Committee.

Alexandre Lebeaut - Director

Alexandre Lebeaut has more than 25 years of relevant experience and leadership in innovation, research and development, ranging from preclinical to market, with successes particularly in the fields of immunology, oncology, immuno-inflammation and infectious diseases. He has held various international positions, mainly in the United States and in particular within Bluebird Bio, Sanofi, Novartis and Schering Plow Research Institute. More recently, Alexandre Lebeaut was "Executive Vice-President R&D and Chief Scientific Officer" at Ipsen in the United States. He currently leads a Maryland-based non-profit organization, I-ACT for Children (Institute for Advanced Clinical Trials for Children), dedicated to pediatric drug development.

Nicolas Poirier — Director representing the shareholder employees

Nicolas Poirier has been appointed Chief Executive Officer of OSE Immunotherapeutics in October 2022 while he has been chief scientific officer of OSE Immunotherapeutics since 2016. He joined the company in 2009 as project leader and then as director of scientific programs. Nicolas Poirier holds a Ph.D. in immunology and has a strong expertise in the development of immunotherapies. His role has been to implement innovative therapeutic strategies on new targets and pathways in immunology addressing severe pathologies with high therapeutic need, thus making a robust contribution to the Company's growth. He is the author of several high-level international publications in the area of immunotherapy.

Gérard Tobelem — Director

Gérard Tobelem won the first Diderot Innovation prize in 2006. He has held industrial, medical and scientific positions, including as Executive Chairman of the French Blood Establishment. Gérard Tobelem has held strategic roles at the French Ministry of Higher Education and Research. He has advised a variety of international pharmaceutical companies on their Research & Development strategies. Until 2018, he was non-executive Chairman of the Board of Directors of Theradiag. Previously, he taught hematology at Paris 7 University and was head of the Department of Blood Disorders at Lariboisière Hospital in Paris.

Addresses of directors

- Dominique Costantini – 286, boulevard Raspail – 75015 Paris
- Maryvonne Hiance – 35, rue Edison – 44000 Nantes
- Elsy Boglioli - 35, rue de Bellechasse - 75007 Paris
- Jean-Patrick Demonsang – 14, rue des Étangs – 44117 Saint-André des Eaux
- Brigitte Dréno – 10, rue Voltaire – 44000 Nantes
- Didier Hoch – 1508, route de Bellegarde – La Sauzée – 42210 Saint Cyr Les Vignes
- Alexandre Lebeaut - 8001 Woodmont Avenue Apt # 417 Bethesda, Maryland 20814 United States
- Nicolas Poirier - 4, impasse de la Rochère - 44119 Grandchamps des Fontaines
- Gérard Tobelem – 113, rue Monge – 75005 Paris

CAPITAL AND VOTING RIGHTS HELD BY THE MEMBERS OF THE BOARD OF DIRECTORS

After potential exercise of all the instruments carrying rights to shares of the Company, shares held in the Company by the directors at March 31, 2023, would be as follows:

- Dominique Costantini will hold 2,053,063 shares representing 9.97 % of the capital and 15.38% of the voting rights
- Maryvonne Hiance (directly and through her family holding company), will hold 454.084 shares representing 2.20 % of the capital and 3.33% of the voting rights
- Elsy Boglioli will hold 20,000 shares representing 0.10% of the capital and 0.08% of the voting rights
- Jean-Patrick Demonsang will hold 70,000 shares representing 0.34% of the capital and 0.38% of the voting rights
- Brigitte Dréno will hold 40,000 shares representing 0.19% of the capital and 0.15% of the voting rights
- Didier Hoch will hold 47,334 shares representing 0.23% of the capital and 0.21% of the voting rights
- Nicolas Poirier will hold 492,802 shares representing 2.39% of the capital and 3.16% of the voting rights
- Gérard Tobelem will hold 114,100 shares representing 0.55% of the capital and 0.55% of the voting rights

LIST OF CORPORATE OFFICES AND POSITIONS HELD BY THE MEMBERS OF THE BOARD OF DIRECTORS IN ALL COMPANIES OVER THE LAST FIVE YEARS

First name – Last name or corporate name of the member	Other corporate offices currently held in other companies	Other corporate offices and positions held in other companies over the last five years and no longer held as of the date of this Universal Registration Document
Dominique Costantini	- Director of Smart Immune	- Director of Abivax - Director of Theradiag SA - Director of Carthera SAS - Director of Sensorion - Director of Theranexus SAS
Maryvonne Hiance	- Vice Chairman of the Atlanpole Biotherapies cluster - Chairman of HealthTech For Care - Chairman of Olgram - Director of Pherecydes Pharma	- Chairman and Vice Chairman of France Biotech
Elsy Boglioli	- Founder and Chief Executive Officer of Bio Up - Independent Director of Gensight - Independent Director of Laverock Therapeutics - Member of the Supervisory Board of Inova Software, Metafora Biosystems, Womed	- None
Jean-Patrick Demonsang	- Chairman of Demonsang Consulting SAS -	- Chairman of Parexi SAS - Chief Executive Officer of Genode Partners SAS - Chairman of the Supervisory Board of G1J Ile-de-France
Brigitte Dréno	- Consulting Firms: BMS, Fabre Oncology	- Deputy Vice-President for Scientific and Technical Culture at the University of Nantes - RHU SUccESS coordinator
Didier Hoch	- Chairman of Pherecydes Pharma - Director of the University of the Underground Charity Foundation - Strategic Advisor for Goliver Therapeutics	- Chief Executive Officer of Pherecydes Pharma (2022) - Independent Director of DBV Technology, Genticel, Germitech - Member of the Strategic Board - Advisory Committee of Myastérix, Curavac - Director of the Fondation pour l'Université Grenoble Alpes
Nicolas Poirier	- Member of the Scientific Board of MabDesign and MAbSillico	- None
Alexandre Lebeaut	- Immunorx Pharma Inc., Director - Object Pharma Inc., Director - Calypso Biotech, Director	- I-ACT for Children, Chief Executive Officer - Vifor Pharma, Director
Gérard Tobelem	- Director of Dendrogenix	- Director of SupBiotech - Director of the Louis Dreyfus business foundation - Chairman of Théradiag SA

12.1.2 Composition of the operational management team

COMPOSITION OF THE EXECUTIVE MANAGEMENT

Dominique Costantini serves as Chairman of the Board of Directors.

Nicolas Poirier was appointed Chief Executive Officer since October 7, 2022 (following the departure of Alexis Vandier) and serves as Chief Scientific Officer.

BIOGRAPHIES OF THE MEMBERS OF THE EXECUTIVE MANAGEMENT

Please refer to paragraph 12.1.1 of the Universal Registration Document.

Nicolas Poirier (PhD) - Chief Executive Officer and Chief Scientific Officer

Nicolas Poirier is assisted by an operational management team including:

- **Dominique Costantini** (MD), Director of Strategy and Development (cf. p137 information related to the Board members)

- **Anne-Laure Autret-Cornet,** Chief Financial Officer.

  Anne-Laure Autret-Cornet graduated from ESSCA Management School and has received the certificate "Corporate Finance" from HEC Paris in 2020. Specialized in Audit-Finance, Anne-Laure has acquired a seven-year experience within Deloitte before joining Effimune in October 2013 as Administrative and Financial Manager. Since May 2016, Anne-Laure was appointed Chief Financial Officer of OSE Immunotherapeutics.

  Anne-Laure Autret-Cornet was elected as new director representing the employee shareholders, her appointment will be submitted to the approval of the next General Assembly Meeting.

- **Silvia Comis** (MD), Head of Clinical development

  Silvia brings 30 years of international experience and leadership in the pharmaceutical industry with a strong expertise in clinical research and development as well as in medical affairs and real-world evidence in oncology, haematology and immuno-oncology. She was recently Senior Medical Director IQVIA, and European Head of Early Products Medical Affairs in oncology at Novartis, involved in all the immuno-oncology programs with clinical innovations.

- **Jean-Pascal Conduzorgues** (PharmD), Industrial Director and Qualified Person

  With a doctorate in pharmacy, he has vast experience as a qualified person (QP), a pharmaceutical qualification required for drugs in Europe. He organizes the subcontractors needed to coordinate the pharmaceutical cases. He was a founder, manager and qualified person of the Montpellier-based CRID Pharma, which became Amatsi and then recently Eurofins, which he headed for 20 years. This company is a pharmaceutical services company specializing in pharmaceutical development (formulation, analytical development, approval of manufacturing processes, ICH stability studies, quality control and pharmaceutical writing) and in drug management for clinical trials. In 2011 he merged CRID Pharma with Avogadro to form Amatsi, a 175-person group located in France and the United States offering all services related to drug development. Since 2013 Jean-Pascal Conduzorgues has had his own consulting firm, Ibero, where he assists with pharmaceutical planning and initiatives by biotechnology companies he chooses to support as a shareholder and consultant, as is the case for OSE Immunotherapeutics.

- **Sophie Fay, Chief External Affairs**

Sophie Fay graduated from ESSEC and holds an MBA. She benefits from 15+ years of a lead experience in pharma and biotech in corporate strategy and market access.

Specific operational departments handle medical, translational, medical-marketing, pharmaceutical and legal activities.

12.1.3 Disclosures about the Management team and directors

To the knowledge of the Board of Directors, over the past five years, none of the members of the Board of Directors, nor the Chief Executive Officer of the Company has been:

- Subject to any sanction;
- Involved in any bankruptcies, receiverships or liquidations, or company placement under judicial administration as a manager or corporate officer;

- Disqualified by a court as a member of an administrative, management or supervisory body or from participating in the management or conduct of the business of an issuer or from intervening in the management or conduct of an issuer's affairs;

- Subject to an incrimination and/or official public sanction by the statutory or regulatory authorities (including designated professional organizations).

12.2 Potential conflicts of interest of the members of the Board of Directors and Executive Management

To the Company's knowledge, there are no existing or potential conflicts of interest between the duties towards the Company, the Chief Executive Officer and the members of the Board of Directors and the private interests and/or duties of the individuals that comprise the administrative, management and executive management bodies. If necessary, Article 19 of the Board of Directors' Internal Rules governs the conflicts of interest of any director. There is no arrangement or agreement entered into with a shareholder, customer, supplier or other under which any of the aforementioned persons has been selected.

There are no family ties between the aforementioned persons.

No restrictions other than legal, statutory or pursuant to the Internal Rules are accepted by any of the aforementioned persons concerning the sale of its stake in the Company's share capital.

13 Compensation and benefits

13.1 Total gross compensation for members of the Board of Directors and Executive Management

In accordance with the law of July 3, 2008, the disclosures presented herein are established by referring to the corporate governance code and additional recommendations regarding communication on the compensation of executive corporate officers of listed companies as defined by Middlenext. The Middlenext Code used as a reference by the Company can be consulted at the address http://www.middlenext.com/IMG/pdf/Code_de_gouvernance_site.pdf. The relevant summary tables from Appendix 2 of AMF recommendation DOC-2021-02 are presented below.

For the 2022 fiscal year, the only executive corporate officers were Dominique Costantini and Nicolas Poirier for the end of 2022. Alexis Peyroles resigned from his mandate of Chief Executive Officer in January 2022 and Alexis Vandier was Chief Executive Officer from July 13 to October 7, 2022.The only compensation paid to executive corporate officers during 2022 was directors' fees for their terms of office as directors.

Dominique Costantini has an open-ended employment contract since July 1, 2014, for her position as Director of Development. She receives a gross annual compensation of €309,470. Variable compensation equal to up to three months' salary is provided for based on the achievement of specific targets.

Nicolas Poirier, Chief Executive Officer, signed an open-ended employment agreement on October 1st, 2009, as a researcher and was appointed Chief Scientific Officer on May 31, 2006. As Chief Scientific Officer, his gross compensation is €250,000, with variable compensation up to three months' salary based on the achievement of specific targets.

Alexis Peyroles, Chief Executive Officer until January 2022, signed an open-ended employment agreement on July 1st, 2014, as Chief Operation Officer. At January 1st, 2022, his gross compensation was €385,000 with variable compensation up to 50% of the gross annual compensation, based on the achievement of specific targets. Alexis Peyroles is no more Chief Executive Officer since January 2022. His severance pay was provisioned in the 2021 accounts.

It should be noted that there was no compensation for a new Chief Executive Officer over the first 6 months of the year because this function was endorsed by the Chairman of the Board of Directors as interim without additional compensation.

Alexis Vandier, Chief Executive Officer between July and October 2022 had signed an open-ended employment agreement on June 13, 2022, as Chief Operating Officer. His gross compensation was 460,000 euros with variable compensation of up to 50% of gross annual compensation depending on the achievement of objectives. Alexis Vandier is no longer Chief Executive Officer since October 7, 2022. A report setting out the principles and criteria for determining, distributing and allocating the fixed, variable and exceptional elements making up the total compensation and benefits for members of the Board of Directors and executive management for the 2022 financial year is presented in Appendix C of this Universal Registration Document. This report will be submitted for the approval of the Annual General Meeting of June 22, 2023, in its resolutions 10 to 15. The reader is invited to refer to it.

TABLE 1: SUMMARY TABLE OF COMPENSATION AND SHARE SUBSCRIPTION WARRANTS ALLOCATED TO EACH EXECUTIVE CORPORATE OFFICER

	2022 fiscal year	2021 fiscal year
Dominique Costantini Chairwoman of the Board of Directors since March 28, 2018		
Compensation due for the fiscal year (table 2)	€404,313 Gross Wages	€394,419 Gross Wages
Valuation of multi-annual variable compensation allocated during the year	N/A	N/A

Valuation of the share subscription warrants* and founders' share warrants allocated during the fiscal year (Table 4)	€34,200	€51,700
Valuation of free shares allocated (table 6)	N/A	N/A
TOTAL	€438,313	€446,119

	2022 fiscal year*
Nicolas Poirier – Chief Executive Officer	
Compensation due for the fiscal year (table 2)	€343,896 Gross Wages
Valuation of multi-annual variable compensation allocated during the year	N/A
Valuation of the share subscription warrants and founders' share warrants allocated during the fiscal year (Table 4)	N/A
Valuation of free shares allocated (table 6)	€917,360 Gross
TOTAL	€1,261,256

*The term starting in 2022, only the 2022 data are presented.

	2022 fiscal year*
Alexis Vandier– Chief Executive Officer	
Compensation due for the fiscal year (table 2)	€216 061 Gross Wages
Valuation of multi-annual variable compensation allocated during the year	N/A
Valuation of the share subscription warrants and founders' share warrants allocated during the fiscal year (Table 4)	N/A
Valuation of free shares allocated (table 6)	N/A
TOTAL	€216 061

*The term lasted between July and October 2022, effective end of term in March 2023.

TABLE 2: SUMMARY OF THE COMPENSATION OF EACH EXECUTIVE CORPORATE OFFICER

Executive Officer	**Compensation for the 2022 fiscal year - In euros**		**Compensation for the 2021 fiscal year - In euros**	
Dominique Costantini	404,113 Gross[1]		394,419 Gross [1]	
	Amounts due	Amounts paid	Amounts due	Amounts paid
Fixed compensation	302,500	302,500	302,500	302,500
Annual variable compensation	75,625	60,500[2]	73,734	71,843[2]
Multi-year variable compensation	N/A	N/A	N/A	N/A
Exceptional compensation	N/A	N/A	1,500	1,500

Directors' fees	25,988	25,988	16,685	16,685
Benefits in kind	0	0	0	0
TOTAL	404,113	388,988	394,310	392,528

[1] On July 1, 2020, Dominique Costantini's employment contract was amended to increase her gross annual compensation to €302,500, excluding variable compensation.
[2] 2022 variable compensation was paid in January 2023 – 80% of goals achieved.

Executive Officer	**Compensation for the 2020 fiscal year In euros**	
Nicolas Poirier	343 896€ Bruts[1]	
	Amounts due	Amounts due
Fixed compensation	250,000	250,000
Annual variable compensation	62 500[2]	56 250[2]
Multi-year variable compensation	N/A	N/A
Patentl compensation	10,500	10,500
Directors' fees	27,146	27,146
Benefits in kind	0	0
TOTAL	350,146	343,896

[1] Nicolas Poirier's employment contract provided for compensation of €250,000 excluded variable compensation.
[2] 2022 variable compensation was paid in January 2023 - 90% of goals achieved.

TABLE 3: GROSS COMPENSATION RECEIVED BY NON-EXECUTIVE CORPORATE OFFICERS AS MEMBERS OF THE BOARD OF DIRECTORS (AND OTHER COMPENSATION)

Name of the non-executive corporate officer	**Amounts allocated in 2021**	**Amounts paid in 2021**	**Amounts allocated in 2022**	**Amounts paid in 2022**
Gérard Tobelem				
Compensation as a member of the Board	**€34,286**	**€34,286**	**€46,429 €**	**€46,429**
Other compensation	10,000 founders' share warrants	10,000 founders' share warrants	10,000 founders' share warrants	10,000 founders' share warrants
Jean-Patrick Demonsang				
Compensation as a member of the Board	**€34,286**	**€34,286**	**€35,714**	**€35,714**
Other compensation	10,000 founders' share warrants	10,000 founders' share warrants	10,000 founders' share warrants	10,000 founders' share warrants
Didier Hoch				
Compensation as a member of the Board	**€30,857**	**€30,857**	**€32,857**	**€32,857**

Other compensation	10,000 founders' share warrants	10,000 founders' share warrants	10,000 founders' share warrants	10,000 founders' share warrants
Elsy Boglioli				
Compensation as a member of the Board	**€12,857**	**€12,857**	**€36,429 €**	**€36,429**
Other compensation	10,000 founders' share warrants **€90,000**	10,000 founders' share warrants	10,000 founders' share warrants	10,000 founders' share warrants
Maryvonne Hiance				
Compensation as a member of the Board	**€22,724**	**€22,724**	**€43,571**	**€43,571**
Other compensation	10,000 founders' share warrants	10,000 founders' share warrants	10,000 founders' share warrants	10,000 founders' share warrants
Brigitte Dréno				
Compensation as a member of the Board	**€21,429**	**€21,429**	**€21,429**	**€21,429**
Other compensation	10,000 founders' share warrants	10,000 founders' share warrants	10,000 founders' share warrants	10,000 founders' share warrants
Alexandre Lebeaut				
Compensation as a member of the Board			**23 529 €**	**23 529 €**
Other compensation			10,000 founders' share warrants	10,000 founders' share warrants
TOTAL	**€289,964** **70,000 founders' share warrants**	**€289,964** **70,000 founders' share warrants**	**€247,101** **70,000 founders' share warrants**	**€247,101** **70,000 founders' share warrants**

TABLE 4: STOCK OPTIONS GRANTED TO EACH EXECUTIVE CORPORATE OFFICER BY THE COMPANY OR ANY COMPANY IN ITS GROUP DURING THE FISCAL YEARS ENDED DECEMBER 31, 2021 AND 2022

Executive corporate officer name	**Plan date**	**Plan number**	**Valuation of share subscription warrants and founders' share warrants according to the method used in the consolidated financial statements**	**Number of share subscription warrants and founders' warrants allocated during the fiscal year**	**Exercise price**	**Exercise period**
Dominique Costantini	06/23/2022	2022 founders' share warrants	€34,200	10,000 founders' share warrants	€6.63	06/23/2027
	6/24/2021	2021 founders' share warrants	€51,700	10,000 founders' share warrants	€11.05	6/24/2026

TOTAL			€85,900	20,000 founders' share warrants		

TABLE 5: STOCK OPTIONS EXERCISED BY EACH EXECUTIVE CORPORATE OFFICER DURING THE FISCAL YEARS ENDED DECEMBER 31, 2022, AND 2021

None

TABLE 6: FREE SHARES GRANTED TO EACH CORPORATE OFFICER DURING THE FISCAL YEARS ENDED DECEMBER 31, 2021, AND 2022

Executive corporate officer name	Plan number and date	Number of shares awarded during the 2021/2022 fiscal years	Valuation of shares according to the method used in the consolidated financial statements	Vesting date	Availability date	Performance conditions
Nicolas Poirier	03/28/2022	150,000	€917,260 €	03/28/2022	03/28/2023	Attendance
TOTAL		150,000	€917,260 €			

TABLE 7: FREE SHARES THAT BECAME AVAILABLE TO EACH EXECUTIVE CORPORATE OFFICER DURING THE FISCAL YEARS ENDED DECEMBER 31, 2021, AND 2022

Corporate officer name	Plan number and date	Number of shares that became available during the year	Vesting conditions
Nicolas Poirier	06/17/2020	100,000 (as of 06/17/2022)	Attendance

TABLE 8: HISTORY OF STOCK OPTIONS GRANTED TO CORPORATE OFFICERS

As of the date of this Universal Registration Document:

	2021 founders' share warrants	2020 founders' share warrants	2019 founders' share warrants	2018 founders' share warrants	2018 share subscription warrants	2017 share subscription warrants
Date of General Shareholders' Meeting or Board of Directors having allocated the plan	Extraordinary General Shareholders' Meeting on 5/29/2020 Board of Directors meeting on 6/24/2021	Extraordinary General Shareholders' Meeting on 6/26/2019 Board of Directors meeting on 6/17/2020	Extraordinary General Shareholders' Meeting on 6/13/2018 Board of Directors meeting on 6/26/2019	Extraordinary General Shareholders' Meeting on 6/14/2017 Board of Directors meeting on 6/13/2018	Extraordinary General Shareholders' Meeting on 6/14/2017 Board of Directors meeting on 6/13/2018	Extraordinary General Shareholders' Meeting on 5/31/2016
Maximum number of warrants authorized by General Shareholders' Meetings	500,000 instruments	500,000 instruments	500,000 instruments	500,000 instruments	500,000 instruments	400,000 instruments
Number of instruments issued	80,000	70,000	60,000*	25,900	42,850	52,000

	2021 founders' share warrants	2020 founders' share warrants	2019 founders' share warrants	2018 founders' share warrants	2018 share subscription warrants	2017 share subscription warrants
Dominique Costantini	10,000	10,000		25,900		
Jean-Patrick Demonsang	10,000	10,000	10,000			
Gérard Tobelem	10,000	10,000	10,000		42,850	
Maryvonne Hiance	10,000	10,000				
Didier Hoch	10,000	10,000	10,000			
Sophie Brouard	10,000	10,000	10,000			
Brigitte Dréno	10,000	10,000	10,000			
Elsy Boglioli	10,000					
Starting point for exercising warrants	Allocation date	Allocation date	Allocation date	Allocation date	Allocation date	Allocation date
Expiration date	6/24/2026	6/17/2025	6/26/2024	6/13/2023	6/13/2023	7/17/2021
Warrant subscription or purchase price	€0	€0	€0	€0	€0.70	€0.60
Number of instruments subscribed	0	0	0	0	0	42,000
Warrant exercise terms	Subscribe common shares	Subscribe common shares	Subscribe common shares	Subscribe common shares	Subscribe common shares	Subscribe common shares
Exercise price	€11.05	€6.14	€3.58	€4.17	€4.17	€4.65
Number of shares subscribed on the date of this Universal Registration Document	0	10,000	0	0	0	42,000
Cumulative number of canceled or lapsed share subscription or purchase warrants	0	0	0	0	0	10,000
Remaining subscription warrants to be issued on the date of this Universal Registration Document	0	0	0	0	0	0

*The 10,000 remaining Founders' share warrants have been allocated to another Director who left since then.

TABLE 9: STOCK OPTIONS GRANTED TO THE TOP 10 NON-CORPORATE OFFICER EMPLOYEES AND OPTIONS EXERCISED BY THEM

Stock subscription or purchase options granted to the first ten employees who are not corporate officers and options exercised by them	Options granted during the fiscal year by the issuer and any Company included in the options' allocation scope, to the first ten employees of the issuer and of any Company included in this scope, to whom the number of options thus granted is the highest (aggregate information)	Options held on the issuer and the Companies referred to above, exercised, during the year, by the ten employees of the issuer and these Companies, whose number of options thus purchased or subscribed is the highest (aggregate information)	Total number of options allocated/shares subscribed or purchased	Weighted average price
41,155 Free Share Allocation plan for 2017		N/A	40,151 vested on 7/18/2018	N/A
150,000 Free Share Allocation plan for 2018-2		N/A	141,800 vested on 3/26/2020	N/A
150,000 Free Share Allocation plan for 2019		N/A	145,300 acquired on 6/27/2020	N/A
250,000 Free Share Allocation plan for 2020		N/A	231,000 free shares allocated on 12/18/2020	N/A
228,700 Free Share Allocation plan for 2022		N/A	223,700 free shares acquired on 03/28/2023	N/A
TOTAL			814,855	

TABLE 10: HISTORY OF FREE SHARE ALLOCATIONS

As of the date of this Universal Registration Document:

- 98,000 free shares granted by the Board of Directors on May 31, 2016;
- 13,851 free shares granted by the Board of Directors on September 8, 2016;
- 150,000 free shares granted by the Board of Directors on December 13, 2016;
- 25,040 free shares granted by the Board of Directors on March 28, 2017;
- 41,155 free shares granted by the Chief Executive Officer on July 18, 2017, authorized by the Board of Directors on June 14, 2017;
- 150,000 free shares granted by the Board of Directors on June 13, 2018 to Alexis Peyroles;
- 38,712 free shares granted by the Board of Directors on December 5, 2018 to Alexis Peyroles and Nicolas Poirier;
- 22,625 free shares granted by the Chief Executive Officer on December 18, 2020 (approved by the Board of Directors on December 10, 2019) to Alexis Peyroles in respect of his variable compensation;
- 141,800 free shares granted by the Chief Executive Officer on March 12, 2020 on the delegation of the Board of Directors on December 5, 2018 (corresponding to the 149,200 free shares approved by the Chief Executive Officer on March 12, 2019 allocated to employees who are not corporate officers of the Company);

- 150,000 free shares granted by the Board of Directors on June 17, 2021 to Alexis Peyroles (corresponding to the 150,000 free shares approved by the Board of Directors on June 17, 2020);
- 100,000 free shares granted by the Board of Directors on June 17, 2021 to Nicolas Poirier (corresponding to the 100,000 free shares approved by the Board of Directors on June 17, 2020);
- 150,000 free shares granted by the Chief Executive Officer on June 27, 2020 under delegation of the Board of Directors on June 17, 2020 (corresponding to the 150,000 free shares approved by the Board of Directors on June 26, 2019 for Alexis Peyroles);
- 145,300 free shares granted by the Chief Executive Officer on June 27, 2020 on the delegation of the Board of Directors on June 26, 2019 (corresponding to the 148,400 free shares approved by the Chief Executive Officer on June 26, 2019 allocated to employees who are not corporate officers of the Company);
- 231,000 free shares granted by the Chief Executive Officer on December 18, 2021 under delegation of the Board of Directors on June 17, 2020 to employees who are not corporate officers of the Company (out of the budget of 244,500 in the Free Share Allocation Plan);
- 11,363 free shares granted by the Chief Executive Officer on December 18, 2021 (approved by the Board of Directors on December 8, 2020 to Alexis Peyroles in respect of his variable compensation);
- Allocation of a maximum of 250,000 free shares to employees who are not corporate officers of the Company, as approved by the Board of Directors on December 7, 2021; validated by the Chief Executive Officer in March 2022;
- Allocation of 150,000 shares from the Free Share Allocation Plan to Nicolas Poirier approved by the Board of Directors on December 7, 2021; validated by the Chief Executive Officer in March 2022.

HISTORY OF FREE SHARE ALLOCATIONS													
INFORMATION ON FREE SHARES													
Meeting date	6/24/2021	6/26/2019	6/13/2018	6/13/2018	6/14/2017	6/13/2018	6/14/2017	6/14/2017	9/17/2014	5/31/2016	5/31/2016	5/31/2016	5/31/2016
Date of the Board of Directors meeting	7/12/2021	6/17/2020	12/8/2020	6/17/2020	12/10/2019	6/26/2019	5/12/2018	6/13/2018	5/31/2016	9/8/2016	12/13/2016	3/28/2017	6/14/2017 (delegation to the Chief Executive Officer on 6/18/2017)
Total number of free shares	400,000	400,000	11,363	100,000	22,625	300,000	38,712	150,000	98,000	13,851	150,000	25,040	41,155
	of which the number allocated to:												
Maryvonne Hiance Director									40,000	0	0	10,926	0
Alexis Peyroles Chief Operating Officer		150,000	11,363		22,625	150,000	18,712	150,000	0	12,162	150,000	0	0
Nicolas Poirier director	150,000			100,000			20,000						
Vesting date of the shares	-	6/17/2021	12/8/2021	6/17/2021	12/18/2020	6/26/2020	12/5/2019	6/13/2019	6/1/2018	9/9/2017	12/13/2017 (100,000 Free Share Allocation plan) 6/13/2018 (for 50,000 Free Share Allocation plan)	3/29/2018	7/18/2018

Lock-up period end date	-	6/17/2022	12/8/2022	6/17/2022	12/10/2021	6/26/2021	5/2020	6/13/2020	6/1/2020	9/9/2018	12/13/2018 (100,000 Free Share Allocation plan) 6/13/2019 (50,000 Free Share Allocation plan)	3/29/2019	7/18/2019
Number of shares vested on 3/31/2021	-	0	0	0	22,625	150,000	38,712	150,000	98,000	13,851	150,000	25,040	40,151
Cumulative number of canceled or lapsed shares		0	0	0	0	0	0	0	0	0	0	0	0
Free shares remaining at the balance sheet date							-	-	-	-	-	-	-

TABLE 11: DETAILS OF THE COMPENSATION CONDITIONS AND OTHER BENEFITS GRANTED TO EXECUTIVE CORPORATE OFFICERS

Executive corporate officers	Date of first appointment	End of term	Service agreement		Employment contract		Supplementary pension plan		Compensation or benefits due or likely to be due as a result of a termination or change of position		Compensation relating to a non-compete clause	
			Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Dominique Costantini *Chairwoman of the Board* *Director*	4/27/2012	GSM for the fiscal year ended 12/31/2023		X	X			X		X		X
Nicolas Poirier *Chief Executive Officer* *Director*	10/07/2022	GSM for the fiscal year ended 12/31/2024		X	X			X		X		X

13.2 Amounts provisioned or recognized by the Company for the purpose of paying pensions, retirement or other benefits

The Company has not provisioned any amounts to pay pensions, retirement and other benefits to corporate officers and/or executive corporate officers who do not otherwise benefit (or have benefited) from a departure or sign-on bonus within the Company.

The share subscription warrants and founders' share warrants granted to corporate officers or executive corporate officers are subject to a detailed breakdown in chapter 15.2 of this Universal Registration Document.

14 Operating procedures of the administrative and management bodies

14.1 Operating procedures and terms of office of the members of the Board of Directors and Executive Management

At the date of this Universal Registration Document, the directors' terms of office are as follows:

First name — Last name or corporate name of the member	Date of first appointment	End of term	Main position in the Company
Dominique Costantini	April 27, 2012	GMS called to approve the financial statements for the fiscal year ended December 31, 2023	Chairwoman of the Board of Directors, Director, Chief Executive Officer
Maryvonne Hiance	May 31, 2016	GSM called to approve the financial statements for the fiscal year ended December 31, 2024	Vice-Chairman of the Board of Directors
Elsy Boglioli	June 24, 2021	GSM called to approve the financial statements for the fiscal year ended December 31, 2023	Director
Jean-Patrick Demonsang	April 10, 2014	GSM called to approve the financial statements for the fiscal year ended December 31, 2022	Director
Brigitte Dreno	June 14, 2017	GSM called to approve the financial statements for the fiscal year ended December 31, 2022	Director
Didier Hoch	May 31, 2016	GSM called to approve the financial statements for the fiscal year ended December 31, 2024	Director
Alexandre Lebeaut	02/18/2022	GSM called to approve the financial statements for the fiscal year ended December 31, 2024	Director
Nicolas Poirier	June 26, 2019	GSM called to approve the financial statements for the fiscal year ended December 31, 2022*	Director representing the employee shareholders
Gérard Tobelem	April 10, 2014	GSM called to approve the financial statements for the fiscal year ended December 31, 2022	Director

* *Nicolas Poirier, previously director representing the employee shareholders, resigned with effect at the General Shareholders' Meeting approving 2022 financial statements, further to his appointment as Chief Executive Officer on October 7, 2022.*

The operating rules of the governance bodies are set out in the statutes in force.

14.1.1 Board of Directors (Articles 19 to 22 of the bylaws)

ARTICLE 19 - BOARD OF DIRECTORS (EXCERPT)

(i) Except as permitted by law, the Company is administered by a Board of Directors with a minimum of three and a maximum of eighteen members.

(ii) During the Company's life span, directors are appointed or reappointed by the Ordinary General Shareholders' Meeting. Notwithstanding, in the event of a merger, directors may be appointed by the Extraordinary General Shareholders' Meeting approving the transaction.

(iii) Directors may or may not be Company shareholders.

(iv) The directors 'term of office is three years and ends at the conclusion of the Ordinary General Shareholders' Meeting called to approve the financial statements of the fiscal year ended and held during the year in which the term of the relevant director expires.

Directors may be re-elected. They may be dismissed at any time by the Ordinary General Shareholders' Meeting.

No one may be appointed director if they are older than 70 and their appointment would mean that more than one-third of the members of the Board of Directors would be over 70. If this proportion is exceeded, the oldest director is deemed to have resigned automatically at the end of the Ordinary General Shareholders' Meeting called to approve the financial statements of the fiscal year during which this threshold was crossed.

Directors may be natural persons or legal entities. Upon their appointment, directors who are legal entities must appoint a permanent representative who is subject to the same conditions and obligations and who incurs the same liabilities as if he or she were a director in his or her own name, without affecting the joint liability of the legal entity he or she is representing.

When the legal entity director ends the term of office of its permanent representative, it must immediately notify the Company, via registered letter, of its decision and provide the name of its new permanent representative. The same applies in the event of the death or resignation of the permanent representative.

The permanent representative of a legal entity director is subject to the same age requirements as apply to natural person directors.

(v) In the event of a vacancy due to death or the resignation of one or more directors, the Board of Directors may make provisional appointments between two General Shareholders' Meetings in order to maintain the same number of directors.

Provisional appointments made in this way by the Board of Directors are subject to ratification by the next Ordinary General Shareholders' Meeting. Failing ratification, the decisions made and actions taken still remain valid.

When the number of directors falls below the legal minimum, the directors still in office must immediately convene the Ordinary General Shareholders' Meeting to fill the number of directors.

A director who is appointed to replace another director stays in office only for the predecessor's remaining term.

Natural person directors may not simultaneously serve on more than five boards of directors or supervisory boards of limited companies (*société anonyme*) headquartered in metropolitan France, except where permitted by law.

A Company employee may only be appointed as director if his or her contract corresponds to active employment. The employee does not lose the benefit of this employment contract. The number of directors with an employment contract with the Company may not exceed one-third of the directors in office.

ARTICLE 20 - CHAIRMANSHIP OF THE BOARD OF DIRECTORS

The Board of Directors elects a chairman from among its natural person members and determines the Chairman's compensation. It sets the term of the Chairman's duties, which may not exceed the Chairman's term as a director. The Chairman may be re-elected.

The Board of Directors may dismiss the Chairman at any time.

No one older than 70 may be appointed Chairman of the Board of Directors. If the Chairman of the Board of Directors turns 70 while in office, he or she will be deemed to have resigned, and a new Chairman will be appointed in accordance with the terms and conditions stipulated in this article.

The Chairman represents the Board of Directors. The Chairman organizes and leads the work of the Board of Directors and reports on it to the General Shareholders' Meeting. The Chairman ensures that the Company bodies operate smoothly and, in particular, ensures that the directors are able to perform their duties.

In the event of a temporary impediment or the death of the Chairman, the Board of Directors may appoint a director to serve as Chairman.

In the event of a temporary impediment, this appointment is granted for a limited period and may be renewed.

In the event of death, it applies until the new Chairman is elected.

ARTICLE 21 - MEETINGS AND PROCEEDINGS OF THE BOARD OF DIRECTORS

BOARD MEETINGS

The Board of Directors meets as often as the corporate interest requires and is convened by the Chairman. If no meeting is held for more than two months, a group of directors comprising at least one-third of the members of the Board of Directors may convene the Board, providing a specific agenda.

Either the Chief Executive Officer, when he or she is not serving as Chairman of the Board of Directors, or the Chief Operating Officers may ask the Chairman to convene the Board of Directors to discuss an established agenda.

The meeting is held at the registered office or any other location.

Notices of meeting may be issued by any means, including verbally.

The Chairman of the Board of Directors chairs the meetings. In the event that the Chairman is unable to perform his or her duties, at each meeting the Board appoints one of its members in attendance to chair the meeting.

At each meeting, the Board may appoint a secretary who does not need to be a Board member.

A register signed by all the members present at the Board meeting is kept.

Directors and any other person called on to attend the meetings of the Board of Directors are bound to secrecy with regard to confidential information that is described as such by the Chairman.

QUORUM AND MAJORITY

The Board of Directors may validly deliberate only if at least half of the directors are present or deemed to be present, subject to the arrangements stipulated in the Rules of Procedure in the event that videoconferencing or another telecommunication medium is used.

Unless stipulated otherwise in these bylaws and subject to the arrangements stipulated in the Rules of Procedure in the event that videoconferencing or another telecommunication medium is used, Board resolutions are passed by a majority vote of the members present or deemed present.

In the event of a tie, the Chairman of the meeting has the casting vote.

For the purposes of calculating the quorum and majority, directors participating in the Board of Directors 'meeting through videoconference or another telecommunication medium in accordance with the terms and conditions outlined in the Board's Rules of Procedure are deemed to be present. Nonetheless, actual presence or presence through a representative is required for any Board proceedings on the approval of the separate financial statements and the group's management report, and for any decisions relating to the dismissal of the Chairman of the Board of Directors, the Chief Executive Officer and the Chief Operating Officer.

REPRESENTATION

Any director may give another director, in writing, may give a proxy to represent him or her at a Board meeting.

Each director may represent only one other director during a single Board meeting.

These provisions apply to the permanent representative of a legal entity.

MINUTES OF THE PROCEEDINGS

The Board of Directors proceedings are reported in minutes issued in a special register, listed and initialed, and kept at the registered office in accordance with the regulatory provisions.

The minutes are signed by the Chairman of the meeting and by a director.

Copies or extracts from the minutes of the Board of Directors proceedings are legally certified by the Chairman or the Chief Executive Officer.

NON-VOTING MEMBERS

During the Company's life span, the Ordinary General Shareholders' Meeting may appoint nonvoting members from among or outside the shareholders.

There may be no more than three nonvoting members.

Nonvoting members are appointed for a one-year term. Their duties end at the conclusion of the Ordinary General Shareholders' Meeting called to approve the financial statements for the fiscal year ended and held during the year in which their term of office expires.

Any outgoing nonvoting member may be re-elected provided that they meet the criteria of this article.

Nonvoting members may be dismissed and replaced at any time by the Ordinary General Shareholders' Meeting without any compensation being due to them. The duties of the nonvoting members also end in the event of death or impediment for a nonvoting member who is a natural person, and in the event of a winding up or initiation of collective insolvency proceedings for a legal entity nonvoting member, or in the event of resignation.

Nonvoting members may be natural persons or legal entities. If the nonvoting member is a legal entity, upon its appointment, it must appoint a permanent representative who is subject to the same conditions and obligations and who incurs the same civil and criminal liabilities as if he or she were a nonvoting member in his or her own name, without affecting the joint liability of the legal entity he or she is representing.

The role of the nonvoting members is to ensure the strict enforcement of the bylaws and present their remarks during the Board of Directors' meetings.

Nonvoting members have an overall advisory and supervisory role in the Company. As part of their role, they may share remarks with the Board and ask to review corporate documents at the Company's registered office.

Nonvoting members must be invited to every Board of Directors' meeting in the same way as the directors.

Nonvoting members have only advisory authority on an individual or collective basis and do not have voting rights on the Board.

Failure to summon the nonvoting member or to send documents to the nonvoting member (s) prior to the meeting of the Board of Directors may in no way be a reason to invalidate the decisions made by the Board of Directors.

ARTICLE 22 - POWERS OF THE BOARD OF DIRECTORS

(i) The Board of Directors determines the Company's business strategies and ensures that they are implemented.

Subject to the powers expressly granted by law to shareholders' meetings and to the extent of the corporate purpose, it examines any issue affecting the proper functioning of the Company and through its proceedings resolves matters that concern it.

In relations with third parties, the Company is bound even for actions by the Board of Directors that do not fall within the corporate purpose unless it proves that the third party knew that the action in question exceeded this purpose or that it could not be unaware of this given the circumstances, it being stated that the mere publication of the bylaws is not sufficient to constitute this proof.

(ii) The Board of Directors may at any time perform the audits and verifications it deems appropriate.

All directors must receive the information required for completing their assignments and they may obtain all documents they consider necessary from the Executive Management.

(iii) The Board of Directors may give any agent of its choice any delegation of authority within the bounds of its powers under the law and these bylaws.

It may decide to create working committees tasked with studying the issues the Board or the Chairman of the Board submits to it.

(iv) The Board of Directors is not qualified to vote on or authorize a bonds issue; these bylaws reserve that power for the General Shareholders' Meeting.

14.1.2 Executive Management (Articles 23 to 26 of the bylaws)

ARTICLE 23 - METHODS OF EXECUTIVE MANAGEMENT

The Company is responsible for its Executive Management, either through the Chairman of the Board of Directors or through another natural person appointed by the Board of Directors who assumes the title of Chief Executive Officer.

The Board of Directors chooses which of these executive management methods to implement. The Board decides on the method of the Executive Management through a majority vote of the directors who are present and deemed present, subject to the special provisions of Article 21 in the event that there are directors participating in the Board meeting via videoconference or another telecommunication medium.

The Board of Directors 'choice is communicated to the shareholders and third parties in accordance with the regulations in force.

The option chosen by the Board of Directors may be reassessed only upon the re renewal or replacement of the Chairman of the Board of Directors or when the Chief Executive Officer's term of office expires.

A change in the method of Executive Management does not require an amendment of the bylaws.

ARTICLE 24 - EXECUTIVE MANAGEMENT

Based on the method selected by the Board of Directors, the Chairman or the Chief Executive Officer takes responsibility for the Company's Executive Management.

The Chief Executive Officer is appointed by the Board of Directors, which sets the length of his or her term of office, determines his or her compensation and, where necessary, the limitations of his or her powers.

The Chief Executive Officer may be dismissed by the Board of Directors at any time. If the Chief Executive Officer who is not the Chairman is dismissed, he or she may be due to damages if the dismissal is decided without just cause.

ARTICLE 25 - POWERS OF THE CHIEF EXECUTIVE OFFICER

The Chief Executive Officer is vested with the broadest powers to act in any situation on behalf of the Company.

The Chief Executive Officer exercises his or her powers within the limits of the corporate purpose, and subject to the powers expressly granted by law to the General Shareholders' Meetings and the Board of Directors.

The Chief Executive Officer represents the Company in its dealings with third parties. The Company is bound even for actions by the Chief Executive Officer that do not fall within the corporate purpose unless it proves that the third party knew that the action in question exceeded this purpose or that it could not be unaware of this given the circumstances, it being stated that the mere publication of the bylaws is not sufficient to constitute this proof.

ARTICLE 26 - CHIEF OPERATING OFFICERS

At the suggestion of the Chief Executive Officer, whether this position is held by the Chairman of the Board of Directors or another person, the Board of Directors may appoint one or more natural persons, selected or not from among the directors and shareholders, responsible for assisting the Chief Executive Officer and given the title Chief Operating Officer.

There may be a maximum of five Chief Operating Officers.

In agreement with the Chief Executive Officer, the Board of Directors determines the scope and duration of the powers granted to the Chief Operating Officers and sets their compensation.

With regard to third parties, the Chief Operating Officer or Chief Operating Officers have the same powers as the Chief Executive Officer.

In the event of a termination of, or inability to perform, the duties of the Chief Executive Officer, the Chief Operating Officers retain their duties and powers until a new Chief Executive Officer is appointed, unless decided otherwise by the Board of Directors.

The Chief Operating Officers may be dismissed at any time on a proposal by the Chief Executive Officer. The dismissal of the Chief Operating Officers may give rise to damages if it is decided without just cause.

14.2 Information on the service contracts between the members of the Board of Directors and the Executive Management and the Company or one of its subsidiaries

14.2.1 Agreements between the Company, a director, the Chief Executive Officer or a Deputy Chief Executive Officer

Dominique Costantini, Chairwoman, signed an employment agreement as Director of Development in 2014. Her gross annual compensation is €302,500 with variable compensation of up to three months' salary depending on the achievement of objectives.

Following the resignation of Alexis Peyroles from his position as Chief Executive Officer, Dominique Costantini was appointed by the Board of Directors on January 14, 2022 as Interim Chief Executive Officer.

Maryvonne Hiance, Vice-Chairwoman, performs an operational role as Director of Public Relations for Executive Management under an employment agreement, with gross annual compensation of €120,000 and variable compensation of up to three months' salary depending on the achievement of objectives. Maryvonne Hiance resigned from her position as Director of Public Relations, effective as of December 31, 2021.

Alexis Peyroles, Director and Chief Executive Officer, signed an open-ended employment agreement as Chief Operating Officer, with a gross annual compensation of €385,000 and variable compensation of up to 50% of fixed compensation depending on the achievement of objectives. Alexis Peyroles stepped down as Chief Operating Officer on January 14, 2022.

Nicolas Poirier, appointed director representing the employee shareholders on June 26,2019, is employed as Chief Scientific Officer. His gross annual compensation is €250.000 from July 1, 2021, with variable compensation of up to three months' salary depending on the achievement of objectives. The Board of Directors appointed Nicolas Poirier as Chief Executive Officer on October 7, 2022. Following the recommendations of the Remuneration Committee, the Board decided to maintain his employment agreement as Chief Scientific Officer during for the duration of his term of Chief Executive Officer.

14.3 Committees

In accordance with Articles 6 and 7 of the Rules of Procedure, the Board has appointed a Compensation and Appointments Committee and an Audit Committee made up of Board members.

The composition of these Committees provides for a term of two years. Committee members are paid €3,000 per year and their chairman is paid €5,000 per year.

Travel and lodging costs incurred by each Committee participant for meetings held outside of Europe will be covered for an amount of €3,000 per meeting, while costs incurred for meetings in Europe will be covered up to €500 per meeting.

14.3.1 Audit Committee

COMPOSITION

The Audit Committee included Jean-Patrick Demonsang (Committee Chairman) and Didier Hoch, whose terms of office were renewed at the Board of Directors meeting on June 24, 2021, for a two-year period.

Jean-Patrick Demonsang and Didier Hoch are both independent members.

OPERATING PROCEDURES

DUTIES

The Audit Committee is responsible for overseeing issues relating to the preparation and audit of accounting and financial information. It is responsible for continually assessing the existence and effectiveness of the Company's financial control and risk control procedures, and has as its duties:

Internal control

- Ensuring that the internal control and risk management systems are effective;
- Verifying the smooth operation with assistance from the Finance Department;
- Reviewing the schedule of internal and external audits;
- Ensure that the Statutory Auditors conduct the statutory audit of the separate financial statements and, where applicable, the consolidated financial statements.

Statutory financial statements and financial information

After regularly reviewing the financial position, the cash position and the commitments appearing in the Company's separate financial statements:

- Reviewing the accounting and financial documents, annual and interim financial statements;
- Overseeing the process of issuing the statutory and consolidated / combined financial statements and the process of preparing the financial information;
- Reviewing the internal control measures;
- Reviewing the material risks for the Company, particularly off-balance sheet risks and commitments;
- Validating the relevance of accounting rules and choices;
- Verifying the relevance of the financial information reported by the Company.

Risk management

- Reviewing any item likely to have material, financial and accounting impacts;
- Reviewing the status of major litigation;
- Review off-balance sheet risks and commitments;
- Reviewing the relevance of the risk monitoring procedures;
- Reviewing any related-party agreements.

Statutory Auditors

- Leading the selection of the Statutory Auditors, managing their compensation and ensuring their independence;
- Ensuring the proper implementation of their assignment;
- Monitoring the statutory audit of the separate financial statements and, where applicable, the consolidated financial statements by the Statutory Auditors;
- Establishing the rules for using the Statutory Auditors for tasks other than the audit of the financial statements and ensuring the proper implementation of their assignment;
- Issue a recommendation on the proposals for the appointment and potential reappointment of the Statutory Auditors presented to the General Shareholders' Meeting, their fees and any issue related to their independence.

INTERNAL RULES

The operating procedures of the Audit Committee are governed by Article 7 of the Internal Rules of the Board of Directors. These Rules of Procedure may be viewed at the Company's registered office upon prior written request.

WORK IN 2022

The Audit Committee met twice in 2022, to review and approve the statutory and consolidated financial statements for fiscal year 2021 (March 28, 2022) and to review and approve the consolidated financial statements for first-half 2022 (September 20, 2022).

14.3.2 Appointments and Compensation Committee

COMPOSITION

The Appointments and Compensation Committee consists of Gérard Tobelem (Committee Chairman), Maryvonne Hiance and Elsy Boglioli, whose terms of office were renewed at the Board of Directors meeting on June 24, 2021, for a two-year period.

The independent members are Gérard Tobelem and Elsy Boglioli.

OPERATING PROCEDURES

DUTIES

The Appointments and Compensation Committee issues recommendations to the Board of Directors on the following topics:

- Advice and assistance regarding compensation, the pension and welfare benefit plan, supplementary pensions, benefits in kind, various cash entitlements of the executive corporate officers, allocations of free or performance shares, stock subscriptions or purchase options;
- The determination of the procedures for setting the variable portion of the compensation of the executive corporate officers, and overseeing the enforcement of these procedures;
- The distribution of the directors' fees, where necessary, to the directors taking into account their attendance record and tasks accomplished on the Board of Directors;
- Any extraordinary compensation of the directors for specific assignments or duties given to them by the Board;
- Any changes to the composition of the Board of Directors or the Executive Management;
- Prevention of conflicts of interest on the Board of Directors;
- Oversight of the establishment of structures and procedures making it possible to apply proper governing practices within the Company;
- Ensuring compliance with ethical principles within the Company and in its relations with third parties;
- Discussions on the classification of independent director for each director when the director is first appointed and every year before the publication of the Universal Registration Document, and presentation of the report of its recommendations to the Board of Directors.

In addition, the Executive Management proposes to it the various stock subscription or purchase option plans, equity warrant plans, founders' warrant allocation plans or free share allocation plans.

INTERNAL RULES

The operating procedures of the Appointments and Compensation Committee is governed by Article 6 of the Board of Directors' Internal Rules. These Internal Rules may be viewed at the Company's registered office upon prior written request.

WORK IN 2022

The Appointments and Compensation Committee met five times in 2022: on January 12, June 23, July 13, November 30 and December 1.

14.3.3 Scientific Advisory Board

In addition, the Company appointed an international Scientific Advisory Board on June 9, 2022, composed of 6 leader experts to guide the Company in its next phases of growth and scientific orientations.

This Scientific Advisory Board is chaired by Wolf Hervé Fridman, director of the Cordeliers Research Center.

The Scientific Advisory Board (SAB) combines the expertise of renowned scientific and international key-opinion leaders in the fields of immunology, immuno-oncology, inflammation and immunotherapy. The SAB works with the Company's leadership team and advise its Board of Directors on its scientific, medical, translational and developmental strategy.

14.4 Statement on corporate governance

In order to comply with the requirements of Article L. 225-37-4 of the French Commercial Code, the Company has designated the Corporate Governance Code which can be consulted on the website www.middlenext.com (the "MiddleNext Code") as a reference code.

Recommendations of the MiddleNext Code	Already adopted	To be adopted	Will not be adopted	Not applicable
I. Supervisory power				
R1: Board of Directors' ethics policy	X			
R2: Conflict of interest	X			
R3: Composition of the Board, independent directors	X			
R4: Board member information	X			
R5: Board member training			X	
R6: Board and committee meetings	X			
R7: Implementation of committees	X			
R8: Implementation of a specialized committee on corporate social/societal and environmental responsibility (CSR)		X		
R9: Implementation of rules of procedure	X			
R10: Directors' selection	X			
R11: Duration of the Directors' term	X			
R12: Directors' compensation	X			
R13: Implementation of an assessment of the Board's work	X			
R14: Relationships with the shareholders	X			
II. Executive power				
R15: Diversity and equity policy within the company		X		
R16: Definition and transparency of the compensation of executive corporate officers	X			
R17: Preparation of managers' succession		X		
R18: Combination of corporate officers and employment contracts	X			
R19 : Severance payments				X

R20 : Supplementary pension schemes				X
R21: Stock options and free shares			X	
R22 : Revue des points de vigilance	X			

R5: The Company considers that the profile, experience and professional environment of the members of the Board of Directors enables them to be up to date with the obligations and best practices in terms of corporate governance.

R8: The Company is involved in CSR activities as described in appendix of this document.

R13: The performance of the Board of Directors is assessed every three years in the form of a self-assessment carried out under the guidance of an outside consultant. This assessment addresses the Board's composition, organization and operating procedures. In addition, once a year, the Board puts a discussion of its operating procedures on the agenda of one of its meetings.

R18: Dominique Costantini has a permanent employment contract as Director of Development. The Company maintains this technical contract as Director of Development, despite the appointment of Dominique Costantini as Chairwoman of the Board of Directors, due to her seniority and the distinct technical functions she exercises in terms of drug development expertise.

R19: N/A. No severance pay has been granted.

R20: The Company does not currently plan to implement a supplementary retirement scheme.

R21: The Company has no stock options. The 2012, 2014, 2015 and 2016 share subscription warrants, and 2015, 2016, 2017, 2018, 2019, 2020, 2021 and 2022 founders' share warrants were granted to management, consultants and employees. Thanks to their technical knowledge, resources or expertise, these people have provided or continue to provide the Company with tools and resources that have helped it grow both scientifically and as a business. These equity warrants and founder warrants do not correspond to a compensation instrument as no performance criterion would be relevant to express the Company's medium- or long-term interest.

The other financial instruments used by the Company (free shares, founders' warrants) are meant to retain key Company employees to help the organization operate smoothly and grow.

R22: The Board of Directors took note of the elements presented in the "points of vigilance" section of the Middlenext Code.

14.5 Changes to the corporate governance

None

15 Employees

15.1 Human resources

15.1.1 Number of employees

At 31 December 2022, the average monthly headcount was 61 employees.

As of the date of this Universal Registration Document, the Company's workforce is 67 employees (excluding interns):

The clinical and regulatory Research & Development Division has 58 persons.

The Administrative Division has 9 persons.

15.2 Employee shareholding and stock options

15.2.1 Share subscription warrants (BSA) and founders' share warrants (BSPCE)

As of the date of this Universal Registration Document, the various share subscription warrants and founders' share warrants plans allow for subscription of new common shares in exchange for one warrant.

ISSUANCE OF 2018 SHARE SUBSCRIPTION WARRANTS

On June 13, 2018, the Board of Directors, making use of the delegation of the General Shareholders' Meeting on June 14, 2017, decided to issue 42,850 2018 share subscription warrants for the benefit of Gérard Tobelem, which can be subscribed until June 13, 2023. This issue canceled and replaced that of the 2016 share subscription warrants.

ISSUE OF 850,000 SHARE SUBSCRIPTION WARRANTS TO THE EIB

In February 2021, the Company signed a loan agreement with the European Investment Bank (EIB) for €25 million, available in three tranches according to the criteria defined in the agreement. The first tranche of €10 million, not subject to conditions, was paid in July 2021 (to the Company). The loan agreement also contains an agreement to issue share subscription warrants to EIB for the first two tranches of the financing, in particular the issue of 850,000 share subscription warrants with respect to the drawdown of the first tranche. An additional 550,000 share subscription warrants could be issued if OSE Immunotherapeutics draws down the second tranche of €10 million. This first tranche of 850,000 share subscription warrants was issued on the basis of the 17th resolution of the Shareholders' Meeting of June 16, 2020.

The terms and conditions of the share subscription warrants are as follows:
- Subscription price: €0.01
- Maturity date: 12 years
- Exercise price: 97.5% of the volume-weighted average of the trading price of an ordinary share during the last 3 (three) trading days prior to the issue pricing date.
- The vesting is immediate upon issuance of the share subscription warrants.
- Parity: 1 share, except in the event of a capital increase, since the number of shares to be issued must always represent the percentage of fully diluted capital upon issuance of the share subscription warrants (anti-dilution clause applicable if the market price is less than €20 per share), with a deduction for the first 1,500,000 shares issued.

For each share subscription warrants issued, a call and put contract is attached to this derivative, the whole in an inseparable package over a period of five years.

The share subscription warrants were issued on July 8, 2021. Except in the usual cases of early exercise, the share subscription warrants may be exercised from July 8, 2026.

The exercise of all 850,000 share subscription warrants (corresponding to all of the share subscription warrants issued, without any additional share subscription warrants to compensate for subsequent capital increases) is likely to result in the issuance of 850,000 new Company shares. Except in the usual cases of early exercise (change of control, payment default), the share subscription warrants may be exercised at any time from July 8, 2026. Share subscription warrants that have not been exercised by July 8, 2033 will lapse.

From July 8, 2026 or in the event of the usual cases of early exercise (change of control, payment default), the EIB will have the option to ask the Company (i) either to exercise its share subscription warrants, (ii) the buyback of all or part of its share subscription warrants at market value (less the exercise price of the share subscription warrants) with a ceiling of €15 million for all share subscription warrants concerned. It is specified that in the event of exercise after July 8, 2026, and in order to avoid the Company incurring an excessive expense related to the repurchase of the share subscription warrants, if the repurchase of the share subscription warrants by the Company results in a cash level of less than €10 million, the EIB's put option will be exercised on a number of share subscription warrants enabling the Company to retain a cash level of €10 million; the Company will have to repurchase the remaining share subscription warrants as soon as its cash level exceeds €10 million.

However, the Company may replace an existing shareholder or a third party to buy back these share subscription warrants at market value. The Company also has a call option enabling it to buy back the EIB share subscription warrants at market value (less the exercise price of the share subscription warrants) in the event of a public offer by a third party resulting in the exit of the managing shareholders, for a period of one month following said exit.

For the purposes of a possible share subscription warrants' buy-back, the market value will be determined, in the absence of an agreement, by an expert who will act in accordance with the international guidelines for valuation of investment funds (IPEV).

The Company also has a right of first refusal enabling it to buy back the EIB’s share subscription warrants if the latter wishes to sell them to a third party.

ISSUANCE OF 550,000 SHARE SUBSCRIPTION WARRANTS TO THE EIB

As part of the loan agreement presented above, the Company has drawn down a €10 million second tranche linked to 550,000 warrants.

The modalities and terms are the same one than for the 850,000 warrants presented above.

The warrants were issued on December 16, 2022. Unless urgent anticipated exercise, the warrants will be exercisable from December 16, 2027. The warrants not exercised at the latest on December 16, 2034, will be obsolete.

ISSUANCE OF 2018 FOUNDERS' SHARE WARRANTS

On June 13, 2018, the Board of Directors, making use of the delegation from the General Shareholders' Meeting of June 14, 2017, decided to issue 25,900 2018 founders' share warrants for the benefit of Dominique Costantini. This issue served to offset the 2017 founders' share warrants which could not have been subscribed or exercised before the end of the exercise period on March 28, 2018 given the market price.

ISSUANCE OF 2019 FOUNDERS' SHARE WARRANTS

On June 26, 2019, the Board of Directors, making use of the delegation from the General Shareholders' Meeting of June 13, 2018, decided to issue 60,000 2019 founders' share warrants, i.e. 10,000 founders' share warrants for the benefit of each non-salaried non-executive director in office on June 26, 2019.

ISSUANCE OF 2020 FOUNDERS' SHARE WARRANTS

On June 17, 2020, the Board of Directors, making use of the delegation from the General Shareholders' Meeting of June 26, 2019, decided to issue 70,000 2020 founders' share warrants, i.e. 10,000 founders' share warrants for the benefit of each non-salaried non-executive director in office on June 17, 2020.

ISSUANCE OF 2021 FOUNDERS' SHARE WARRANTS

On June 24, 2021, the Board of Directors, making use of the delegation from the General Shareholders' Meeting of June 26, 2019, decided to issue 80,000 2021 founders' share warrants, i.e. 10,000 founders' share warrants for the benefit of each non-salaried non-executive director in office on June 24, 2021.

ISSUANCE OF 2022 FOUNDERS' SHARE WARRANTS

On June 23, 2022, the Board of Directors, making use of the delegation from the General Shareholders' Meeting of June 23, 2022, decided to issue 80,000 2022 founders' share warrants, i.e. 10,000 founders' share warrants for the benefit of each non-salaried non-executive director in office on June 22, 2022.

Plan details

	EIB share subcription warrants	**2022 founders' share subscription warrants**	**2021 founders' share subscription warrants**	**EIB share subscription warrants**	**2020 founders' share subscription warrants**	**2019 founders' share subscription warrants**	**2018 founders' share subscription warrants**	**2018 share subscription warrants**
Date of General Shareholders' Meeting or Board of Directors having allocated the plan	**Extraordinary General Shareholders' Meeting on 6/23/2022** **Board of Directors meeting on 12/02/2022**	**Extraordinary General Shareholders' Meeting on - 6/23/2022** **Board of Directors meeting on 6/23/2022**	**Extraordinary General Shareholders' Meeting on 5/29/2020** **Board of Directors meeting on 6/24/2021**	**Extraordinary General Shareholders' Meeting on 6/16/2020** **Board of Directors meeting on 12/8/2020**	**Extraordinary General Shareholders' Meeting on 6/26/2019** **Board of Directors meeting on 6/17/2020**	**Extraordinary General Shareholders' Meeting on 6/13/2018** **Board of Directors meeting on 6/26/2019**	**Extraordinary General Shareholders' Meeting on 6/14/2017** **Board of Directors meeting on 6/13/2018**	**Extraordinary General Shareholders' Meeting on 6/14/2017**
Maximum number of warrants authorized by General Shareholders' Meetings	Cap of €1,500,000 nominal value	80,000	80,000	Cap of €1,500,000 nominal value	70,000	60,000	500,000	500,000
Number of warrants issued	550,000	80,000	80,000	850,000	70,000	60,000	25,900	42,850
Starting point for exercising warrants	Allocation date	Allocation date	Allocation date	Allocation date	Allocation date	Allocation date	Allocation date	Allocation date
Expiration date	16-Dec-34	23-June-27	24-June-26	08-July-33	17-June-25	26-June-24	13-June-23	13-June-23
Warrant subscription or purchase price	€0.01	€0	€0	€0.01	€0	€0	€0	€0.70
Number of warrants subscribed	550,000	0	0	850,000	10,000	0	0	0

	EIB share subcription warrants	2022 founders' share subscription warrants	2021 founders' share subscription warrants	EIB share subscription warrants	2020 founders' share subscription warrants	2019 founders' share subscription warrants	2018 founders' share subscription warrants	2018 share subscription warrants
Warrant exercise terms	Subscribe common shares	Subscribe common shares	Subscribe common shares	Subscribe common shares	Subscribe common shares	Subscribe common shares	Subscribe common shares	Subscribe common shares
Exercise price	€7.19	€6.63	€11.05	€10.59	€6.14	€3.58	€4.17	€4.17
Number of shares subscribed on the date of this Universal Registration Document	0	0	0	0	10,000	0	0	0
Cumulative number of canceled or lapsed share subscription or purchase warrants	0	0	0	0	0	0	0	0
Remaining subscription warrants to be issued on the date of this Universal Registration Document	0	-	0	0	0	0	0	0

15.2.2 Free share allocations

See Tables 6, 7 and 10 in section 13.1 of this Universal Registration Document.

15.3 Incentive and profit-sharing contracts

The Company's employees do not benefit from any incentive or profit-sharing contracts.

16 Main shareholders

16.1 Changes in shareholding structure

16.1.1 Changes in shareholding over 2 years

To the knowledge of the Board of Directors, the change in the shareholding structure is as follows:

Name	December 31, 2022			December 31, 2021		
	Number of shares	% Capital	% Voting Rights	Number of shares	% Capital	% Voting rights
Emile Loria	3,010,944	16,25%	12,37%	3,199,353	17,27%	13,25%
Dominique Costantini	2,007,163	10,83%	16,38%	2,007,163	10,83%	16,50%
Alexis Peyroles (1)	929,862	5,02%	6,83%	918,499	4,96%	6,20%
Maryvonne Hiance (2)	424,084	2,29%	3,49%	424,084	2,29%	3,41%
Nicolas Poirier	192,802	1,04%	1,17%	192,802	1,04%	0,98%
Mandataires sociaux et autres salariés	495,024	2,67%	3,16%	489,663	2,64%	3,30%
Public	11,467,522	61,89%	0 ,00%	11,295,837	60,97%	56,36%
Total	**18,527,401**	**100%**	**43%**	**18,527,401**	**100%**	**100%**

(1) Directly and indirectly through the intermediary of his asset management company Aperana Consulting.

(2) Directly and indirectly through her asset management company HIANCE MD2A.

16.1.2 Distribution of capital on the registration date of this Universal Registration Document

To date, the share capital stands at €3,780,220.20 divided into 18,901,101 shares, fully subscribed.

16.2 Double voting rights

In accordance with Article L. 225-123 of the French Commercial Code, and unless specified otherwise by the bylaws, shareholders who have owned registered shares for more than two years automatically receive double voting rights. Because no special provision has been stipulated in the bylaws, double voting rights have entered into force for shareholders who met the legal conditions within two years from the Company's first listing, i.e. March 30, 2017.

16.3 Control of the issuer

As of the date of this Universal Registration Document, the Company is not controlled by one shareholder or a group of shareholders.

Out of the ten members of the Board of Directors, seven are independent, the duties of the Chairman and Chief Executive Officer are separated within the Company (this position is temporarily assumed by the same person until the recruitment of a new Chief Executive Officer), and at the Board of Directors meeting on March 27, 2015, this person created two special committees, an Audit Committee and an Appointments and Compensation Committee, which are described above in paragraph 16.3 of this document. The Company has not implemented any other measures to ensure that this control is not exercised improperly.

16.4 Agreements that may lead to a change in control

None

17 Related-party transactions

17.1 Significant agreements with related parties

17.1.1 Agreement between Company subsidiaries and shareholders

OSE PHARMA INTERNATIONAL (OPI)

OSE Pharma International, a limited company (*société anonyme*) with its registered office in Switzerland (known as OPI SA) has share capital of 100,000 Swiss francs and was created in February 2012. Its corporate purpose is the acquisition, holding, operation, development and marketing of intellectual property rights in biotechnology; research and development of products and treatments resulting from such rights, the conduct of studies and clinical trials, the granting of licenses; the identification and the building of relationships involving partners and scientific, financial, manufacturing and governmental investors; investment in companies active in the same sector (in compliance with the Swiss Federal Law on Acquisition of Real Estate by Persons Resident Abroad - LFAIE); all of which in the Americas. Its main asset is worldwide rights relating to the composition of peptides. It has no employees.

In July 2012, OPI (represented by Guy Chatelain) signed a licensing and marketing contract with OSE Pharma for the Tedopi® project (OSE-2101). This first contract gives OSE Pharma the commercial rights to market the product in Europe as well as responsibility for international development in Europe and the USA. OSE Pharma will set up an international development team and will seek to obtain the green light from the two Registration Agencies (EMA and FDA) in both Europe and the USA. The two companies, both controlled by Emile Loria since 2012, have always had the same common goal, i.e. the international clinical development of Tedopi®, for which OSE Pharma is responsible. Initial meetings between the two agencies verified that the international development strategy could be conducted as a Phase 3 trial with a common trial protocol.

The understanding between OSE Pharma and OPI has been identified as a crucial requirement for the continuation and success of the project, both in terms of funding and in terms of potential industrial partnerships across all territories and the expansion of the project to cover other cancers of interest. Since OSE Pharma is responsible for clinical development and has the required management team and expert know-how, this company acquired OPI in April 2014.

In April 2014, OSE Pharma acquired, via the acquisition of OPI, the assets, worldwide rights and know-how of OSE-2101 technology for all cancers of interest expressing HLA-A2. OPI SA in Geneva is now a subsidiary of OSE Pharma, and OPI shareholders are now OSE Pharma shareholders.

17.1.2 Transactions with related parties

Dominique Costantini

Dominique Costantini, Chairwoman of the Board of Directors, has an open-ended employment contract as Director of Development, with gross annual compensation of €302,500 and variable compensation up to three months' salary depending on the achievement of objectives.

At December 31, 2022, Dominique Costantini received for the year 2022: €400,331 gross, including a €71,843 bonus for fiscal year 2020.

The Board of Directors meeting of June 23, 2022, granted 10,000 2022 founders' share warrants to each director, including to Mrs. Costantini.

Nicolas Poirier

Nicolas Poirier, Chief Executive Officer since October 7, 2022, is employed as Chief Scientific Officer. Gross compensation under this employment agreement is of €250,000 with variable compensation up to three months ’salary depending on the achievement of objectives.

On December 7, 2021, the Board of Directors wished to grant Nicolas Poirier an incentive in the form of 150,000 free shares for his leadership of the Research team. These free shares were granted on March 28, 2022.

18 Financial information concerning the issuer's assets, liabilities, financial position and profit or loss

18.1 Financial information concerning the Historical financial information's assets, liabilities, financial position and profit or loss

Fiscal year 2020 historical financial information (annual financial statements and consolidated financial statements) as well as auditors' reports, appear in the Company's 2020 Universal Registration Document, registered with the AMF on April 15, 2021, under number D. 21-0310 and incorporated for reference purposes.

Fiscal year 2021 historical financial information (annual financial statements and consolidated financial statements) as well as auditors' reports, appear in the Company's 2021 Universal Registration Document, registered with the AMF on April 15, 2022, under number D. 22-0298 and incorporated for reference purposes.

18.1.1 Historical financial information

18.1.1.1 Statutory Auditors' report on the consolidated financial statements for the fiscal year ended December 31, 2022

RBB BUSINESS ADVISORS

ERNST & YOUNG et Autres

OSE Immunotherapeutics

Exercice clos le 31 décembre 2022

Rapport des commissaires aux comptes sur les comptes consolidés

RBB BUSINESS ADVISORS
133 bis, rue de l'Université
75007 Paris
S.A. au capital de € 150 000
414 202 341 R.C.S. Paris

Commissaire aux Comptes
Membre de la compagnie
régionale de Paris

ERNST & YOUNG et Autres
Tour First
TSA 14444
92037 Paris-La Défense cedex
S.A.S. à capital variable
438 476 913 R.C.S. Nanterre

Commissaire aux Comptes
Membre de la compagnie
régionale de Versailles et du Centre

OSE Immunotherapeutics
Exercice clos le 31 décembre 2022

Rapport des commissaires aux comptes sur les comptes consolidés

A l'Assemblée Générale de la société OSE Immunotherapeutics,

Opinion

En exécution de la mission qui nous a été confiée par vos assemblées générales, nous avons effectué l'audit des comptes consolidés de la société OSE Immunotherapeutics relatifs à l'exercice clos le 31 décembre 2022, tels qu'ils sont joints au présent rapport.

Nous certifions que les comptes consolidés sont, au regard du référentiel IFRS tel qu'adopté dans l'Union européenne, réguliers et sincères et donnent une image fidèle du résultat des opérations de l'exercice écoulé ainsi que de la situation financière et du patrimoine, à la fin de l'exercice, de l'ensemble constitué par les personnes et entités comprises dans la consolidation.

L'opinion formulée ci-dessus est cohérente avec le contenu de notre rapport au comité d'audit.

Fondement de l'opinion

Référentiel d'audit

Nous avons effectué notre audit selon les normes d'exercice professionnel applicables en France. Nous estimons que les éléments que nous avons collectés sont suffisants et appropriés pour fonder notre opinion.

Les responsabilités qui nous incombent en vertu de ces normes sont indiquées dans la partie « Responsabilités des commissaires aux comptes relatives à l'audit des comptes consolidés » du présent rapport.

Indépendance

Nous avons réalisé notre mission d'audit dans le respect des règles d'indépendance prévues par le Code de commerce et par le Code de déontologie de la profession de commissaire aux comptes sur la période du 1er janvier 2022 à la date d'émission de notre rapport, et notamment nous n'avons pas fourni de services interdits par l'article 5, paragraphe 1, du règlement (UE) n° 537/2014.

Observation

Sans remettre en cause l'opinion exprimée ci-dessus, nous attirons votre attention sur la note 3.1 « Base de préparation des états financiers consolidés » de l'annexe des comptes consolidés qui présente les éléments sous-tendant l'application du principe de continuité d'exploitation de la société.

Justification des appréciations - Points clés de l'audit

En application des dispositions des articles L. 823-9 et R. 823-7 du Code de commerce relatives à la justification de nos appréciations, nous portons à votre connaissance les points clés de l'audit relatifs aux risques d'anomalies significatives qui, selon notre jugement professionnel, ont été les plus importants pour l'audit des comptes consolidés de l'exercice, ainsi que les réponses que nous avons apportées face à ces risques.

Les appréciations ainsi portées s'inscrivent dans le contexte de l'audit des comptes consolidés pris dans leur ensemble et de la formation de notre opinion exprimée ci-avant. Nous n'exprimons pas d'opinion sur des éléments de ces comptes consolidés pris isolément.

Reconnaissance des produits d'exploitation issus des accords de collaboration

Risque identifié	Notre réponse
Le chiffre d'affaires de votre groupe est principalement issu des accords de collaboration mis en place avec des sociétés pharmaceutiques partenaires. Ces accords incluent diverses composantes, d'une part, des montants facturables à la signature et, d'autre part, des montants facturables lors du franchissement de certains objectifs de développement prédéfinis ou bien encore d'objectifs commerciaux ou réglementaires. Comptablement, les montants facturables au titre de la signature du contrat sont soit immédiatement enregistrés en chiffre d'affaires lorsque votre groupe n'a pas d'engagements de développement futurs, soit, lorsque votre groupe n'a pas transféré l'ensemble des droits, étalés sur la durée estimée de l'implication de votre groupe dans les développements futurs, laquelle fait l'objet de révisions périodiques. Les montants facturables liés au franchissement d'un objectif défini contractuellement sont comptabilisés en chiffre d'affaires à la date à laquelle la condition contractuelle est remplie.	Nos travaux ont porté sur l'intégralité des contrats en cours et clos au cours de la période. Nos contrôles ont plus particulièrement consisté à : ▶ analyser les clauses contractuelles et les traitements comptables applicables aux montants facturables à la signature et aux montants facturables au franchissement d'objectifs ; ▶ étudier les hypothèses utilisées dans la reconnaissance du chiffre d'affaires, notamment les dates de finalisation des travaux de recherche et développement de votre groupe ; ▶ étudier le montant des frais de recherche et développement encouru, par rapprochement des coûts avec le grand livre analytique ;

La comptabilisation de ces contrats s'appuie donc sur des estimations et des hypothèses de la direction concernant notamment :

- l'estimation des dates de franchissement des objectifs ;
- le montant estimé des frais de recherche et développement à engager après la signature ;

Nous avons donc considéré que la reconnaissance du chiffre d'affaires issu des accords de collaboration, représentant l'essentiel du chiffre d'affaires de votre groupe, est un point clé de l'audit.

- étudier le montant des frais de recherche et développement restant à encourir au travers d'entretiens avec la direction financière et par examen du budget qui a été validé par le conseil d'administration ;
- rapprocher le budget avec celui de l'année précédente et analyser les variations ;
- vérifier l'exactitude arithmétique du calcul du chiffre d'affaires.

Evaluation des actifs incorporels relatifs à la R&D : OSE-127

Risque identifié	Notre réponse
La valeur nette comptable de l'actif incorporel OSE-127 relatif à la recherche et au développement en cours (R&D) s'élève au 31 décembre 2021 à M€ 15,7. Cet actif immobilisé est constitué de la molécule OSE 127 (ex. Effi-7), issue de l'acquisition de la société Effimune. Les actifs incorporels en cours sont soumis à un test de dépréciation lorsque des circonstances indiquent que la recouvrabilité de leur valeur comptable est mise en doute ou a minima une fois par an. Une perte de valeur est comptabilisée à concurrence de l'excédent de la valeur comptable sur la valeur recouvrable de l'actif. Comme explicité dans la note 4.1.1, ce test de dépréciation sur la molécule OSE-127 a été réalisé en utilisant la méthode de l'actualisation des flux futurs de trésorerie afin d'analyser la valeur d'utilité des actifs. Ces flux de trésorerie prévisionnels prennent en considération plusieurs hypothèses clés : horizon temporel, probabilités de réussite, taux d'actualisation, taux d'imposition. Les conclusions de ces tests ont conduit à une absence de dépréciation. Nous avons considéré que la détermination de la valeur recouvrable des actifs incorporels relatifs à la R&D est un point clé de l'audit en raison (i) de leur importance dans les comptes de votre groupe, (ii) des estimations nécessaires pour déterminer les flux futurs de trésorerie et (iii) des estimations et hypothèses utilisées, notamment en ce qui concerne les probabilités de réussite et le taux d'actualisation, pour déterminer leur valeur d'utilité.	Notre approche d'audit concernant les actifs incorporels relatifs à la R&D repose principalement sur des analyses sur (i) le *business plan* établi par la direction du groupe et incluant différentes hypothèses opérationnelles ainsi que les probabilités de réalisation de ces flux de trésorerie prévisionnels et (ii) le modèle financier contribuant à déterminer la valeur recouvrable de chacun des actifs utilisés par votre groupe. Nous avons focalisé notre attention sur les éléments suivants : - Les principales hypothèses opérationnelles incluses dans le *business plan* : nous avons pris connaissance des estimations et des hypothèses retenues et les avons rapprochées avec les informations prévisionnelles communiquées par les sociétés pharmaceutiques partenaires. Nous avons également vérifié l'exactitude arithmétique du *business plan* produit par la direction. Nous avons rapproché ce *business plan* avec le budget approuvé par votre conseil d'administration. - Les probabilités de réussite : nous avons examiné les différentes probabilités de réussite retenues et comparé celles-ci aux pratiques observées dans le secteur des biotechnologies. - Le taux d'actualisation : nous avons apprécié le taux d'actualisation retenu, en incluant dans notre équipe d'audit des experts en évaluation financière.

- Le taux d'imposition : nous avons apprécié le taux d'imposition retenu en incluant dans notre équipe d'audit des experts en fiscalité.
- Les tests de sensibilité : nous avons examiné l'analyse de sensibilité de la valeur d'utilité effectuée par la direction, à une variation des principales hypothèses retenues.
- Enfin, nous avons vérifié que la note 4.1.1 de l'annexe des comptes consolidés donnait une information appropriée.

Caractère exhaustif des dépenses de recherche et développement sous-traitées (études cliniques)

Risque identifié	Notre réponse
Votre groupe poursuit des programmes de recherche précliniques et cliniques en collaboration avec des centres de recherche et d'essais cliniques sous contrat. Au 31 décembre 2022, les frais de sous-traitance de recherche et développement s'élèvent à M€ 17,9. Les dépenses de recherche et développement engagées à ce titre sont systématiquement reconnues en charges selon l'avancement des projets. A la clôture, sur la base des informations transmises par les prestataires ou des calendriers de réalisation prévus aux contrats, la direction détermine les avancements au *prorata temporis* de chacune des prestations de recherche. Compte tenu de l'importance des dépenses de recherche et développement et de leur méthode d'estimation à la clôture de l'exercice, nous avons considéré leur caractère exhaustif comme un point clé de notre audit.	Nos travaux ont notamment consisté à prendre connaissance des éléments justifiant les estimations clés utilisées par la direction pour déterminer le montant des charges à provisionner dans les comptes à la clôture de l'exercice. Dans ce cadre, nous avons : - pris connaissance du processus de contrôle interne de suivi de l'avancement des charges mis en place par votre société afin d'identifier et d'estimer les coûts à provisionner à la clôture de l'exercice ; - étudié les contrats significatifs conclus avec les centres de recherche et d'essais cliniques, ainsi que les éléments établis par la direction justifiant des coûts des essais réalisés ; - étudié les débouclages des provisions de l'année précédente afin d'examiner la cohérence des estimations réalisées par la direction ; - examiné la cohérence du stade d'avancement des projets et le calcul de la charge afférente, au regard des informations transmises par les centres de recherche et d'essais cliniques ou issues de l'analyse réalisée par la direction sur la base des calendriers de réalisation prévus aux contrats ; - analysé, le cas échéant, les factures émises après la clôture afin d'examiner l'absence de décalage avec les estimations réalisées.

Vérifications spécifiques

Nous avons également procédé, conformément aux normes d'exercice professionnel applicables en France, aux vérifications spécifiques prévues par les textes légaux et réglementaires des informations relatives au groupe, données dans le rapport de gestion du conseil d'administration.

Nous n'avons pas d'observation à formuler sur leur sincérité et leur concordance avec les comptes consolidés.

Autres vérifications ou informations prévues par les textes légaux et réglementaires

Format de présentation des comptes consolidés destinés à être inclus dans le rapport financier annuel

Nous avons également procédé, conformément à la norme d'exercice professionnel sur les diligences du commissaire aux comptes relatives aux comptes annuels et consolidés présentés selon le format d'information électronique unique européen, à la vérification du respect de ce format défini par le règlement européen délégué n° 2019/815 du 17 décembre 2018 dans la présentation des comptes consolidés destinés à être inclus dans le rapport financier annuel mentionné au I de l'article L. 451-1-2 du Code monétaire et financier, établis sous la responsabilité du Directeur General. S'agissant de comptes consolidés, nos diligences comprennent la vérification de la conformité du balisage de ces comptes au format défini par le règlement précité.

Sur la base de nos travaux, nous concluons que la présentation des comptes consolidés destinés à être inclus dans le rapport financier annuel respecte, dans tous ses aspects significatifs, le format d'information électronique unique européen.

Par ailleurs, il ne nous appartient pas de vérifier que les comptes consolidés qui seront effectivement inclus par votre société dans le rapport financier annuel déposé auprès de l'AMF correspondent à ceux sur lesquels nous avons réalisé nos travaux.

Désignation des commissaires aux comptes

Nous avons été nommés commissaires aux comptes de la société OSE Immunotherapeutics par votre assemblée générale du 17 septembre 2014 pour le cabinet RBB BUSINESS ADVISORS et par décision de l'associé unique du 27 avril 2012 pour le cabinet ERNST & YOUNG et Autres.

Au 31 décembre 2022, le cabinet RBB BUSINESS ADVISORS était dans la neuvième année de sa mission sans interruption et le cabinet ERNST & YOUNG et Autres dans la onzième année dont huit années depuis que les titres de la société ont été admis aux négociations sur un marché réglementé

Responsabilités de la direction et des personnes constituant le gouvernement d'entreprise relatives aux comptes consolidés

Il appartient à la direction d'établir des comptes consolidés présentant une image fidèle conformément au référentiel IFRS tel qu'adopté dans l'Union européenne ainsi que de mettre en place le contrôle interne qu'elle estime nécessaire à l'établissement de comptes consolidés ne comportant pas d'anomalies significatives, que celles-ci proviennent de fraudes ou résultent d'erreurs.

Lors de l'établissement des comptes consolidés, il incombe à la direction d'évaluer la capacité de la société à poursuivre son exploitation, de présenter dans ces comptes, le cas échéant, les informations nécessaires relatives à la continuité d'exploitation et d'appliquer la convention comptable de continuité d'exploitation, sauf s'il est prévu de liquider la société ou de cesser son activité.

Il incombe au comité d'audit de suivre le processus d'élaboration de l'information financière et de suivre l'efficacité des systèmes de contrôle interne et de gestion des risques, ainsi que le cas échéant de l'audit interne, en ce qui concerne les procédures relatives à l'élaboration et au traitement de l'information comptable et financière.

Les comptes consolidés ont été arrêtés par le conseil d'administration.

Responsabilités des commissaires aux comptes relatives à l'audit des comptes consolidés

Objectif et démarche d'audit

Il nous appartient d'établir un rapport sur les comptes consolidés. Notre objectif est d'obtenir l'assurance raisonnable que les comptes consolidés pris dans leur ensemble ne comportent pas d'anomalies significatives. L'assurance raisonnable correspond à un niveau élevé d'assurance, sans toutefois garantir qu'un audit réalisé conformément aux normes d'exercice professionnel permet de systématiquement détecter toute anomalie significative. Les anomalies peuvent provenir de fraudes ou résulter d'erreurs et sont considérées comme significatives lorsque l'on peut raisonnablement s'attendre à ce qu'elles puissent, prises individuellement ou en cumulé, influencer les décisions économiques que les utilisateurs des comptes prennent en se fondant sur ceux-ci.

Comme précisé par l'article L. 823-10-1 du Code de commerce, notre mission de certification des comptes ne consiste pas à garantir la viabilité ou la qualité de la gestion de votre société.

Dans le cadre d'un audit réalisé conformément aux normes d'exercice professionnel applicables en France, le commissaire aux comptes exerce son jugement professionnel tout au long de cet audit. En outre :

- il identifie et évalue les risques que les comptes consolidés comportent des anomalies significatives, que celles-ci proviennent de fraudes ou résultent d'erreurs, définit et met en œuvre des procédures d'audit face à ces risques, et recueille des éléments qu'il estime suffisants et appropriés pour fonder son opinion. Le risque de non-détection d'une anomalie significative provenant d'une fraude est plus élevé que celui d'une anomalie significative résultant d'une erreur, car la fraude peut impliquer la collusion, la falsification, les omissions volontaires, les fausses déclarations ou le contournement du contrôle interne ;

- il prend connaissance du contrôle interne pertinent pour l'audit afin de définir des procédures d'audit appropriées en la circonstance, et non dans le but d'exprimer une opinion sur l'efficacité du contrôle interne ;

- il apprécie le caractère approprié des méthodes comptables retenues et le caractère raisonnable des estimations comptables faites par la direction, ainsi que les informations les concernant fournies dans les comptes consolidés ;

- il apprécie le caractère approprié de l'application par la direction de la convention comptable de continuité d'exploitation et, selon les éléments collectés, l'existence ou non d'une incertitude significative liée à des événements ou à des circonstances susceptibles de mettre en cause la capacité de la société à poursuivre son exploitation. Cette appréciation s'appuie sur les éléments collectés jusqu'à la date de son rapport, étant toutefois rappelé que des circonstances ou événements ultérieurs pourraient mettre en cause la continuité d'exploitation. S'il conclut à l'existence d'une incertitude significative, il attire l'attention des lecteurs de son rapport sur les informations fournies dans les comptes consolidés au sujet de cette incertitude ou, si ces informations ne sont pas fournies ou ne sont pas pertinentes, il formule une certification avec réserve ou un refus de certifier ;

- il apprécie la présentation d'ensemble des comptes consolidés et évalue si les comptes consolidés reflètent les opérations et événements sous-jacents de manière à en donner une image fidèle ;

- concernant l'information financière des personnes ou entités comprises dans le périmètre de consolidation, il collecte des éléments qu'il estime suffisants et appropriés pour exprimer une opinion sur les comptes consolidés. Il est responsable de la direction, de la supervision et de la réalisation de l'audit des comptes consolidés ainsi que de l'opinion exprimée sur ces comptes.

Rapport au comité d'audit

Nous remettons au comité d'audit un rapport qui présente notamment l'étendue des travaux d'audit et le programme de travail mis en œuvre, ainsi que les conclusions découlant de nos travaux. Nous portons également à sa connaissance, le cas échéant, les faiblesses significatives du contrôle interne que nous avons identifiées pour ce qui concerne les procédures relatives à l'élaboration et au traitement de l'information comptable et financière.

Parmi les éléments communiqués dans le rapport au comité d'audit figurent les risques d'anomalies significatives, que nous jugeons avoir été les plus importants pour l'audit des comptes consolidés de l'exercice et qui constituent de ce fait les points clés de l'audit, qu'il nous appartient de décrire dans le présent rapport.

Nous fournissons également au comité d'audit la déclaration prévue par l'article 6 du règlement (UE) n° 537/2014 confirmant notre indépendance, au sens des règles applicables en France telles qu'elles sont fixées notamment par les articles L. 822-10 à L. 822-14 du Code de commerce et dans le Code de déontologie de la profession de commissaire aux comptes. Le cas échéant, nous nous entretenons avec le comité d'audit des risques pesant sur notre indépendance et des mesures de sauvegarde appliquées.

Paris et Paris-La Défense, le 28 avril 2023

Les Commissaires aux Comptes

RBB BUSINESS ADVISORS	ERNST & YOUNG et Autres
Marc Baijot	Cédric Garcia

18.1.1.2 *Statutory Auditors' report on the annual financial statements for the fiscal year ended December 31, 2022*

RBB BUSINESS ADVISORS

ERNST & YOUNG et Autres

OSE Immunotherapeutics

Exercice clos le 31 décembre 2022

Rapport des commissaires aux comptes sur les comptes annuels

RBB BUSINESS ADVISORS
133 bis, rue de l'Université
75007 Paris
S.A. au capital de € 150 000
414 202 341 R.C.S. Paris

Commissaire aux Comptes
Membre de la compagnie
régionale de Paris

ERNST & YOUNG et Autres
Tour First
TSA 14444
92037 Paris-La Défense cedex
S.A.S. à capital variable
438 476 913 R.C.S. Nanterre

Commissaire aux Comptes
Membre de la compagnie
régionale de Versailles et du Centre

OSE Immunotherapeutics
Exercice clos le 31 décembre 2022

Rapport des commissaires aux comptes sur les comptes annuels

A l'Assemblée Générale de la société OSE Immunotherapeutics,

Opinion

En exécution de la mission qui nous a été confiée par vos assemblées générales, nous avons effectué l'audit des comptes annuels de la société OSE Immunotherapeutics relatifs à l'exercice clos le 31 décembre 2022, tels qu'ils sont joints au présent rapport.

Nous certifions que les comptes annuels sont, au regard des règles et principes comptables français, réguliers et sincères et donnent une image fidèle du résultat des opérations de l'exercice écoulé ainsi que de la situation financière et du patrimoine de la société à la fin de cet exercice.

L'opinion formulée ci-dessus est cohérente avec le contenu de notre rapport au comité d'audit.

Fondement de l'opinion

Référentiel d'audit

Nous avons effectué notre audit selon les normes d'exercice professionnel applicables en France. Nous estimons que les éléments que nous avons collectés sont suffisants et appropriés pour fonder notre opinion.

Les responsabilités qui nous incombent en vertu de ces normes sont indiquées dans la partie « Responsabilités des commissaires aux comptes relatives à l'audit des comptes annuels » du présent rapport.

Indépendance

Nous avons réalisé notre mission d'audit dans le respect des règles d'indépendance prévues par le Code de commerce et par le Code de déontologie de la profession de commissaire aux comptes sur la période du

1er janvier 2022 à la date d'émission de notre rapport, et notamment nous n'avons pas fourni de services interdits par l'article 5, paragraphe 1, du règlement (UE) n° 537/2014.

Observation

Sans remettre en cause l'opinion exprimée ci-dessus, nous attirons votre attention sur le paragraphe « continuité d'exploitation » de la note « Règles et méthodes comptable » de l'annexe aux comptes annuels qui présente les éléments sous-tendant l'application du principe de continuité d'exploitation de la société

Justification des appréciations - Points clés de l'audit

En application des dispositions des articles L. 823-9 et R. 823-7 du Code de commerce relatives à la justification de nos appréciations, nous portons à votre connaissance les points clés de l'audit relatifs aux risques d'anomalies significatives qui, selon notre jugement professionnel, ont été les plus importants pour l'audit des comptes annuels de l'exercice, ainsi que les réponses que nous avons apportées face à ces risques.

Les appréciations ainsi portées s'inscrivent dans le contexte de l'audit des comptes annuels pris dans leur ensemble et de la formation de notre opinion exprimée ci-avant. Nous n'exprimons pas d'opinion sur des éléments de ces comptes annuels pris isolément.

Reconnaissance des produits d'exploitation issus des accords de collaboration

Cf. note « Produits d'exploitation » de l'annexe des comptes annuels

Risque identifié	Notre réponse
Les produits d'exploitation de votre société sont principalement issus des accords de collaboration mis en place avec des sociétés pharmaceutiques partenaires. Ces accords incluent diverses composantes, d'une part, des montants facturables à la signature et, d'autre part, des montants facturables lors du franchissement de certains objectifs de développement prédéfinis, ou bien encore d'objectifs commerciaux ou réglementaires. Comptablement, les montants facturables au titre de la signature du contrat sont soit immédiatement enregistrés en produits lorsque votre société n'a pas d'engagements de développement futurs, soit, lorsque votre société n'a pas transféré l'ensemble des droits, étalés sur la durée estimée de l'implication de votre société dans les développements futurs, laquelle fait l'objet de révisions périodiques. Les montants facturables liés au franchissement d'un objectif défini contractuellement sont comptabilisés en produits à la date à laquelle la condition contractuelle est remplie. La comptabilisation de ces contrats s'appuie donc sur des estimations et hypothèses de la direction concernant notamment :	Nos travaux ont porté sur l'intégralité des contrats en cours et clos au cours de la période. Nos contrôles ont ainsi consisté à : ▶ étudier les hypothèses utilisées pour la reconnaissance du chiffre d'affaires, notamment les dates de finalisation des travaux de recherche et développement de votre société; ▶ étudier le montant des frais de recherche et développement encouru, par rapprochement des coûts avec le grand livre analytique ; ▶ étudier le montant des frais de recherche et développement restant à encourir, au travers d'entretiens avec la direction financière et par examen du budget qui a été validé par votre conseil d'administration ; ▶ rapprocher le budget avec celui de l'année précédente et analyser les variations ; ▶ vérifier l'exactitude arithmétique du calcul du chiffre d'affaires.

La comptabilisation de ces contrats s'appuie donc sur des estimations et hypothèses de la direction concernant notamment :

- l'estimation des dates de franchissement des objectifs ;
- le montant estimé des frais de recherche et développement à engager après la signature.

Dès lors, nous avons considéré que la reconnaissance des produits d'exploitation issus de ces contrats de collaboration constituait un point clé de l'audit.

Evaluation du fonds commercial

Cf. note « Immobilisations incorporelles » de l'annexe des comptes annuels

Risque identifié	Notre réponse
Comme mentionné dans la note « Immobilisations incorporelles » des parties « Règles et méthodes comptables » et « Notes relatives à certains postes du bilan » de l'annexe des comptes annuels, le fonds commercial est inscrit au bilan pour une valeur nette comptable de K€ 42 734. Il est comptabilisé au coût d'acquisition. Ce fonds commercial a été affecté aux molécules, FR104 et OSE-127, issues de l'acquisition de la société Effimune. Lorsque la valeur actuelle de cet actif est inférieure à la valeur comptable, une dépréciation est constituée du montant de la différence. Comme explicité dans la note « Immobilisations incorporelles », ce test de dépréciation a été réalisé en utilisant la méthode de l'actualisation des flux futurs de trésorerie afin d'analyser la valeur d'utilité des actifs. Ces flux de trésorerie prévisionnels prennent en considération plusieurs hypothèses clés : horizon temporel, probabilités de réussite, taux d'actualisation, taux d'imposition. La réalisation de ces tests a conduit la direction à conclure à une absence de dépréciation. Compte tenu de l'importance du fonds commercial et de l'impact significatif qu'aurait une évolution des estimations et des hypothèses, notamment en ce qui concerne les probabilités de réussite et le taux d'actualisation, sur la valeur d'utilité, nous avons considéré l'évaluation du fonds commercial comme un point clé de l'audit.	Notre appréciation de la valeur du fonds commercial est fondée sur le processus mis en place par votre société pour déterminer la valeur d'utilité de cet actif. Nos travaux ont notamment consisté à : - prendre connaissance de la méthodologie retenue par la direction pour évaluer la valeur d'utilité de cet actif ; - analyser le *business plan* élaboré par la direction, en rapprochant les éléments prévisionnels utilisés provenant du budget approuvé par votre conseil d'administration ; - examiner les différentes probabilités de succès retenues et comparer celles-ci aux pratiques observées dans le secteur des biotechnologies ; - apprécier le taux d'actualisation retenu, en incluant des experts en évaluation financière dans notre équipe d'audit. Des tests de sensibilité ont ainsi été réalisés par la société et examinés par nos soins ; - apprécier le taux d'imposition retenu en incluant des experts en fiscalité dans notre équipe d'audit ; - vérifier les calculs réalisés par la direction de votre société dans le *business plan* et le modèle financier établis ; - étudier les tests de sensibilité : nous avons apprécié l'analyse de sensibilité de la valeur d'utilité effectuée par la direction, à une variation des principales hypothèses retenues ;

vérifier que les notes « Immobilisations incorporelles » des parties « Règles et méthodes comptables » et « Notes relatives à certains postes du bilan » donnaient une information appropriée.

Evaluation des titres de participation

Cf. note « Immobilisations financières » de l'annexe des comptes annuels

Risque identifié	Notre réponse
Comme mentionné dans les notes « Immobilisations financières » des parties « Règles et méthodes comptables » et « Notes relatives à certains postes du bilan » de l'annexe des comptes annuels, les titres de participation sont inscrits au bilan pour une valeur nette comptable de K€ 50 000. Ils sont comptabilisés à la date d'entrée au coût d'acquisition ou à la valeur d'apport. Les titres de participation sont constitués essentiellement des titres de l'entité OSE Pharma International (OPI) qui possède les droits sur la molécule OSE-2101. Lorsque la valeur actuelle de ces actifs est inférieure à la valeur comptable, une dépréciation est constituée du montant de la différence. La valeur actuelle de ces actifs, comme exposé dans la note « Immobilisations financières », est établie sur la base d'éléments prévisionnels via la réalisation de flux futurs de trésorerie (DCF) issus des *business plans* établis par la direction. Les flux de trésorerie retenus pour tester les titres de participation de l'entité OPI incluent les projections de la direction pour la molécule OSE-2101 dont l'entité OPI détient les droits d'exploitation. Ces flux de trésorerie prévisionnels prennent en considération plusieurs hypothèses clés : horizon temporel, probabilités de réussite, taux d'actualisation, taux d'imposition. La réalisation de ces tests a conduit la direction à conclure à une absence de dépréciation. Les perspectives de rentabilité et les incertitudes inhérentes à certaines hypothèses requièrent l'exercice du jugement de la direction afin de confirmer l'évaluation faite de la valeur nette comptable des titres de participation.	Notre appréciation de l'évaluation de la valeur des titres de participation est fondée sur le processus mis en place par votre société pour déterminer la valeur d'utilité de ces actifs. Nos travaux ont notamment consisté à : ► prendre connaissance de la méthodologie retenue par la direction pour évaluer la valeur d'utilité de ces actifs ; ► analyser le *business plan* élaboré par la direction, ces évaluations reposant sur des éléments prévisionnels ; ► apprécier les différentes probabilités de réussite retenues et comparer celles-ci aux pratiques observées dans le secteur des biotechnologies, notamment dans le domaine de l'oncologie ; ► étudier la pertinence du taux d'actualisation retenu, en incluant des experts en évaluation financière dans notre équipe d'audit. Des tests de sensibilité ont ainsi été réalisés par la direction de votre société et examinés par nos soins ; ► apprécier le taux d'imposition retenu en incluant des experts en fiscalité dans notre équipe d'audit ; vérifier les calculs réalisés par la direction de votre société dans le *business plan* et le modèle financier établis.

Compte tenu de l'importance des titres de participation et de l'impact significatif qu'aurait une évolution des estimations et des hypothèses, notamment en ce qui concerne les probabilités de réussite et le taux d'actualisation sur leur valeur actuelle, nous avons considéré l'évaluation des titres de participation comme un point clé de l'audit.

Caractère exhaustif des dépenses de recherche et développement sous-traitées (études cliniques)

Cf. « Frais de recherche et développement » de l'annexe des comptes annuels.

Risque identifié	Notre réponse
Votre société poursuit des programmes de recherche en collaboration avec des centres de recherche sous contrat. Au 31 décembre 2022, les frais de sous-traitance de recherche et développement s'élèvent à m€ 17,9. Les dépenses de recherche et développement engagées à ce titre sont systématiquement comptabilisées en charges selon l'avancement des projets. A la clôture de l'exercice, sur la base des informations transmises par les prestataires ou des calendriers de réalisation prévus aux contrats, la direction détermine les avancements au *prorata temporis* de chacune des prestations de recherche. Compte tenu de l'importance des dépenses de recherche et développement et de leur méthode d'estimation à la clôture de l'exercice, nous avons considéré leur évaluation comme un point clé de l'audit.	Nos travaux ont notamment consisté à prendre connaissance des éléments justifiant les estimations clés utilisées par la direction pour déterminer le montant des charges à provisionner dans les comptes à la clôture de l'exercice. Dans ce cadre, nous avons : ▶ pris connaissance du processus de contrôle interne de suivi relatif à l'avancement des charges mis en place par votre société afin d'identifier et d'estimer les coûts à provisionner à la clôture de l'exercice ; ▶ étudié les contrats significatifs conclus avec les centres de recherche et d'essais cliniques, ainsi que les éléments établis par la direction justifiant des coûts des essais réalisés ; ▶ étudié, le cas échéant, les débouclages de provisions de l'année précédente afin d'examiner la cohérence des estimations passées de la direction ; ▶ examiné la cohérence du stade d'avancement des projets et le calcul de la charge afférente, au regard des informations transmises par les prestataires ou issues de l'analyse réalisée par la direction sur la base des calendriers de réalisation prévus aux contrats ; analysé, le cas échéant, les factures émises après la clôture, afin d'examiner l'absence de décalage avec les estimations réalisées.

Vérifications spécifiques

Nous avons également procédé, conformément aux normes d'exercice professionnel applicables en France, aux vérifications spécifiques prévues par les textes légaux et réglementaires.

Informations données dans le rapport de gestion et dans les autres documents sur la situation financière et les comptes annuels adressés aux actionnaires

Nous n'avons pas d'observation à formuler sur la sincérité et la concordance avec les comptes annuels des informations données dans le rapport de gestion du conseil d'administration et dans les autres documents sur la situation financière et les comptes annuels adressés aux actionnaires.

Nous attestons de la sincérité et de la concordance avec les comptes annuels des informations relatives aux délais de paiement mentionnées à l'article D. 441-6 du Code de commerce.

Informations relatives au gouvernement d'entreprise

Nous attestons de l'existence, dans la section du rapport de gestion du conseil d'administration consacrée au gouvernement d'entreprise, des informations requises par les articles L. 225-37-4, L. 22-10-10 et L. 22-10-9 du Code de commerce.

Concernant les informations fournies en application des dispositions de l'article L. 22-10-9 du Code de commerce sur les rémunérations et avantages versés ou attribués aux mandataires sociaux ainsi que sur les engagements consentis en leur faveur, nous avons vérifié leur concordance avec les comptes ou avec les données ayant servi à l'établissement de ces comptes et, le cas échéant, avec les éléments recueillis par votre société auprès des entreprises contrôlées par elle qui sont comprises dans le périmètre de consolidation. Sur la base de ces travaux, nous attestons l'exactitude et la sincérité de ces informations.

Autres informations

En application de la loi, nous nous sommes assurés que les diverses informations relatives à l'identité des détenteurs du capital ou des droits de vote vous ont été communiquées dans le rapport de gestion.

Autres vérifications ou informations prévues par les textes légaux et réglementaires

Format de présentation des comptes annuels destinés à être inclus dans le rapport financier annuel

Nous avons également procédé, conformément à la norme d'exercice professionnel sur les diligences du commissaire aux comptes relatives aux comptes annuels et consolidés présentés selon le format d'information électronique unique européen, à la vérification du respect de ce format défini par le règlement européen délégué n° 2019/815 du 17 décembre 2018 dans la présentation des comptes annuels destinés à être inclus dans le rapport financier annuel mentionné au I de l'article L. 451-1-2 du Code monétaire et financier, établis sous la responsabilité du Directeur General.

Sur la base de nos travaux, nous concluons que la présentation des comptes annuels destinés à être inclus dans le rapport financier annuel respecte, dans tous ses aspects significatifs, le format d'information électronique unique européen.

Il ne nous appartient pas de vérifier que les comptes annuels qui seront effectivement inclus par votre société dans le rapport financier annuel déposé auprès de l'AMF correspondent à ceux sur lesquels nous avons réalisé nos travaux.

■ **Désignation des commissaires aux comptes**

Nous avons été nommés commissaires aux comptes de la société OSE Immunotherapeutics par votre assemblée générale du 17 septembre 2014 pour le cabinet RBB BUSINESS ADVISORS et par décision de l'associé unique du 27 avril 2012 pour le cabinet ERNST & YOUNG et Autres.

Au 31 décembre 2022, le cabinet RBB BUSINESS ADVISORS était dans la neuvième année de sa mission sans interruption et le cabinet ERNST & YOUNG et Autres dans la onzième année dont huit années depuis que les titres de la société ont été admis aux négociations sur un marché réglementé.

Responsabilités de la direction et des personnes constituant le gouvernement d'entreprise relatives aux comptes annuels

Il appartient à la direction d'établir des comptes annuels présentant une image fidèle conformément aux règles et principes comptables français ainsi que de mettre en place le contrôle interne qu'elle estime nécessaire à l'établissement de comptes annuels ne comportant pas d'anomalies significatives, que celles-ci proviennent de fraudes ou résultent d'erreurs.

Lors de l'établissement des comptes annuels, il incombe à la direction d'évaluer la capacité de la société à poursuivre son exploitation, de présenter dans ces comptes, le cas échéant, les informations nécessaires relatives à la continuité d'exploitation et d'appliquer la convention comptable de continuité d'exploitation, sauf s'il est prévu de liquider la société ou de cesser son activité.

Il incombe au comité d'audit de suivre le processus d'élaboration de l'information financière et de suivre l'efficacité des systèmes de contrôle interne et de gestion des risques, ainsi que le cas échéant de l'audit interne, en ce qui concerne les procédures relatives à l'élaboration et au traitement de l'information comptable et financière.

Les comptes annuels ont été arrêtés par le conseil d'administration.

Responsabilités des commissaires aux comptes relatives à l'audit des comptes annuels

■ **Objectif et démarche d'audit**

Il nous appartient d'établir un rapport sur les comptes annuels. Notre objectif est d'obtenir l'assurance raisonnable que les comptes annuels pris dans leur ensemble ne comportent pas d'anomalies significatives. L'assurance raisonnable correspond à un niveau élevé d'assurance, sans toutefois garantir qu'un audit réalisé conformément aux normes d'exercice professionnel permet de systématiquement détecter toute anomalie significative. Les anomalies peuvent provenir de fraudes ou résulter d'erreurs et sont considérées comme significatives lorsque l'on peut raisonnablement s'attendre à ce qu'elles puissent, prises individuellement ou en cumulé, influencer les décisions économiques que les utilisateurs des comptes prennent en se fondant sur ceux-ci.

Comme précisé par l'article L. 823-10-1 du Code de commerce, notre mission de certification des comptes ne consiste pas à garantir la viabilité ou la qualité de la gestion de votre société.

Dans le cadre d'un audit réalisé conformément aux normes d'exercice professionnel applicables en France, le commissaire aux comptes exerce son jugement professionnel tout au long de cet audit. En outre :

- il identifie et évalue les risques que les comptes annuels comportent des anomalies significatives, que celles-ci proviennent de fraudes ou résultent d'erreurs, définit et met en œuvre des procédures d'audit face à ces risques, et recueille des éléments qu'il estime suffisants et appropriés pour fonder son opinion. Le risque de non-détection d'une anomalie significative provenant d'une fraude est plus élevé que celui d'une anomalie significative résultant d'une erreur, car la fraude peut impliquer la collusion, la falsification, les omissions volontaires, les fausses déclarations ou le contournement du contrôle interne ;
- il prend connaissance du contrôle interne pertinent pour l'audit afin de définir des procédures d'audit appropriées en la circonstance, et non dans le but d'exprimer une opinion sur l'efficacité du contrôle interne ;
- il apprécie le caractère approprié des méthodes comptables retenues et le caractère raisonnable des estimations comptables faites par la direction, ainsi que les informations les concernant fournies dans les comptes annuels ;
- il apprécie le caractère approprié de l'application par la direction de la convention comptable de continuité d'exploitation et, selon les éléments collectés, l'existence ou non d'une incertitude significative liée à des événements ou à des circonstances susceptibles de mettre en cause la capacité de la société à poursuivre son exploitation. Cette appréciation s'appuie sur les éléments collectés jusqu'à la date de son rapport, étant toutefois rappelé que des circonstances ou événements ultérieurs pourraient mettre en cause la continuité d'exploitation. S'il conclut à l'existence d'une incertitude significative, il attire l'attention des lecteurs de son rapport sur les informations fournies dans les comptes annuels au sujet de cette incertitude ou, si ces informations ne sont pas fournies ou ne sont pas pertinentes, il formule une certification avec réserve ou un refus de certifier ;
- il apprécie la présentation d'ensemble des comptes annuels et évalue si les comptes annuels reflètent les opérations et événements sous-jacents de manière à en donner une image fidèle.

Rapport au comité d'audit

Nous remettons au comité d'audit un rapport qui présente notamment l'étendue des travaux d'audit et le programme de travail mis en œuvre, ainsi que les conclusions découlant de nos travaux. Nous portons également à sa connaissance, le cas échéant, les faiblesses significatives du contrôle interne que nous avons identifiées pour ce qui concerne les procédures relatives à l'élaboration et au traitement de l'information comptable et financière.

Parmi les éléments communiqués dans le rapport au comité d'audit figurent les risques d'anomalies significatives, que nous jugeons avoir été les plus importants pour l'audit des comptes annuels de l'exercice et qui constituent de ce fait les points clés de l'audit, qu'il nous appartient de décrire dans le présent rapport.

Nous fournissons également au comité d'audit la déclaration prévue par l'article 6 du règlement (UE) n° 537/2014 confirmant notre indépendance, au sens des règles applicables en France telles qu'elles sont fixées notamment par les articles L. 822-10 à L. 822-14 du Code de commerce et dans le Code de déontologie de la profession de commissaire aux comptes. Le cas échéant, nous nous entretenons avec le comité d'audit des risques pesant sur notre indépendance et des mesures de sauvegarde appliquées.

Paris et Paris-La Défense, le 28 avril 2023

Les Commissaires aux Comptes

RBB BUSINESS ADVISORS

Marc Baïjot

ERNST & YOUNG et Autres

Cédric Garcia

18.1.2 Change of accounting reference date

Not applicable

18.1.3 Accounting standards

See Part 3 of Section 18.1.6 "Consolidated financial statements"

18.1.4 Change of accounting standards

Not applicable

18.1.5 Annual financial statements for the fiscal year ended December 31, 2022

Assets in €K	**31/12/2022**	**31/12/2021**
Non-current assets		
Intangible assets	42,901	42,882
Tangible assets	743	926
Non-current financial assets	51,074	51,241
Total non-current assets	**94,718**	**95,050**
Current assets		
Stocks and receivables		
Receivables	9,409	8,894
Marketable securities	86	82
Cash and cash equivalents	25,522	33,493
Prepaid expenses	3,452	2,964
Total current assets	**38,468**	**45,433**
Current conversion difference		2
Total assets	**133,186**	**140,484**

Liabilities in K€	**31/12/2022**	**12/31/2021**
Stated capital	3,705	3,705
Share premium	132,332	132,327
Legal reserve	-	-
Retained earnings	(42,667)	(30,500)
Net result	(14,139)	(12,166)
Total shareholders' equity	**79,232**	**93,365**
Conditioned advances	14,425	14,425
Total other equity	**14,425**	**14,425**
Provision for risks	681	477
Provision for charges	432	421
al provision for risks and charges	**1,113**	**898**
Current financial liabilities	26,263	17,253
Other current financial liabilities	505	389

Trade payables	8,493	9,594
Fiscal ans social debts	2,535	3,737
Other debts and accruals	33	
Deffered income	588	822
Total current debts	**38,417**	**31,796**
Exchange difference		0
Total liabilities	**133,186**	**140,484**

Income statement

P&L in K€	**31/12/2022**	**31/12/2021**
Turnover	3,303	6,147
Other revenues	17,074	21,427
Total Revenues	**20,377**	**27,574**
Other purchase ans external expenses	26,980	31,178
Staff cost	8,476	9,471
Tax expenses	153	164
Depreciation for amortisation and provision	1,614	869
Other expenses	1,854	2,074
Total Operating costs	**39,077**	**43,756**
Operating Profit/Loss	**(18,700)**	**(16,183)**
Financial products	30	35
Financial expenses	703	422
Financial result	**(673)**	**(388)**
Profit/Loss Before Tax	**(19,374)**	**(16,571)**
Exceptional product	91	286
Exceptional expenses	289	226
Exceptional result	**(198)**	**60**
Income Tax	(5,432)	(4,344)
Net Profit/Loss	**(14,139)**	**(12,166)**

18.1.6 Consolidated financial statements for the fiscal year ended December 31, 2022

Consolidated balance sheet

ASSETS in €k	**Note**	**12/31/2022**	**12/31/2021**
Intangible assets			
R&D	1.1	48,784	51,122
Tangible assets	1.2	743	926
Right-of-use assets	1.3	4,236	4,513
Financial assets	1.4	635	936
Deferred tax assets	10.1	182	173
Total intangible assets		**54,581**	**57,670**
Trade receivables			

Other accounts receivables	2.2	403	772
Current financial assets	2.3	11,177	9,854
Cash and cash equivalents	2.1	25 620	33,579
Total tangible assets		**37,200**	**44,206**
TOTAL ASSETS		**91,781**	**101,876**

LIABILITIES in €K		**12/31/2022**	**12/31/2021**
Stated capital	4.1	3,705	3,705
Share premium	4.1	65,611	65,605
Treasury stock	4.4	(549)	(160)
Reserves and retained earnings		(18,349)	(4,411)
Consolidated result		(17,760)	(16,850)
Total shareholders' equity		**32,658**	**47,890**
Non-current financial liabilities	5	37,231	30,801
Lease non-current liabilities	5	3,586	3,965
Non-current deferred tax liabilities	10.1	1,514	1,748
Non-current provisions	7	524	710
Total non-current debts		**42,856**	**37,224**
Current financial liabilities	5	3,093	1,611
Lease current liabilities	5	883	756
Trade payables	6.1	8,539	9,607
Tax due liabilities	6.2	21	14
Other payables	6.2	2,916	3,724
Other debts and accruals	6.3	816	1,050
Total current debts		**16,268**	**16,761**
TOTAL LIABILITIES		**91,781**	**101,876**

Statement of comprehensive income

P&L IN K€	**Note**	**December 31, 2022**	**December 31, 2021**
Turnover	8.1	18,302	26,306
Other operating income	8.1	0	0
Total Revenues		**18,302**	**26,306**
Research and development expenses	8.2	(26,893)	(30,550)
Overhead expenses	8.3	(6,672)	(8,608)
Expenses related to shares payments	8.4	(3,130)	(3,773)
OPERATING PROFIT/LOSS - CURRENT		**(18,392)**	**(16,625)**
Other operating expenses		(84)	0
OPERATING PROFIT/LOSS		**(18,476)**	**(16,625)**
Financial products	9	2,079	267
Financial expenses	9	(1,624)	(856)
PROFIT/LOSS BEFORE TAX		**(18,022)**	**(17,213)**
Income Tax	10.3	263	364
NET PROFIT/LOSS		**(17,760)**	**(16,850)**

Of which consolidated net result attributable to shareholders		***(17,760)***	***(16,850)***
Net earnings attributable to shareholders			
Weighted average number of shares outstanding	12	**18,527,401**	**18,154,978**
Basic earnings per share		**(0.96)**	**(0.93)**
Diluted earnings per share		**(0.96)**	**(0.93)**

IN K€	**2022**	**2021**
NET RESULT	**(17,760)**	**(16,850)**
Amounts to be recycled in the income statement:		
Unrealized gains on securities available for sale, net of tax		
Currency conversion difference	(61)	(55)
Amounts not to be recycled in the income statement:	122	25
Other comprehensive income in the period	**61**	**(29)**
GLOBAL PROFIT/LOSS	**(17,699)**	**(16,879)**

Statement of changes in consolidated equity

In K€	**Share capital**	**Share premium**	**Currency translation transactions**	**Own shares**	**Retained earnings and result**	**Total consolidated equity**
Consolidated equity as at December 31st, 2020	**3,597**	**65,449**	**(104)**	**(93)**	**(7,485)**	**61,364**
Consolidated result					(16,850)	(16,850)
Actuarial difference					25	25
Currency translation			(55)			(55)
Global consolidated result	**0**	**0**	**(55)**	**0**	**(16,825)**	**(16,879)**
Capital variation - warrants	8	187				195
Capital variation - BSPCE	2	59				61
Capital increase – free shares	98	(98)				0
Retrospective impact – Change in accounting method (net of tax)					144	144
Impact ID on currency translation patent OPI			9			9
Warrant subscription		9				9
Share based payments					2,944	2,944
Own shares transactions				(67)	110	43
Consolidated equity as at December 31st, 2021	3,705	65,605	(150)	(160)	(21,111)	47,890
Consolidated result					(17,760)	(17,760)
Actuarial difference					122	122
Currency translation			(61)			(61)
Global consolidated result	0	0	(61)	0	(17,638)	(17,699)
ID impact on currency translation transaction Patent OPI			(9)			(9)
Warrant subscription		6				6
Payment in shares					2,728	2,728
Transactions on treasury shares				(390)	132	(258)
Consolidated equity as at December 31st, 2022	**3,705**	**65,611**	**(220)**	**(549)**	**(35,890)**	**32,658**

Consolidated Cash Flow Statement

In K€		December 31, 2022	December 31, 2021
	CONSOLIDATED RESULT	**(17,760)**	**(16,850)**
+/-	Depreciation, amortization and provision expenses	2,744	2,337
+	Amortization on "right-of-use"	742	687
+/-	Shares based payments (1)	2,728	2,944
	CASH FLOW BEFORE TAX	**(11,545)**	**(10,881)**
+	Financial charges	(3,066)	634
-	Income tax expenses	(263)	(364)
-	Tax paid	(236)	(332)
+/-	Working capital variation (2)	(3,142)	1,025
	CASH FLOW FROM OPERATING ACTIVITIES (A)	**(18,252)**	**(9,919)**
-	Tangible assets increase	(274)	(472)
+/-	Financial assets variation	0	0
+/-	Mutual finds units accounted in current financial assets	0	0
+/-	Loans and advances variation	300	(355)
	CASH FLOW FROM INVESTING ACTIVITIES (B)	**26**	**(827)**
+	Capital increase (including share premium)		265
+/-	Own shares transactions	6	
+	Warrant subscription		
+	Loan subscription	12,056	15,281
-	Loan repayment	(1,010)	(40)
-	Lease debt repayment (3)	(785)	(549)
-	Financial charges		
	CASH FLOW FROM FINANCING ACTIVITIES (C)	**10,267**	**14,957**
+/-	Currency translation transactions (D)		
	CASH VARIATION E = (A + B + C + D)	**(7,959)**	**4,211**
	CASH OPENING BALANCE (F)	33,579	29,368
	CASH CLOSING BALANCE (G)	25,620	33,579

(1) Warrants and free shares awards granted in 2022 and valuated for 2,728 K€

(2) Mainly explained by:

- Decrease in trade receivable for 369 K€
  Increase in other current assets for 1,323 K€
- Decrease in trade accounts payable for 1,067 K€
- Decrease in social and tax payable for 808 K€
- Decrease in other debts for 234 K€

(3) Explained by IFRS16 application, which corresponds to reimbursement of lease debt for 785 K€

Notes to the consolidated financial statements

1 INFORMATION ON THE COMPANY PRESENTING THE FINANCIAL STATEMENTS

OSE Immunotherapeutics (the "Group" or the "Company") is a biotechnology company focused on developing innovative immunotherapies acting on activator or suppressor cells to stimulate or inhibit the immune response for immuno-oncology and autoimmune diseases and transplantation. It has a portfolio of innovative clinical and preclinical products and agreements with international pharmaceutical groups. The registered office of OSE Immunotherapeutics is in Nantes. Teams are based in Nantes and Paris.

OPI, a wholly-owned subsidiary of OSE Immunotherapeutics, is a company governed by Swiss law, founded in February 2012, which owns the rights to Tedopi® (OSE-2101), which it acquired from Biotech Synergy (US) in April 2012. OPI grants OSE Immunotherapeutics the license to Tedopi® (OSE-2101).

OSE Immunotherapeutics Inc. is a company governed by US law, founded in April 2017, in order to serve as a point of support for international scientific collaboration.

2 HIGHLIGHTS

2.1 Authorization of compassionate use in several European countries for Tedopi® in non-small cell lung cancer (NSCLC) after failure with immunotherapy

In October 2022, the Company announced authorizations for compassionate use of Tedopi® in NSCLC from Health Agencies in Europe - in France, Italy and Spain - in third line post-chemotherapy and immunotherapy. The significant medical need for new therapeutic options in NSCLC patients post-ICI failure associated with promising efficacy, safety and quality of life data resulted in authorizations for compassionate use of Tedopi® in third line after a sequential treatment with chemotherapy and immunotherapy.

Meetings should be held with the European and American Health agencies to valider the new Phase 3 confirmatory trial protocol in NSCLC in second line after secondary resistance to a combination of chemotherapy + immunotherapy.

2.2 New data on Tedopi® in Phase 3 clinical trial in NSCLC presented at the 2022 ESMO conference

In September 2022, the Company presented new data on the benefit/risk evaluation of Tedopi® versus chemotherapy standard treatment in patients with NSCLC after failure of an immune checkpoint inhibitor, at the 2022 conference.

2.3 Servier and OSE Immunotherapeutics announce the completion of patient enrollment in the Phase 2a clinical trial of OSE-127/S95011 in primary Sjögren syndrome

On November 3, 2022, Servier and the Company announced the completion of patient enrollment in the Phase 2a clinical trial conducted by Servier evaluating the efficacy and safety of monoclonal antibody OSE-127/S95011 in primary Sjögren's syndrome.

This international, randomized, double-blind, placebo-controlled, Phase 2a study is designed to evaluate the efficacy and tolerance of the monoclonal antibody named OSE-127/S95011 in primary Sjögren's syndrome. The study includes 48 patients across a score of centers located in the United States, Australia and Europe. Results are expected in 2023.

2.4 OSE Immunotherapeutics announces first patient dosed with anti-PD1 monoclonal antibody OSE-279 in a Phase 1 /2 clinical trial in advanced solid tumors and lymphomas

In December 2022, the Company announced that the first patient had been dosed in the Phase 1/2 clinical trial evaluating OSE-279, a high affinity anti-PD1 blocking monoclonal antibody, in patients with advanced solid tumors or lymphomas.

This first-in-human open label Phase 1/2 dose escalation and expansion study aims to determine the Maximum Tolerated Dose and/or the recommended Phase 2 dose of OSE-279 as a monotherapy in advanced solid tumors or lymphomas. Secondary objectives include assessment of OSE-279's antitumor activity, evaluation of the safety profile, pharmacokinetic and receptor occupancy or pharmacodynamic profile.

2.5 BI 765063/OSE-172: OSE Immunotherapeutics and its partner Boehringer Ingelheim announced first patient dosed in a Phase 1 expansion trial of SIRPa antagonist monoclonal antibody BI 765063 targeting myeloid cells in immuno-oncology

In May 2022, the Company announced a new Phase 1 expansion clinical trial, which triggered a €10 million milestone payment from Boehringer to OSE Immunotherapeutics, with BI 765063, a first-in-class SIRPα inhibitor on the SIRPα/ CD47 myeloid pathway. The expansion trial is conducted in combination with Boehringer Ingelheim's anti-PD1 antibody ezabenlimab in advanced hepatocellular carcinoma (HCC) and head and neck squamous cell carcinoma (HNSCC), both new indications in oncology. BI 765063 is being evaluated in parallel in Europe in advanced colorectal cancer and endometrium cancer.

2.6 Acceptance of the IND (Investigational New Drug) in the United States for VEL-101/FR104 received by Veloxis Pharmaceuticals, the Company's partner in transplantation, and a €5 million milestone payment

On January 31, 2022, Veloxis Pharmaceuticals, Inc. received acceptance of the New Investigational Drug (IND) application in the United States to set up a clinical trial of VEL-101/FR104 (CD 28 antagonist) sponsored and conducted by Veloxis in the United States.

As part of the global licensing agreement signed in April 2021, this first step triggered a €5 million milestone payment from Veloxis Pharmaceuticals, Inc. to OSE Immunotherapeutics. This payment has been received in Q1 2022.

2.7 Presentation of the latest preclinical efficacy data of OSE-127, IL-7 receptor antagonist in Acute Lymphoblastic Leukemia (ALL) at the 2022 ASH congress

In December 2022, the Company presented the the latest preclinical data on the use of its anti-IL-7 receptor (IL-7R) antagonist OSE-127 for the treatment of B- and T-Cell Acute Lymphoblastic Leukemia (B- and T-ALL) at the American Society of Hematology (ASH) annual meeting. This oral presentation has received the merit-based "Abstract Achievement Award" from the peer-review committee.

2.8 Presentation of two posters at the 2022 SITC congress and an oral presentation at the 2022 AACR and PEGS congresses

In November 2022, the Company presented scientific updates in oral and poster presentations selected for international conferences: the Society for Immunotherapy of Cancer (SITC) 37th Annual Meeting in Boston, MA, November 8 – 12 and the Protein & Antibody Engineering Summit (PEGS) Europe 14th Annual Meeting in Barcelona, Spain, November 14 – 16. The communications feature the latest research on pre-IND programs from the pioneering Myeloid and BiCKI® platforms, namely presentations on OSE-230 (first pro-resolutive monoclonal antibody) in chronic inflammation, CLEC-1 (new myeloid immune checkpoint) and BiCKI®-IL-7 (new bifunctional therapy targeting PD1 and IL-7) in immuno-oncology.

2.9 Publication in "Science Advances" of data on CLEC-1, a new immune myeloid checkpoint

In November 2022, the Company announced the publication of data in the peer-reviewed journal Science Advances on a first-in-class preclinical program with CLEC-1, its novel myeloid immune checkpoint target for cancer immunotherapy.

2.10 Presentation of 4 posters at the 2022 annual ASCO meeting

In June 2022, OSE Immunotherapeutics presented 4 posters at the 2022 ASCO meeting:

- NSCLC Atalante-1 Phase 3 Trial Beyond Checkpoint Inhibitor Neoepitope Specific Immunotherapy Tedopi® Shows Significant Patient-Reported Outcomes Versus Chemotherapy
- Positive Interim Results in Phase 2 Trial with Tedopi® in Pancreatic Cancer in Maintenance Strategy Post-FOLFIRINOX (GERCOR)

2.11 CLEC-1: Presentation of an update in immunology research in London: "Immuno-Oncology Summit Europe" and il Boston: "Tumor Myeloid-Directed Therapies Summit."

In May and June 2022, the Company was invited to provide an update on its R&D programs in immuno-oncology at two dedicated international conferences in May and June. The Company's broad presence in scientific cancer research events confirms its expertise in the highly attractive field of myeloid cells and macrophages, identified as poor prognostic factors in oncology and in immune escape mechanisms of cancer immunotherapies.

2.12 Nicolas Poirier appointed Chief Executive Officer

In October 2022, Nicolas Poirier was appointed new Chief Executive Officer, effective immediately.

Throughout his career, Dr. Nicolas Poirier has demonstrated both his expertise as an international scientific leader, pioneering the discovery and development of innovative immunotherapies, and in-depth knowledge of the biotech sector through various strategic leadership roles. He has been instrumental in the development of OSE Immunotherapeutics, notably as the initiator of 5 programs in the Company's portfolio that are now in clinical stage. He also played a major role in the signature of 4 strategic pharmaceutical partnerships for OSE Immunotherapeutics.

2.13 Creation of an international Scientific Advisory Board (SAB)

In June 2022, the Company created a Scientific Advisory Board (SAB) combining the expertise of renowned scientific and international key-opinion leaders in the fields of immunology, immuno-oncology, inflammation and immunotherapy.

The SAB will work with the Company's leadership team and advise its Board of Directors on its scientific, medical, translational and developmental strategy. The SAB members include Pr. Wolf-Hervé Fridman (Université de Paris), Dr. Sophie Brouard (CRTI, Nantes), Dr. Bernard Malissen (CIML, Marseille), Pr. Miriam Merad (Mount Sinai, New-York), Pr. Charles Serhan (Harvard, Boston) and Dr. Jennifer Wargo (MD Anderson Cancer Center, Houston).

2.14 OSE received a €10 million payment corresponding to the second tranche of the financing granted by the European Investment Bank (EIB)

In December 2022, the Company announced a €10 million drawdown corresponding to the second tranche of the financing granted by the European Investment Bank (EIB). The finance contract was signed on February 12, 2021.

This financing will further support the progress and expansion of OSE Immunotherapeutics' lead clinical development programs in therapeutic areas with high unmet medical needs.

2.15 Allocation and issuance of share subscription warrants/founders' share warrants

During the financial year, the Company allocated 80,000 founders' share warrants and issued 550,000 share subscription warrants (see Section 4.2 of the consolidated financial statements).

3 ACCOUNTING POLICIES AND PRINCIPLES

3.1 Basis of preparation of the consolidated financial statements

The consolidated financial statements of OSE Immunotherapeutics, the consolidating entity, and its subsidiaries, OPI and OSE Immunotherapeutics Inc (the "Group"), approved by the Board of Directors on April 27, 2023, are presented in thousands of euro (000) and were prepared in accordance with International Financial Reporting Standards (IFRS) as adopted by the European Union.

The Board of Directors adopted the going concern assumption, in view of the following:

- Cash and cash equivalents available at December 31, 2022, stood at €25,6 thousand
- Financing of the 2022 research tax credit of €5,4 thousand
- An equity financing line with Vester Finance allowing the Company to raise a minimum of €3.4 million by December 31, 2023 (cf §15.1 Financing)
- Decrease in costs and implementation of a plan to reduce operational and social expenses
- Agreement on loans with "La Région Pays de la Loire » and with a banking pool for a total amount of €3.8 million ((cf §15.1 Financing)

Consequently, this cash enables the Company to finance its development costs over the next twelve months.

Lastly, as a listed company, and as authorized by the last General Shareholders' Meeting, the Company has the option, if needed, to use the financial instruments to which listed companies have access.

3.2 Reporting date

Consolidated entities' reporting date is December 31 which is the Group's reporting date.

3.3 Standards and interpretations applicable from January 1, 2022

The Group applied the following standards and interpretations adopted by the European Union:

- Amendments to IFRS 3 (Reference to the conceptual frame)
- Amendments to IAS 16 (Product prior to the intended use)
- Amendments to IAS 37 (Onerous contracts, contract enforcement costs)

3.4 Standards, amendments and interpretations adopted by the European Union and applicable to fiscal years beginning on or after January 1, 2022, and not adopted in advance by the Company

The Company did not adopt in advance other standards, amendments, revisions and interpretations of published standards effective for annual periods beginning on or after January 1, 2023. Management does not expect these standards to have a material impact on the Company's financial statements.

3.5 Key accounting estimates and judgments

The preparation of financial statements in accordance with IFRS requires judgments, estimates and assumptions to be made which affect the amounts and disclosures that appear in the financial statements. Actual results may prove to be very different from these estimates depending on the various assumptions or conditions and, where applicable, a sensitivity analysis may be carried out if the difference is significant.

Estimates and assumptions

- **Valuation of free share allocation plans (AGA), share subscription warrants (BSA) and founders' share warrants (BSPCE)**

The fair value of the free share allocation plans, share subscription warrants and founders' share warrants allocated is measured on the basis of a valuation model that takes into consideration the probability of the plans' vesting requirements being met.

The fair value of the share subscription warrants and founders' share warrants granted is measured on the basis of actuarial valuation models.

These models require the Company to use certain calculation assumptions such as the expected volatility of the share price (see Note 4.3).

- **Recognition of corporate tax**

The Company is liable to pay income tax in France for its business activities.

Deferred tax assets mainly relate to tax loss carryforwards which are only recognized to the extent that it is probable that future taxable profits will be available. The Group must use its judgment to determine the probability of the existence of future taxable profits.

These deferred tax assets are recognized within the limit of tax liabilities recognized in the form of deferred tax liabilities, payment of which may be avoided by the Company, and the thresholds provided for by tax legislation (see Note 10).

- **Revenue recognition**

Within the context of a sale or licensing agreement, the Company may defer recognition of a portion of revenue, irrespective of the payments received (see Note 8.1). Determining the duration of this deferral requires the use of estimates.

- **Intangible assets arising from the acquisition of Effimune**

The fair value of intangible assets associated with the FR104 and OSE-127 molecules was estimated on the basis of business plans reflecting management's best estimate (see Note 1.1).

- **Estimation and recognition of R&D expenses provisioned under trade payables**

R&D expenses are systematically recognized as expenses as the research programs progress. Based on the information supplied by service providers or by work schedules provided for in contracts, on the reporting date, Management determines the progress of each of the research services on a pro rata basis and, where necessary, settles the expenses for the fiscal year.

The research tax credit for the fiscal year amounted to €5.432 thousand.

3.6 Financial statements and transactions in foreign currencies

Each consolidated entity decides on the operating currency in line with its own economic environment and the conditions under which it conducts its business transactions.

Financial statements in foreign currencies

The financial statements of entities whose operating currency differs from the presentation currency are converted using the closing rate method. This conversion is as follows:

- Assets and liabilities are converted into the presentation currency, i.e. into euros at closing rates.
- Income and expenses are converted using the average rate for the period. The Group used an annual average, considering this to be an acceptable approximation of the conversion applicable on the date of each transaction.

Foreign exchange gains and losses arising from this conversion are recognized in other comprehensive income under "foreign exchange gains and losses."

Transactions in foreign currencies

Transactions in foreign currencies are converted into the presentation currency at the current rate on the transaction date. Monetary items are converted at the foreign exchange rate on the annual reporting date and the effects of these revaluations are recognized in profit or loss for the period.

3.7 Intangible assets

Intangible assets are recognized in the balance sheet when they satisfy IAS 38 recognition criteria.

Intangible assets acquired are recognized at their acquisition cost, on the assumption that recognition criteria (reliable valuation and probability that economic benefits will be generated by the asset) have been met.

R&D expenses

- Research expenses are systematically recognized as expenses.
  Under IAS 38, development expenses are only recognized as intangible assets if all the following criteria have been met:

  (a) technical feasibility needed to complete the development project,
  (b) the Company's intention to complete the project and use the asset,
  (c) ability to use the intangible asset,
  (d) demonstration of the probability of future economic benefits attached to the asset,
  (e) availability of technical, financial and other resources to complete the project, and
  (f) reliable assessment of development expenses.

Given the uncertainty surrounding the technical feasibility of the completion of the research in progress, the Company's development expenses do not currently meet the IAS 38 criteria and are therefore recognized as expenses over the period during which the research commitment was made.

- Acquired R&D projects are recognized as intangible assets at their fair value, even in the absence of marketing authorization. These assets fall into two categories:

- They are classed as assets with a defined useful life when they generate economic benefits. In this case, their fair value as recognized in the balance sheet less, where applicable, the remaining value, is amortized over the period of use expected by the Company.

- Other cases include non-current assets in development which are not amortized but are subject to annual impairment tests.

Patents

Costs relating to filing existing patents, incurred by the Company until said patents are obtained, are recognized as expenses, in line with the position taken for recognizing R&D expenses.

3.8 Testing non-current assets for impairment

Intangible assets and property, plant and equipment with a finite life are tested for impairment when circumstances indicate that the recoverability of their carrying amount has been put into doubt and this test is conducted at least once a year on the reporting date (see Note 4.1.1). An impairment is recognized for the difference between the carrying amount and the recoverable amount of the asset.

The recoverable amount of an asset is its fair value fewer selling costs or, if higher, its value in use.

3.9 Financial assets

Financial assets within the scope of IFRS 9 are classed and measured in three categories:

- Amortized cost
- Fair value through other comprehensive income
- Fair value through profit or loss

Upon initial recognition, financial assets are measured at their fair value plus, in the case of investments which are not recognized at fair value through profit or loss, any directly attributable transaction costs.

The Company determines the classification of its financial assets upon initial recognition and, once authorized and appropriated, reviews this classification at each annual reporting date.

3.9.1 Non-current financial assets

Non-current financial assets include long-term financial assets, in particular:
- Cash SICAVs (money market funds);
- Loans and receivables;
- And the "cash portion" of the liquidity contract associated with share buybacks.

Loans and receivables

This category of non-current financial assets includes advances and collateral deposits pledged to third parties. Repayable advances and collateral deposits are non-derivative financial assets. They are recognized at amortized cost using the effective interest rate method in accordance with IFRS 9.

Loans and receivables are impaired when a loss event occurs, their carrying amount reduced to the sum of the cash flows expected.

3.9.2 Current financial assets

Current financial assets include trade and other receivables, other current assets, cash and cash equivalents and current financial instruments.
These assets are recognized by type, based on the following rules.

Trade receivables

Trade receivables are initially recorded and recognized at the fair value of the consideration received or receivable. Where applicable, receivables are impaired to take recovery risk into consideration.

Current financial instruments

The Company classes its investments in current financial instruments in one of these three categories:

- **Investments held to maturity recorded at amortized cost**

The Company did not hold any of this type of investment over the period.

- **Assets at fair value through profit or loss**

They are held-for-trading assets, i.e. assets acquired by the Company intended for short-term sale. The objective is to realize a capital gain.
These assets are part of a portfolio of financial instruments managed together and for which there is a practice of short-term selling. They are measured at fair value and changes in fair value are recognized through profit or loss.

These financial assets are recognized at their fair value without deducting the transaction costs that may be incurred when they are sold. Realized or unrealized gains or losses, associated with the change in fair value of these assets are recognized through profit or loss under Income from cash or cash equivalents.

- **Financial assets at fair value through other comprehensive income**

The Company did not hold any of this type of investment over the period.

Cash and cash equivalents

Cash equivalents are highly liquid, short-term investments, which are easily convertible into a known amount of cash, and which are subject to negligible risk of change of value.

Cash and cash equivalents include cash at bank and in hand, as well as cash investments in transferable securities or term deposits maturing in less than three months and with a very low sensitivity to interest rate risk.

When preparing the statement of cash flows, cash and cash equivalents comprise bank sight deposits, highly liquid short-term investments, net of bank overdrafts. In the balance sheet, bank overdrafts are shown as borrowings under financial liabilities.

3.10 Consolidated shareholders' equity

Consolidated shareholders' equity is the shareholders' equity of consolidated group entities.

Ordinary shares are classified as equity. Capital transaction costs directly attributable to the issue of new shares or options are recognized in equity as a deduction from the proceeds of the issue.

3.11 Treasury shares

The acquisition cost of the OSE Immunotherapeutics shares held by the Group is recognized as a deduction from consolidated equity.

Since April 8, 2015, for a two-year period, automatically renewable for subsequent one-year periods, OSE Immunotherapeutics has charged an organization with implementing a liquidity contract that complies with the Ethics charter drafted by the French Association of Investment Firms (*Association française des entreprises d'investissement*) and approved by the AMF in a decision dated March 21, 2011.

At December 31, 2022, OSE Immunotherapeutics securities held through the liquidity account, as well as the profits or losses generated over the fiscal year on transactions conducted by the liquidity contract manager were reclassified as shareholders' equity. The cash portion of the liquidity account is classed under "Other financial assets."

3.12 Share-based payments

The Group introduced compensation plans paid out in equity instruments in the form of share subscription warrants, Company founders' share warrants or free shares awarded to employees, management, consultants, service providers and members of the Board of Directors.

In application of IFRS 2, for share-based payment transactions settled in equity instruments, the Company measures the related compensation, at the fair value of the goods and services received, unless such fair value cannot be reliably estimated.
In order to apply these last provisions, the amount of benefits granted is measured using the Bjerksund & Stensland model and is recognized under expenses, over the period in which the rights to benefit from the equity instruments vest, offset by increases in equity.

The fair value of the share subscription warrants granted is determined by applying the option-pricing model described in Note 4.3.

The fair value of the free shares awarded is measured on the basis of a valuation model that takes into consideration the probability of the plans' vesting requirements being met.

3.13 Financial liabilities

A financial liability is defined as a contractual obligation to deliver cash or another financial asset to another entity. A financial instrument can be classed as a financial liability (debt, derivative financial instrument) or an equity instrument.
The acquisition price of a financial liability is the amount actually paid, net of transaction costs (unless measured at fair value through profit or loss) and net of any redemption premiums.

There are three categories of financial liabilities:

- **Liabilities measured at amortized cost**

These include trade payables, tax and social security debts, loans and other financial liabilities, such as repayable advances and bank loans. They are recognized at amortized cost using the effective interest rate method.

The portion of financial liabilities maturing in less than one year is shown under "Current financial liabilities."

- **Liabilities measured at fair value through profit or loss**

The Company did not hold any of this type of investment over the period.

- **Liabilities measured optionally at fair value under the through profit or loss**

The Company did not hold any of this type of investment over the period.

3.14 Public funding

The Company received public funding in the form of conditional advances and grants. Details of this funding are supplied in Note 5.

Public grants are recognized as assets where there is reasonable assurance that:

The Company will comply with the conditions attached to the grants; and
Grants will be received.
Operating subsidies that offset the expenses incurred by the Group are recognized in the income statement, less R&D expenses, as the costs are incurred for the research programs in question.

Interest-free conditional advances are intended to fund research programs. They are repayable, in full, if the project is a success and, in part, if the program fails.
Repayable advances for which the contractual rate does not constitute a market rate are treated as financial liabilities to be measured at amortized cost at each reporting date, by discounting all future cash payments at the prevailing market rate of interest or in the contract.
The difference between the current value of the advance at the market rate and the amount of cash received from the public body constitutes a grant within the meaning of IAS 20. This difference must be recognized as an income-related grant and recognized in the income statement, less R&D expenses, as the costs are incurred for the research programs in question.
These advances are recognized as non-current financial liabilities and current financial liabilities depending on their maturity. In the event of a marked failure, the debt waiver granted is recorded as a subsidy.

3.15 Provisions for liabilities and charges

Provisions for liabilities and charges are commitments arising from disputes and other risks, with uncertain timing and amounts, that the Company may face in the course of its activities.

A provision is recognized when the Company has a legal or constructive obligation to a third party arising from a past event and when it is probable or certain that this will result in an outflow of funds to said third party, with no equivalent consideration expected from the latter, and when the future outflows of liquidity can be reliably estimated.

The amount recognized as a provision is the best estimate of the expenditure needed to discharge the obligation, discounted on the reporting date.

Pension-related commitments

On leaving the Company, employees receive a pension in accordance with legal requirements and the applicable collective agreement.

The valuation and accounting methods used by the Group are those set out by IAS 19 “Employee benefits.”

Following the application of the IFRIC ruling of May 2021, the company has opted for a new method of measuring these commitments ("IFRIC") for the financial year relating to the distribution of rights to benefits for plans whose benefits are subject to the combination of length of service, a maximum capped amount and presence at the entity when he or she reaches retirement age.

In accordance with this standard:

- expenses relating to defined-contribution schemes are recognized as the expenses are incurred;
- the obligations of each defined benefit plan are determined according to the new IFRIC method. These calculations are based on assumptions relating to mortality, staff turnover and projections of wage increases. They take the economic situation in individual countries into consideration;
- actuarial gains and losses are recognized as other comprehensive income.

3.16 Revenue

To date, the Company’s revenue is mainly generated by licensing agreements with pharmaceutical companies. Generally speaking, these contracts are made up of different components, such as amounts billable on signing and amounts billable when certain predefined development targets have been met, one-off funding payments to finance R&D expenses and the assignment of royalties on future product sales. Royalties on future product sales are a percentage of the net sales generated by the partner.

Amounts billable on signing the contract, for the assignment of a molecule’s intellectual property rights, are immediately recognized as revenue when the contract comes into force where the amounts are non-refundable and the Company has no future development commitments.

Revenue related to development services carried out on behalf of the client acquiring the intellectual property rights, are initially recognized as deferred income and spread over the estimated length of the Company’s involvement in future development, which is subject to periodic reviews.

Amounts billable once certain predefined development targets have been met are recognized in full as revenue when these objectives are actually achieved, provided that the Company is not contractually liable for any development services on behalf of the client that has acquired the intellectual property after these objectives have been met. On the downside, all or some of the amounts billed when a development target is met, may be spread over the estimated duration of the Company’s involvement in future development, which is subject to periodic reviews.

3.17 Leases

OSE Immunotherapeutics has leases (as a tenant) mainly for offices and other equipment.

Under operating leases, within the meaning of IFRS 16, the Group recognizes right of use assets and lease liabilities for all these leases, apart from short-term leases (12 months or less) and those relating to low-value assets.

Payments under these leases not recognized in the balance sheet are recognized as operating expenses on a straight-line basis over the lease term.

At the start of the lease, the liability for future lease payments is discounted using a marginal borrowing rate corresponding to a risk-free rate adjusted by a margin that is representative of the risk specific to each Group entity.

As lease payments are spread over the lease term, the Company applies a discount rate based on the term of these payments.

Payments taken into consideration when assessing liability for future lease payments excludes non-lease components and includes fixed amounts that OSE Immunotherapeutics expects to pay to the lessor over the probable lease term.

Once the lease has commenced, the liability for future lease payments reduces as lease payments are made and increases as interest is added. The liability is revalued, where applicable, to reflect a new assessment or change to future lease payments.

Once the lease has commenced, the right of use asset, initially valued at cost, is amortized on a straight line basis over the lease term and, where applicable, is subject to an impairment test.

3.18 Income tax

Income tax is the total amount of tax payable by the different Group companies, corrected for deferred tax.

Deferred tax is recognized using the balance sheet approach, in accordance with IAS 12, for all temporary differences arising from the difference between the tax base and the carrying amount of assets and liabilities appearing in the financial statements (apart from, for example, goodwill, etc.). They are not discounted.

Deferred tax assets are recognized to the extent that it is probable that future profits will be sufficient to absorb tax loss carryforwards or up to the amount of deferred tax liabilities, within the limit of current thresholds.

3.19 Research tax credit

Research tax credits are granted by the French Government to companies to encourage them to carry out technical or scientific research. Companies that can prove that they have incurred expenses that meet the required criteria receive a tax credit which can be used to pay their corporate tax liability for the fiscal year in which the expenses were incurred and for the three subsequent fiscal years, or if applicable, any surplus can be refunded.

The research tax credit is shown in the income statement, fewer R&D expenses, in accordance with IAS 20.

3.20 Segment information

The application of IFRS 8 “Operating segments” did not have any impact on the Group’s segment information. The Group considers that it operates only in one aggregate segment: Research & Development on pharmaceutical products with a view to their future sale.

In addition, most of the research and development activity is located in France alongside the Company’s principal operational decision-makers who measure performance against the cash consumed by its activities.

For these reasons, the Group's management does not believe it to be opportune to set up separate operating segments in its internal reporting.

3.21 Other comprehensive income

Income and expenses for the period recognized direct in equity are shown under "Other comprehensive income."

For the periods presented, this heading includes translation adjustments related to the activities of entities with operations in Switzerland and the United States, as well as actuarial losses on employee benefits.

3.22 Earnings per share

Basic earnings per share are calculated over all the periods shown based on shares outstanding in OSE Immunotherapeutics which is legally considered to be the parent company.

Diluted earnings per share are calculated by adding the weighted average number of shares outstanding to the number of shares that would result from the conversion of all ordinary shares with a potentially dilutive effect.

If taking instruments giving future access to equity (BSA, etc.) into account when calculating diluted earnings per share, generates an anti-dilutive effect, these instruments are not taken into consideration.

At the reporting dates presented, taking into account a net loss, the diluted earnings per share was -€0.93 per share, identical to the diluted earnings (see Note 12).

1 NOTES TO THE FINANCIAL STATEMENTS

NOTE 1: NON-CURRENT ASSETS

1.1 Intangible assets

In €k	12/31/2021	Increase	Decrease	Amortizations	12/31/2022
R&D expenses acquired implemented	35,273	-	-	(2,356)	32,917
R&D expenses acquired (ongoing)	15,700				15,700
Other intangible assets	149	40	-	(21)	167
	51,122	**40**	**-**	**(2,356)**	**48,784**

In 2016, following the acquisition of Effimune, the Company valued two molecules, FR104 and OSE-127. These molecules were valued on the basis of future cash flow estimates.

Impairment tests are carried out once a year on non-current assets with an indefinite useful life or which cannot be amortized.

As part of the signature of a worldwide licensing agreement with Veloxis Pharmaceuticals, the Company sold the worldwide rights to develop, manufacture, register and market the FR104 molecule in all transplantation indications. In accordance with IAS 38.97, which specifies that an asset must begin to be amortized when it can be used in the manner intended by management, the transfer of rights entails the start of the amortization of this molecule.

The amortization period used corresponds to the end of the product's term of protection (product, process, administration methods, etc.) by intellectual property rights, in particular patents. This protection is provided until December 2036, excluding any extensions related to obtaining marketing authorizations.

At December 31, 2022, the amortization recorded in the financial statements amounted to €3,983 thousand.

The value in use of these two molecules, at December 31, 2022, was measured using the discounted cash flow method (DCF). These are the two main assumptions made:

OSE127

(Based on the license agreement signed with Servier)

- 16-year time horizon (with no terminal value);
- Probabilities of success used consistent with the probabilities of success generally observed in the field of autoimmune diseases (Sjögren's Syndrome and ulcerative colitis);
- 10% tax rate (in accordance with the new tax regime for income from the sale or licensing of patents);
- USA/Europe/Japan population with 0.2% of the population affected by Sjogren's Syndrome and 0.3% affected by UC;
- Maximum market share of 10% for Sjögren's Syndrome and 7% for UC.

FR104

(Based on the license agreement signed with Veloxis Pharmaceuticals)

- 16-year time horizon (with no terminal value);
- Probabilities of success used consistent with the probabilities of success generally observed in the field of autoimmune diseases and in transplantation;
- 10% tax rate (in accordance with the new tax regime for income from the sale or licensing of patents);
- USA/EUROPE/JAPAN and China/Korea/Taiwan/Macao/HK population living with a renal transplant to date, or GVHD;
- Maximum market share of 20% for renal transplants, and 80% for GVHD.

The following sensitivity tests were performed:

- Discount rate: sensitivity analysis performed within a range of 14% to 16% with a respective impact of plus or minus €15 million not resulting in an impairment of the net carrying amount of these molecules;
- Probability of success: sensitivity analysis conducted within a range of plus or minus 10% not resulting in an impairment of the net carrying amount of these molecules;
- Market share: sensitivity analysis conducted within a range of 5% more, or less, not resulting in an impairment of the net carrying amount of these molecules;
- Price: sensitivity analysis conducted within a range of 5% more, or less, not resulting in an impairment of the net carrying amount of these molecules.

1.2 Property, plant and equipment

Property, plant and equipment break down as follows:

In €k	12/31/2021	Increase	Decrease	12/31/2022
Gross values				
Buildings	396	159	241	314
Equipment and tools	1,327	107		1,434
Office and computer equipment, furniture	225	53	2	277
Ongoing fixed assets	0	72	72	0
	1,948	**392**	**315**	**2,025**
Amortization				
Buildings	157	171	158	170
Equipment and tools	687	252		939
Office and computer equipment, furniture	138	37	2	173
	981	**459**	**159**	**1,282**
Depreciation				
Buildings	40	0	40	0
Equipment and tools	0	0	0	0
Office and computer equipment, furniture	0	0	0	0
Net values	**40**	**0**	**40**	**0**
Buildings	199	0	0	144
Equipment and tools	640	0	0	496
Office and computer equipment, furniture	87	0	0	104
Ongoing fixed assets	0	72	72	0
	926	**72**	**72**	**743**

The Company mainly invested in laboratory and office equipment.

1.3 Rights of use

The Company identified one new lease (falling within the scope of the standard) for the 2022 financial year, with the following characteristics:

- A lease relating to real estate in France in France. The incremental borrowing rate used was 1.15%.

Rights of use break down as follows:

IN €K	12/31/2021	Increase	Decrease	12/31/2022
Gross values (real estate assets)				
Lease agreement (Nantes Lot 1)	537	0	0	537
Lease agreement (Nantes Lot 2)	208	0	0	208
Lease agreement (Nantes Lot 3)	127	0	0	127
Lease agreement (Paris Suffren Lot 1) *	406	0	406	0
Lease agreement (Paris Suffren Lot 2) **	296	0	296	0
Leasing (Cytek Cytometre)	281	0	0	281

Lease agreeement (Paris Catalogne) **	4,052	0	0	4,052
Lease agreement (La Chapelle sur Erdre) ***	0	466	0	466
	5,908	**466**	**702**	**5,672**
Amortization				
Lease agreement (Nantes Lot 1)	310	103	0	413
Lease agreement (Nantes Lot 2)	96	35	0	131
Lease agreement (Nantes Lot 3)	30	30	0	60
Lease agreement (Paris Suffren Lot 1) *	395	0	395	0
Lease agreement (Paris Suffren Lot 2) **	296	0	296	0
Leasing (Cytek Cytometre)	107	70	0	177
Lease agreeement (Paris Catalogne)	150	450	0	601
Lease agreement (La Chapelle sur Erdre) ***	0	54	0	54
	1,384	**742**	**691**	**1,436**
Impairment				
Lease agreement (Paris Suffren Lot 1) *	11	0	11	0
Lease agreement (Paris Suffren Lot 2) **	0	0	0	0
	11	**0**	**11**	**0**
Net Values				
Lease agreement (Nantes Lot 1)	227	0	103	124
Lease agreement (Nantes Lot 2)	112	0	35	78
Lease agreement (Nantes Lot 3)	97	0	30	67
Lease agreement (Paris Suffren Lot 1) *	(0)	0	(0)	0
Lease agreement (Paris Suffren Lot 2) **	0	0	0	0
Leasing (Cytek Cytometre)	174	0	70	104
Lease agreeement (Paris Catalogne)	3,902	0	450	3,451
Lease agreement (La Chapelle sur Erdre) ***	0	466	54	412
	4,513	**466**	**742**	**4,236**

** Effective lease date 1/31/2022*
*** Effective lease date 1/31/2022*
**** Effective lease date 12/15/2021 (1/1/2022)*

1.4 Non-current financial assets

In €k	12/31/2021	Increase	Decrease	12/31/2022
Deposits and guarantees	581	35	(92)	524
Liquidity contract - cash balances	355	1,402	(1,646)	111
Total non-current financial assets	**936**	**1,438**	**(1,738)**	**635**

NOTE 2: CURRENT ASSETS

2.1 Available cash and cash equivalents and current financial assets

In €k	12/31/2022	12/31/2021
Bank accounts	18,512	22,481
Term deposit	7,108	11,098
Cash on deposit	**25,620**	**33,579**
Current financial liabilities (bank accounts)	(2)	(1)
Net cash	**25,617**	**33,578**

The Company invests in non-risky term accounts that meet the definition of cash equivalents (available in the short term).

2.2 Trade receivables

In €k	12/31/2022	12/31/2021
Trade receivables	403	772
Total net trade receivables	**403**	**772**

The change in trade receivables is mainly due to decreased rebilling end of 2022, to development costs and related invoices to Boehringer Ingelheim for OSE-172/BI 765063 (€394 thousand at December 31, 2022 versus €585 thousand at December 31, 2021) and to Servier (net credit position for €64 thousand at December 31, 2022 due to an advance received against €12 thousand of net debit receivable at December 31, 2021).

2.3 Other current assets

Other current assets break down as follows:

In €k	12/31/2022	12/31/2021
Value-Added Tax **(1)**	1,741	1,715
Trade debtors **(2)**	98	151
Prepaid expenses **(3)**	3,452	2,964
Prepaid income **(4)**	454	671
Government - tax receivable **(5)**	-	9
Research tax credit **(5)**	5,432	4,344
Total	**11,177**	**9,854**

(1) Value-added tax includes VAT refund claims of €215 thousand, for FNP VAT of €319 thousand and €316 thousand for deductible VAT on services.
(2) "Trade debtors" mainly comprises €98 thousand of trade discounts and rebates receivable.
(3) Prepaid expenses are mainly composed of research and development expenses, including €521 thousand on OSE-127 progress, €811 thousand on OSE-230 progress, €94 thousand on OSE-172 progress, €96 thousand on OSE-279 progress and €410 thousand on BiCKI progress.
(4) "Prepaid income" mainly comprises grants receivable amounting to €448 thousand.
(5) The Research Tax Credit item comprises the tax receivable relating to the 2022 research tax credit.

NOTE 3: FINANCIAL ASSETS AND LIABILITIES AND IMPACT ON INCOME

The Company's financial assets were measured as follows as at December 31, 2022:

	12/31/2022				
IN €K	**Balance sheet**	**Fair value**	**Fair value through the income statement**	**Loans and receivables**	**Liabilities at amortized cost**
Non-current financial assets	635	635		635	
Rights of use	4,236	4,236		4,236	
Trade receivables	403	403		403	
Other current assets	7,885	7,885		7,885	
Cash and cash equivalents	25,620	25,620		25,620	
Total financial assets	**38,779**	**38,779**	**-**	**38,779**	**-**
Non-current financial liabilities	37,231	37,231	4,229		33,003
Non-current lease liabilities	3,586	3,586			3,586
Current financial liabilities	3,093	3,093			3,093
Current lease liabilities	883	883			883
Trade payables	8,539	8,539			8,539
Total financial liabilities	**53,333**	**53,333**			**49,104**

	Impacts on the income statement at December 31, 2022	
IN €K	Interest	Change in fair value
Assets at fair value through the income statement	0	0
Loans and receivables		
Assets at amortized cost		0
Cash and cash equivalents	15	
Total	**15**	**0**
Lease liabilities at amortized cost	68	
Liabilities at fair value through profit or loss	0	(1,816)
Liabilities measured at amortized cost	1,305	
Total	**1,372**	**(1,816)**

NOTE 4: CAPITAL

4.1 Issued capital

Date	Nature of transactions	Capital in €	Issue premium in €	Number of shares created	Number of shares making up the capital	Nominal value in €	Stated capital in €
At December 31, 2020		**3,596,607**	**65,448,952**	**7,934,097**	**17,983,038**	**0.20**	**3,596,607**

June	Capital increase - Share subscription warrants (1)	400	8,900	2,000	17,985,038	0.20	3,597,007
June	Capital increase - Share subscription warrants (2)	6,000	133,500	30,000	18,015,038	0.20	3,603,007
June	Capital increase - Share subscription warrants (3)	1,000	22,250	5,000	18,020,038	0.20	3,604,007
June	Capital increase - Founders' share warrants (4)	2,000	59,400	10,000	18,030,038	0.20	3,606,007
June	Capital increase - Free Share Allocation (5)	30,000	(30,000)	150,000	18,180,038	0.20	3,636,007
June	Capital increase - Free Share Allocation (6)	20,000	(20,000)	100,000	18,280,038	0.20	3,656,007
June	Capital increase - Share subscription warrants (7)	1,000	22,250	5,000	18,285,038	0.20	3,657,007
July	Share subscription warrants - EIB (8)		8,500	0	18,285,038	0.20	3,657,007
December	Capital increase - Free Share Allocation (9)	46,200	(46,200)	231,000	18,516,038	0.20	3,703,207
December	Capital increase - Free Share Allocation (10)	2,273	(2,273)	11,363	18,527,401	0.20	3,705,480
	At December 31, 2021	**3,705,480**	**65,605,279**	**8,478,460**	**18,527,401**	**0.20**	**3,705,480**
	At December 31, 2022	**3,705,480**	**65,605,279**	**8,478,460**	**18,527,401**	**0.20**	**3,705,480**

On December 31, 2022, the share capital stood at €3,705,480. It is divided into 18,527,401 fully subscribed and paid up ordinary shares with a par value of €0.20.

4.2 Equity instruments authorized but not issued

The Combined General Shareholders' Meeting of June 16, 2020, gave the Board of Directors full authority to increase the capital, on one or more occasions, by a maximum of 500,000 new shares:

At December 31, 2020, the Board of Directors had not yet allocated 500,000 of the 500,000 equity instruments.

The Combined General Shareholders' Meeting of June 24, 2021, gave the Board of Directors full authority to increase the capital, on one or more occasions, by a maximum of 500,000 new shares.

On June 24, 2021, the Board of Directors (under the delegation of June 16, 2020) decided to issue 80,000 2021 founders' share warrants to non-salaried, non-executive directors (i.e. 10,000 founders' share warrants per director).

On March 28, 2022, the Board of Directors, further to the Board of Directors of December 7, 2021 (under the delegation of June 24, 2021), decided to issue and grant 150,000 free shares to Nicolas Poirier as director representing the employee shareholders and 228,700 free shares to non-executive director employees.

The Combined Shareholders' Meeting of June 23, 2022, gave the Board of Directors full authority to increase the capital, on one or more occasions, by a maximum of 500,000 new shares.

On June 23, 2022, the Board of Directors (under the delegation of June 23, 2022) decided to issue 80,000 2022 founders' share warrants to non-salaried non-executive directors (i.e. 10,000 founders' share warrants per director).

On July 13, 2022, the Board of Directors (under the delegation of June 23, 2022) decided to issue 60,000 2022 warrants to the Scientific Advisory Board (i.e. 10,000 warrants per member).

On December 6, 2022, the Board of Directors (under the delegation of June 23, 2022) decided to grant 1,852 free shares (i.e. 185,000 shares) preferably to Nicolas Poirier.

As of December 31, 2022, there remain:

- 420,000 equity instruments under the authority of the Combined General Shareholders' Meeting of June 16, 2020
- 500,000 equity instruments under the authority of the Combined General Shareholders' Meeting of June 24, 2021
- 314,800 equity instruments under the authority of the Combined General Shareholders' Meeting of June 23, 2022

4.3 Share subscription warrants, founders' share warrants and free shares

4.3.1 - Share subscription warrants/Founders' share warrants

The Company issued the following share subscription warrant and founders' share warrant plans:

Type		Creation date	Exercise price	Subscription period	Total created				Subscriptions during the fiscal year					
						2015 and before	2016	2017	2018	2019	2020	2021	2022	Total subscribed and/or exercised at 12/31/2022
	Share subscription warrants and founders' share warrants													
2012 share subscription warrants		*11/29/13*	*€1*	*11/29/2013-02/28/2014*	*40,000*	*40,000*		-						*40,000*
Share subscription warrants 2014 1		*06/02/14*	*€8*	*06/02/2014-06/30/2014*	*118,649*	*118,649*		-						*118,649*
Share subscription warrants 2014 2		*07/01/14*	*€8*	*07/01/2014-07/16/2014*	*33,333*	*33,333*		-						*33,333*
2014 3 share subscription warrants		*3/27/15*	*€8*	*03/27/2015-09/30/2016*	*120,000*	*100,000*	*10,000*	-						*110,000*
Share subscription warrants 2014 4		*3/27/15*	*€8*	*Undetermined*	*125,000*	*36,744*	*88,256*	-						*125,000*
Share subscription warrants 2014 5		*3/27/15*	*€8*	*04/01/2016-10/01/2016*	*25,000*	-	*25,000*	-						*25,000*
Share subscription warrants 2014 7		*12/01/15*	*€8*	*12/01/2015-09/30/2016*	*50,000*		*39,000*	-						*39,000*
EFFIMUNE share subscription warrants 2010-2		*10/29/10*	*€5.8*	*12/08/2011-12/07/2016*	*23,620*	*23,620*		-						*23,620*
EFFIMUNE share subscription warrants 2014-2		*07/01/14*	*€7*	*07/01/2014-06/30/2019*	*30,700*		*30,700*	-						*30,700*
EFFIMUNE share subscription warrants 2014-1		*11/25/14*	*€7*	*11/25/2014-11/24/2019*	*3,500*		*3,500*	-						*3,500*
Share subscription warrants 2015		*3/27/15*	*€10.8*	*03/27/2015-05/30/2015*	*136,222*	*136,222*		-						*136,222*
Share subscription warrants 2017		7/18/17	€4.65	07/18/2017-07/17/2021	52,000			30,000	12,000					42,000
Founders' share warrants 2018		6/13/18	€4.17	06/13/2018-06/13/2023	25,900				25,900					25,900
Share subscription warrants 2018		6/13/18	€4.17	06/13/2018-06/13/2023	42,850									-
Founders' share warrants 2019		6/26/19	€3.58	06/26/2019-06/26/2024	60,000					60,000				60,000
Founders' share warrants 2020		6/17/20	€6.14	06/17/2020-06/17/2025	70,000						70,000			70,000
Founders' share warrants 2021		6/24/21	€11.05	6/24/21-6/24/26	80,000							80,000		80,000
Founders'share warrants 2022		6/23/22	€6.63	6/23/22-6/23/27	80,000								80,000	80,000
Shae subscription warrants 2022		7/13/22	€6.25	7/13/22-7/13/27	60,000								60,000	60,000
	Total share subscription warrants and founders' share warrants				**2,003,034**	**488,568**	**196,456**	**30,000**	**37,900**	**60,000**	**70,000**	**930,000**	**140,000**	**1,102,924**

* Share subscription warrants do not qualify as equity instruments.

The table below specifies the assumptions used for the valuation of the share subscription warrant and founders' share warrant plans set up for previous years:

	2017 share subscription warrants	2018 share subscription warrants	2018 founders' share warrants	2019 founders' share warrants	2020 founders' share warrants	2021 founders' share warrants
Date of GM establishing plan	5/31/2016	6/14/2017	6/14/2017	6/13/2018	6/26/19	6/24/21
Number of authorized shares	52,000	42,850	25,900	60,000	70,000	80,000
Subscription price	€0.60	€0.70	€0.00	€0.00	€0.00	€0,00
Subscription date	7/18/2017	6/13/2018	6/13/2018	6/26/2019	6/17/2020	6/24/21
Vesting of share subscription warrants	on subscription	on subscription	on subscription	on subscription	on subscription	on subscription
Exercise price	€4.65/share	€4.17/share	€4.17/share	€3.58/share	€6.14/share	€11.85/share
Option type	American	American	American	American	American	American
Spot rate	€4.05	€4.09	€4.09	€3.52	€6.16	€11.32
Maturity	4 years	5 years	5 years	5 years	5 years	5 years
Volatility	46.98%	47.08%	47.08%	44.67%	50.05%	53.94%
EUR interest rate	0.1494%	0.3812%	0.3812%	-0.2062%	-0.3107%	-0.2509%
Dividend yield	0%	0%	0%	0%	0%	0%
Estimated fair value per share subscription warrant	1.30	1.64	1.64	1.32	2.59	5.17
Number of options subscribed	42,000	0	25.900	60.000	70.000	80.000
Subscription price	€0.60	€0.70	0.00	0.00	0.00	0.00
Number of options exercised	42.000	-	-	-	10.000	
Contractual expiration date	7/17/2021	6/13/23	6/13/23	6/26/2024	6/17/25	6/24/23
Vesting period	none	none	none	none	none	none

During 2022, the Group introduced the plan described below:

- Issuance dated June 23, 2022, of 80,000 2022 founders' share warrants (i.e. 10,000 founders' share warrants per non-salaried non-executive directors in office at June 23, 2022).

	2022 founders' share warrants
Date of GM establishing plan	6/23/2022
Number of authorized shares	80,000
Subscription price	€0.00
Subscription date	6/23/2022
Vesting of share subscription warrants/founders' warrants	on subscription
Exercise price	€6.63/share
Option type	American
Spot rate	€6.64

Maturity	5 years
Volatility	58.87%
EUR interest rate	1.9422%
Dividend yield	0%
Estimated fair value per share subscription warrant/founders' share warrant	3.42
Number of options subscribed	80,000
Subscription price	0.00
Number of options exercised	-
Contractual expiry date	6/23/2027
Vesting period	none

- Issuance dated July 13, 2022, of 60,000 share subscription warrants to the Scientific Advisory Board's members.

	2022 subscription share warrants
Date of GM establishing plan	7/13/2022
Number of authorized shares	60,000
Subscription price	€0.00
Subscription date	6/23/2022
Vesting of share subscription warrants/founders' warrants	on subscription
Exercise price	€6.25/share
Option type	American
Spot rate	€6.23
Maturity	5 years
Volatility	55.17%
EUR interest rate	1.5951%
Dividend yield	0%
Estimated fair value per share subscription warrant/founders' share warrant	3.01
Number of options subscribed	60,000
Subscription price	0.70
Number of options exercised	-
Contractual expiry date	7/13/2027
Vesting period	none

4.3.2 – Free shares

The Company issued the following free share plans:

Allocation date	Exercise period	Total allocated	Exercised during the fiscal year	Total non-exercised and expired
			2022	
Free Share Allocation				
3/28/2022	3/28/2022-3/28/2023	228,700		
3/28/2022	3/28/2022-3/28/2023	150,000		
12/06/2022	12/06/22-12/06/2023	185,200		
Total Free share allocation		**563,900**	**-**	**-**

On March 28, 2022, the Board of Directors allocated free shares with the following characteristics:

Allocation to Nicolas Poirier:

- Number of shares allocated (existing or to be issued): 150,000,
- Value of the share on the allocation date (according to the market price): €8.00,
- Vesting period and employment requirement: 1 year,
- Lock-up period: 1 year.

Allocation to employees:

- Number of shares allocated (existing or to be issued): 228,700,
- Value of the share on the allocation date (according to the market price): €8.00,
- Vesting period and employment requirement: 1 year,
- Lock-up period: 1 year.

On December 6, 2022, the Board of Directors allocated free shares with the following characteristics:

Allocation to Nicolas Poirier:

- Number of shares allocated (existing or to be issued): 185,200,
- Value of the share on the allocation date (according to the market price): €6.96,
- Vesting period and employment requirement: 1 year,
- Lock-up period: 1 year.

These free shares are linked to performance conditions whose probability of achievement is difficult to assess, the assumption was made on a probability of achievement at 0%.

4.3.3 - Corporate officers, employees and consultants

The expense recognized on December 31, 2022, for benefits paid in equity instruments to corporate officers, employees and consultants stood at €2,728 thousand, associated with the 2022 free share allocation plans and the 2022 founders' share warrant plan.

The employer's contribution in relation to free shares stood at €402 thousand. Thus, expenses associated with share-based payments totaled €3,130 thousand.

All these benefits were granted to corporate officers, employees and consultants.

Share subscription warrants/founders' share warrants measured at the fair value of the options determined using the Bjerksund & Stensland model.

Free share allocations were measured using a model that considers the probability of achieving related vesting conditions.

The valuation of the conditions of the plans was measured by an external service provider.

4.4 Company's buyback of its own shares

The Combined General Shareholders' Meeting of June 23, 2022, authorized, for a period of eighteen months with effect from the Meeting, the Board of Directors to implement, on one or more occasions, a share buyback program in accordance with the provisions of Article L. 225-209 of the French Commercial Code and pursuant to the General Regulation of the French Financial Markets Authority (AMF), for in the circumstances described below:

Share buyback objective:

- To boost liquidity in Company shares through the intermediary of an investment services provider acting independently under a liquidity contract in accordance with the AMAFI Ethics charter recognized by the French Financial Markets Authority;
- The allocation of shares to employees or corporate officers of the Company or of French companies or groups of companies related to it in accordance with legal requirements, particularly within the context of sharing in the fruits of the Company's expansion, employee share ownership plans or Company savings plans, stock options or the free allocation of shares or in any other circumstance permitted by regulations;
- The delivery of shares in payment, or exchange, in connection with acquisitions;
- Ensuring the coverage of debt securities giving access to equity;
- The cancellation of shares by reducing the share capital, particularly for the purposes of optimizing net earnings per share, subject to the adoption of the 35th resolution below, intended to authorize the Board of Directors to reduce the share capital;
- The implementation of any market practice that would be permitted by the French Financial Markets Authority and, more generally speaking, the completion of any transaction that complies with current regulations.

Maximum purchase price: €21.60 per share, not including costs and commissions, capped at €10 million overall.

Maximum number of shares that can be purchased: 10% of the total number of shares making up the Company's share capital, on the date of the share buyback. When the shares are acquired with the aim of boosting trading and liquidity, the number of shares taken into consideration when calculating the 10% cap provided for above, corresponds to the number of shares purchased, less the number of shares resold during the authorization period.

Summary of shares bought and sold in 2022:

2022					
	1st quarter	2nd quarter	3rd quarter	4th quarter	Total
Securities purchased	89,665	42,716	49,137	59,488	241,006
Price (in euros)	7,43	6,86	6,20	6,43	6,83
Total amount (in K€)	**666**	**293**	**305**	**383**	**1,646**
Securities Sold	80,172	30,597	27,344	62,416	200,529
Price (in euros)	7,53	6,98	6,63	6,47	6,99
Total amount (in K€)	**604**	**213**	**181**	**404**	**1,402**

On December 31, 2022, the Company held 70,095 OSE Immunotherapeutics shares, acquired for a total of €438 thousand. Sales of treasury shares generated a net gain on disposal of €112 thousand in 2022. Management fees for these treasury shares amounted to €15 thousand (€14 thousand after deduction of deferred taxes).
These amounts have been restated in equity in accordance with IAS 32. Treasury shares in shareholders' equity therefore amounted to €549 thousand at December 31, 2022.

NOTE 5: FINANCIAL LIABILITIES

Financial liabilities are presented in the table below which distinguishes between non-current and current liabilities:

IN €K	12/31/2021	Increase	Decrease	Other transactions *	12/31/2022	Interest at 12/31/2022
BPI EFFIMAB Advance	4,688	75			4,763	(75)
BPI EFFICLIN Advance	6,464	92			6,556	(92)
Guaranteed loan	5,932			(1,695)	4,237	
BPI COVEPIT Advance	911	6			916	(6)
BPI CAPACITY / COVEPIT 2 Advance	3,008	16		(247)	2,777	(16)
EIB LOAN	5,810	10,000	(2,056)		13,754	
EIB LOAN – Subscription share warrant component	3,989	2,056	(1,816)		4,229	
Non-current financial liabilities	**30,801**	**12,244**	**(3,872)**	**(1,942)**	**37,231**	**(188)**
Nantes Lot 1 Lease	124			(111)	13	
Nantes Lot 2 Lease	78			(35)	43	
Nantes Lot 3 Lease	69			(31)	38	
Paris Suffren Lot 1 Lease	(0)				(0)	
Place de Catalogne Lease	3,595			(491)	3,104	
Leasing Cytometre	98			(68)	30	
La Chapelle sur Erdre		466		(108)	358	

Non-current lease liabilities	**3,965**	**466**		**(844)**	**3,586**	
BPI EFFIMAB Advance						
BPI EFFICLIN Advance						
Guaranteed loan	1,093		(1,034)	1,695	1,753	(43)
BPI COVEPIT Advance						
BPI CAPACITY / COVEPIT 2 Advance				247	247	
EIB LOAN	517	1,073	(500)		1,090	
Bank overdrafts	1	1			2	
Current financial liabilities	**1,611**	**1,074**	**(1,534)**	**1,942**	**3,093**	**(1,117)**
Nantes Lot 1 Lease	117		(107)	111	122	(4)
Nantes Lot 2 Lease	42		(36)	35	41	(2)
Nantes Lot 3 Lease	32		(29)	31	34	(2)
Paris Suffren Lot 1 Lease	10		(10)		0	
Place de Catalogne Lease	476		(414)	491	553	(54)
Leasing Cytometre	79		(69)	68	78	(3)
La Chapelle sur Erdre			(52)	108	56	(3)
Current lease liabilities	**756**		**(717)**	**844**	**883**	**(68)**
Total financial liabilities	**37,133**	**13,784**	**(6,123)**		**44,794**	**(1,372)**

** This column includes the current/non-current breakdown of the year.*

The table below shows the schedule of financial liabilities:

IN €K	Less than 1 year	December 2024	December 2025	December 2026	December 2027 and after	Total
BPI EFFIMAB Advance	-			765	3,998	**4,688**
BPI EFFICLIN Advance	-		699	1,351	4,506	**6,464**
Guaranteed loan	1,753	1,798	1,798	642		**7,025**
BPI COVEPIT Advance	-	64	227	227	398	**911**
BPI CAPACITY / COVEPIT 2 Advance	247	1,000	1,000	777		**3,008**
EIB LOAN	1,090			17,982		**10,315**
Bank overdrafts	2					**1**
Financial liabilities	**3,093**	**2,861**	**3,723**	**21,745**	**8,901**	**32,412**
Nantes Lot 1 Lease	122	13	-	-		**134**
Nantes Lot 2 Lease	41	35	8			**84**
Nantes Lot 3 Lease	34	31	7	-		**71**
Place de Catalogne Lease	553	484	478	471	1,671	**3,657**
Leasing Cytometre	78	30	-	-	-	**108**

La Chapelle sur Erdre	56	53	52	52	201	**414**
Lease liabilities	**883**	**646**	**545**	**523**	**1,872**	**4,470**
Total financial liabilities	**3,976**	**3,507**	**4,269**	**22,267**	**10,775**	**44,794**

Lease liabilities (see Note 1.3)

Jador

Financial liabilities

Repayable advances

The amount of repayable advances indicated corresponds to the amounts received by the Company. However, their repayment is subject to the success of the product developed in each of the aid programs.

French Government-guaranteed loan

To address the financial consequences of the COVID-19 pandemic, on May 5, 2020, a French Government-guaranteed loan of €6,960,000 was granted, split between three banks (CIC, CM and BNP).

These loans meet the conditions of the Rectifying Finance Law for 2020, n°2020-289, of March 23, 2020, and the specifications defined in the decree dated March 23, 2020, providing the French Government guarantee to credit and financial institutions under that law.

This funding is one-year cash loan immediately made available to the borrower for the full amount on the date that the funds are transferred into their current account. Capital will be repaid and interest and ancillary costs paid in a single installment on the annual repayment date, with the option for the borrower to apply to spread the outstanding amount due on the repayment date over a further four years. Management exercised the option allowing it to repay this loan at a maturity of five years.

The optional amortization amendments to French Government-guaranteed loans enabling the repayment to be spread over five years were signed at the end of March 2021.

The funds received and conditions are as follows:

- Crédit Mutuel = €2,300,000 received on May 6, 2020. 48 monthly payments with a first due on May 6, 2022 and a final payment on May 5, 2026. (Fixed rate: 0.70% / APR: 1.39% per year).
- BNP = €2,300,000 received on May 6, 2020. 48 monthly payments with a first due on May 6, 2022 and a final payment on May 5, 2026. (Fixed rate: 0.70% / APR: 1.39% per year).
- CIC = €2,360,000 received on May 18, 2020. 48 monthly payments with a first due on June 15, 2022 and a final payment on May 15, 2026. (Fixed rate: 0.70% / APR: 1.39% per year).

EIB loan

Tranche 1

In early July 2021, the Company received the payment of €10 million for the first tranche of the loan granted by the European Investment Bank (EIB) on February 12, 2021.

This type of financing, granted by the EIB, and benefiting from a guarantee from the European Commission under the European Fund for Strategic Investments (known as the "Juncker Plan"), aims to support developed research and innovation projects by companies with high growth potential.

This first tranche bears a fixed annual interest rate of 5% paid annually, with a maturity of five years.

The first tranche is accompanied by the issue of share subscription warrants (BSA) entitling EIB in the event of exercise, to subscribe to 850,000 shares of the Company (i.e. 4.44% of the share capital on an undiluted basis). The share subscription warrants T1 are not subject to a request for admission to trading on any market.

The subscription price is €0.01 per share subscription warrant, i.e. €8,500.

The EIB has a put option on these share subscription warrants. The terms of this option are as follows:

Warrant EIG (put)	
Option type	Put option
Underlying	Warrants
Quantity	850,000
Warrant selling price	Spot share OSE – Exercise price
Date of attribution	7/08/2021
Period of exercise	7/08/2021-7/09/2026
Option capped to a €15 million payment (this option will be exercised, when appropriate, for the quantity of warrants allowing to obtain a €15 million payment, the remaining warrant being kept by the EIB	
Option condition of exercise	Change of control of the issuer
	Reached maturity
	Reimbursement of the loan
	Nonpayment of the issuer

The Company also has a call option on these share subscription warrants. The terms of this option are as follows:

Warrant EIG (call)	
Option type	Call option
Underlying	Warrants
Quantity	850,000
Warrant selling price	Spot share OSE – Exercise price
Date of attribution	7/08/2021
Period of exercise	7/08/2021-7/09/2033
Option condition of exercise	Exit i.e. Transfer of all shares from key shareholders to a third party
	Warrants have to be exercisable and not exercised

The valuation of the share subscription warrants T1 on the issue date (July 8, 2021) breaks down as follows:

- Share subscription warrants issued, excluding additional options - part (1): +€5.89 /share
- EIB put option - part (2): +€0.00/share
- Company call option - part (3): - €0.96/share

A total of **€4.93/share**. For all the 850,000 share subscription warrants T1 issued, the valuation therefore amounts to €4.19 million.

The valuation of share subscription warrants T1 at December 31, 2022 breaks down as follows:

- Share subscription warrants issued, excluding additional options - part (1): +€3.70/share

- EIB put option - part (2): +€0.00/share

- Company call option - part (3): -€0.82/share

A total of **€2.88/share**. For all the 850,000 share subscription warrants T1 issued, the valuation therefore amounts to €2.45 million.

Given the characteristics of the loan contract, this financial instrument is considered as a hybrid instrument consisting of a host (debt) and embedded derivatives (call and put share subscription warrants).

- The debt (corresponding to the Tranche 1) is measured using the amortized cost method including issue costs corresponding to the fair value of the share subscription warrants (on the issue date) for €4.19 million and taking into account an effective interest rate of 18.56%.
- The share subscription warrants T1 are derivative liabilities to be measured at fair value through profit or loss at each closing date (i.e. €1.54 thousand at December 31, 2022.)

Tranche 2

In early December 2022, the Company received the payment of €10 million for the second tranche of the loan granted by the European Investment Bank (EIB) on February 12, 2021.

This second tranche bears a fixed annual interest rate of 5% paid annually, with a maturity of five years.

This loan is recognized on the date it is granted at fair value and then subsequently recognized at amortized cost. The effective interest rate (TEI) of Tranche 2 was estimated at 10.48%.

The second tranche (T2) is accompanied by the issue of share subscription warrants (share subscription warrants T2) entitling EIB in the event of exercise, to subscribe to 550,000 shares of the Company (i.e.2.97% of the share capital on an undiluted basis). The share subscription warrants T2 are not subject to a request for admission to trading on any market.

The subscription price is €0.01 per share subscription warrant, i.e. €5,500.

These share subscription warrants T2 are accompanied by a put option of the share subscription warrants to the hand of the EIB. The terms of this option are as follows:

Warrant EIG (put) Tranche 2	
Option type	Put option
Underlying	Warrants
Quantity	550,000
Warrant selling price	Spot share OSE – Exercise price
Date of attribution	12/01/2022
Period of exercise	12/01/2022-12/01/2027
Option capped to a €15 million payment (this option will be exercised, when appropriate, for the quantity of warrants allowing to obtain a €15 million payment, the remaining warrant being kept by the EIB	
Option condition of exercise	Change of control of the issuer
	Reached maturity
	Reimbursement of the loan
	Nonpayment of the issuer

These share subscription warrants T2 are accompanied by a call option of the share subscription warrants to the hand of the EIB. The terms of this option are as follows:

Warrant EIG (call) Tranche B	
Option type	Call option
Underlying	Warrants
Quantity	550,000
Warrant selling price	Spot share OSE – Exercise price
Date of attribution	12/01/2022
Period of exercise	12/01/2022-12/01/2027
Option condition of exercise	Exit i.e. Transfer of all shares from key shareholders to a third party
	Warrants have to be exercisable and not exercised

NOTE 6: CURRENT DEBTS

6.1. Trade payables

IN €K	**12/31/2022**	**12/31/2021**
Trade payables	4,563	2,955
Accrued invoices	3,977	6,652
Total trade payables	**8,539**	**9,607**

This item decreased slightly compared to December 31, 2021, in line with the increase in subcontracting expenses related to research on OSE-127, OSE-172 and OSE-279.

6.2. Tax and social security liabilities

IN €K	**12/31/2022**	**12/31/2021**
Staff costs	1,608	2,012
Social security and other social organizations	858	1,554
Other taxes, duties and similar payments	449	158
Current tax liability	2,916	3,724
Other payables	21	14
Tax and social security liabilities	**2,937**	**3,737**

The decrease in tax and social security liabilities is in line with the provision in 2021 related to the departure of the previous Chief Executive Officer.

6.3. Other current liabilities

IN €K	12/31/2022	12/31/2021
Deferred income	812	1,046
Other	3	4
Total other debts and accruals	**816**	**1,050**

The deferred income item is stable compared to the previous reporting date. This item is mainly composed of:

- €531 thousand related to the CAPA Building grant (linked to the progress of costs incurred)
- €56 thousand under the collaboration and licensing agreement signed with Boehringer Ingelheim (OSE-172), corresponding to the estimated costs remaining to be incurred by the Group in 2022.

NOTE 7: CURRENT AND NON-CURRENT PROVISIONS

Provisions break down as follows:

IN €K	12/31/2021	Increase through the income statement	Decrease through the income statement	Impact of change in method through retained earnings	12/31/2022
Provision for pension commitments [(1)]	**421**	11			**432**
Provision for risks and litigation	**289**	1,247	(1,044)	(401)	**91**
	710	**1,258**	(1,044)	(401)	**524**

(1) of which the effect of actuarial gains and losses of €11 thousand

Provision for pension commitments

The pension commitment provision is measured in accordance with the applicable collective agreement, i.e. the pharmaceutical industry collective agreement, and according to the new IFRIC method. The assumptions made were as follows:

- Mortality table: regulatory table TH (men)/TF (women) 00-02,
- Estimated retirement age: 62,
- Ratio of wage increases: 2%,
- Staff turnover: low turnover,
- Discount rate: 3.84%,

- Social security contribution rates: between 39% and 46% depending on the category.

The impact of a change in method is considered immaterial and was recognized in the reserve for €160 thousand.
On December 31, 2022, the average monthly headcount stood at 57, compared with 53 on December 31, 2021.

NOTE 8: OPERATING INCOME

8.1. Revenue from collaboration agreements

As of December 31, 2022, the breakdown of operating income is as follows:

IN €K	**2022**		**2021**	
	Revenue	Deferred income	Revenue	Deferred income
BI Agreement				
Milestones	9,800		7,330	
Re-invoicing of direct costs	2,505	281	4,023	240
Servier agreement				
Milestones			5,000	
Re-invoicing for chemical batch production	831		1,047	
Veloxis agreement				
Upfront	5,000		6,620	
Reagent sales	72		2,287	
Labexchange Die/ Laborgerate-borse GmbH agreement				
Final product sales	4			
Total	**18,302**	**281**	**26,306**	**240**

Revenue amounted to €18,302 thousand and consisted of income from agreements with our industrial partners:

Boehringer Ingelheim (BI):

The analysis of the contract with BI, according to the IFRS.15 standard, highlighted two performance obligations:

- An OSE technology license related to OSE-172 for the development and commercialization,
- A development service.

The transaction price is composed as follows:

- An upfront,
- A development milestone,
- Royalties,
- Re-invoicing of a part of the development costs.

The transaction price is allocated to the two performance obligations identified with the residual method.

The revenue allocated to the license is recognized at the date of the license transfer, corresponding to the date of agreement signature. Nevertheless, the revenue assessment allocated to the license is variable, given the uncertainty linked to the achievement of milestones and to royalties.

To each milestone achievement, this one becoming highly probable, it can be integrated to the transaction price et thus recognized in revenue.
In addition, as long as OSE Immunotherapeutics participates in development, part of the transaction price must be allocated to development services.

Consequently, for 2022 and following the payment of the milestone 4 (following enrollment of the first patient in the phase 1 expansion clinical trial), the following revenue was recognized:

- €9,800 thousand related to the intellectual property by application of the residual method,
- €2,595 thousand related to the re-invoicing of development costs including a margin percentage (double digit) and recognized according to the costs incurred.

Servier

The contract with Servier, signed in December 2016, covers a collaboration, options and a license option on the product OSE-127. This contract included 3 phases:

- Before exercising the option 1, OSE Immunotherapeutics must complete the phase 1 common to all applications of OSE-127 but does not grant any right on its intellectual property (IP).
- Further to the option 1exercise, OSE Immunotherapeutics grants Servier a partial development license to conduct the phase 2 study in the Sjögren syndrome. This phase 2 is conducted by Servier alone. On its side, OSE Immunotherapeutics has to achieve the “option 2 plan” corresponding in particular to the phase 2 study in ulcerative colitis (UC).
- Upon the exercise of option 2, OSE will grant an exclusive development and commercialization license to Servier covering the whole IP related OSE-127.

Financial modalities of this contract are the following:

- Upfront fee: € 10.25M
- Option 1 exercise: €10M
- Option 2 exercise: €20M
- Development milestones
- Royalties
- Re-invoicing of a part of IP costs

Even if OSE Immunotherapeutics retained the legal ownership of the IP and the decision-making power over the development activities it conducts, it would actually transfer control of the IP to Servier as soon as the contract was signed by granting Servier options:

- Exercisable at any time and
- The option 2 results in the transfer to Servier of all IP rights on OSE-127.

Therefore, the development activities were conducted on an underlying IP controlled by Servier and should be considered as services provided by OSE to Servier.

Two obligations were therefore included in this contract:

- An assignment of IP with right of return,
- Provision of development services.

An amendment was signed in March 2020 with the main following modifications:

- The option 2 of €20M has been split in:
  - A first €5M milestone paid to OSE upon enrollment of the first patient in the phase 2 study in Sjögren syndrome.
  - The option 2 of €15M can be exercised by Servier according to the results of one or the other phase 2 study.
- The phase 2 study in UC conducted by OSE can be resized at OSE discretion.

Thus, since the signing of the amendment with Servier in March 2020, OSE is no longer required to provide development services. Thus, from this date, the amounts received from Servier will be fully allocated to the license.

Then, for the year 2021 and following dosing of the first patient in the phase 2 study in Sjögren syndrome, the Company received the second €5M milestone payment. In accordance with the accounting treatment described below, this amount was fully allocated to the license and recognized in revenue for the 2021 financial year.

In addition, during the 2022 financial year, the Company re-invoiced €831,000 thousand of manufacturing costs for clinical batches and part of the IP costs.

Veloxis

The analysis of the contract with Veloxis, with regard to IFRS 15 standard, highlights two performance obligations:

- Transfer of intellectual property (FR104 molecule),
- Sales of products related to the molecule FR104.

The transaction price is allocated to the two performance obligations identified in proportion to the specific sales price of each of these obligations. A two-digit margin is applied on the sales of the product.

The revenue allocated to the license is recognized at the date of the license transfer, corresponding to the date of signature of the contract.

The revenue allocated to the sales of the product is recognized at the date of its delivery.

Consequently, for the 2022 year, it was recognized as revenue:

- €72,000 thousand related to the sale of reagents including a margin and recognized on delivery,
- €5,000 thousand allocated to the transfer of IP by application of the residual method.

For deferred income, see Note 6.1. Other current liabilities.

8.2. Research and development expenses

R&D expenses in €K	31/12/2022	31/12/2021
Subcontractor	18,248	23,235
Fees	2,603	2,398
Consumables and small equipment	1,473	1,056
Advertising and press relation	105	164
Payroll expenses	5,844	4,712
Depreciation and provisions	2,708	1,933
Provision for risks/litigation	105	260
Taxes	75	59
Royalties	1,250	1,820
Others	315	272
R&D expenses	**32,725**	**35,909**
CIR	(5,432)	(4,344)
Subsidy income	(399)	(1,015)
Total R&D expenses adjusted	**26,893**	**30,550**

Subcontracting expenses decreased compared to 2021, in line with the product development phases, and in particular the Phase 2 clinical trial for OSE-127, the Phase 1 clinical trial for OSE-172, costs of CMC for OSE-230 and OSE-279.

The activity of the Laboratory in Nantes increased as shown by increased consumables in 2022 compared with 2021.

The increase in fees is correlated with the changes in patent portfolio, mainly on OSE-230, OSE-127, Tedopi®, new BiCKI® platform and CLEC.

As for 2021, the item “royalties” corresponds to the accounting of a provision for the INSERM royalty fees on FR104, triggered by the milestone invoiced to Veloxis in 2022.

After deduction of the research tax credit and subsidies, the total amount of R&D expenses thus decreased to reach €26,893 thousand.

8.3. Overhead expenses

IN €K	12/31/2022	12/31/2021
Fees	2,388	2,924
Consumables and small equipment	43	36
Advertising and press relation	46	68
Employee expenses	1,953	3,927
Depreciation and provisions	736	659
Provision for Risks/Litigation	82	29

Taxes	78	105
Directors' fees	350	231
Others	997	630
Total overhead expenses	**6,672**	**8,751**

Fees include legal, financial (financial communication, accounting, etc.) and human resources services. The decrease compared to 2021 is mainly due to a decrease in recruitment services, outsourcing of functions and the fees of lawyers relating to the EIB loan.

The decrease in overhead expenses is directed due to the decrease in employee expenses.

The increase in depreciation item is mainly due to the new leases for Paris Place de Catalogne (started on January 4, 2021) and La Chapelle sur Erdre (started on January 1,2022) restated in IFR16 standard (cf. note 1.3).

The "Other" item includes rental expenses, up following the signing of two new leases.

8.4. Expenses related to share-based payments

.Allocation of financial instruments in 2022 breaks down as follows:

IN €K	**12/31/2022**	**12/31/2021**
Expenses related to share-based payments	3,130	3,773

Expenses of €3,130 thousand include €2,728 thousand in expenses relating to corporate officers, employees or consultants (see Note 4.3) and €402 thousand in employer's contribution on free shares.

8.5. Employee benefits expenses

The employee benefits expenses allocated to research and development expenses for €5,844 thousand and to overhead for €1,953 thousand break down as follows:

IN €K	**12/31/2022**	**12/31/2021**
Salary and wage benefits	7,673	8,561
Directors' fees	350	231
Pension commitments	124	78
	8,147	**8,870**
Expenses related to employee share-based payments	2,718	3,360
	2,718	**3,360**

On December 31, 2022, the average monthly headcount stood at 57, compared with 53 on December 31, 2021.

NOTE 9: NET FINANCIAL INCOME

In K€	31/12/2022	31/12/2021
Foreign exchange gain	248	58
Revenue on cash equivalents	15	7
Other financial income	1,816	201
Change in fair value of marketable securities	0	1
Total financial income	**2,079**	**267**
Foreign exchange loss	252	20
Interest expense	1,304	829
Interest on lease liabilities	68	7
VMP depreciation allowance	0	0
Total financial expenses	**1,624**	**856**
Total Financial income	**454**	**(588)**

The variation in net financial income was mainly due to:

- Change in fair value of the warrants' liability derivative as part of the BEI contract.
- Increase in interest following the drawing of the second tranche of the EIB loan.

NOTE 10: CORPORATE TAX

10.1. Deferred tax assets

The Company recognized a deferred tax asset for OPI (Swiss subsidiary) valued at €1.3 million calculated on the basis of a 13.99% tax rate (Swiss rates under ordinary law applied since January 1, 2020).

At December 31, 2022, deferred tax assets stood at €182 thousand.

10.2. Net deferred tax liabilities

Given its level of development, the Company only recognizes deferred tax assets in the amount of its tax liabilities recognized as deferred tax liabilities, payment of which may be avoided by the Company, even in the absence of any profit forecast. As of December 31, 2022, the amount of tax loss carryforwards amounts to €93.1 million.

In 2016, the Company recognized a deferred tax liability for the FR104 and OSE-127 molecules, valued at €52.6 million. Consequently, the Company recognized its deferred tax assets at the level of its deferred tax liabilities. As at December 31, 2018, the net deferred tax liability amounted to €2,010 thousand.

Since January 1, 2019, under the 2019 finance act modifying the tax regime for income from the sale or licensing of patents, the Company applied a deferred tax rate of 10% when calculating deferred tax liabilities and assets generated in France.

In light of the administrative clarifications of April 22, 2020, profits eligible for the preferential regime may be offset against tax loss carryforwards as of December 31, 2019. As a result, deferred tax assets on tax loss carryforwards were recognized in the amount of deferred tax liabilities (with the application of the cap on tax loss carryforwards). Deferred tax assets on recognized tax loss carryforwards at December 31, 2022 amounted to €3,347 thousand.

As a result, as of December 31, 2022, the net deferred tax liability amounted to €1,514 thousand.

10.3. Income tax expense

At December 31, 2022, the Group generated income (net of tax) of €263 thousand, which breaks down as follows:

- Net deferred tax income of €264 thousand, mainly corresponding to:
    - A decrease in the deferred tax liabilities of €232 thousand between December 31, 2021, and December 31, 2022 (of which an increase of €2 thousand in the net deferred tax income on the cancellation of Euronext fees and €234 thousand in the additional allocation of losses carried forward following the inclusion of the VELOXIS agreement),
    - An increase in deferred tax assets of €19 thousand between December 31, 2021, and December 31, 2022, related to OPI patents,
    - A decrease in deferred tax liabilities related to the OCI impacts of actuarial differences of €14 thousand.
- Income tax expense of €1 thousand.

The tax proof breaks down as follows:

Consolidated result (IFRS) 31/12/2022	
Net income before tax	(18,023)
Tax rate	10%
Theoretical tax	1,802
Permanent differences	1,240
Swiss tax rate	19
Other tax or tax credit	(1)
Deferred tax on recognized deficit	(0)
Deferred tax on non-recognized deficit	(2,815)
Other	(19)
Income tax	263

Income tax accounted	(263)
Net effective tax rate	*1.46%*

NOTE 11: COMMITMENTS

11.1. Commitments received under licensing and distribution contracts where applicable

Under licensing and distribution agreements, Boehringer Ingelheim, Servier, Rafa, CKD and Veloxis agreed to pay the Company:

- One-off payments when certain development milestones and revenue are reached;
- Royalties on product sales.

11.2. Commitments in view of sublicensing contracts with Selexis

Under commercial licensing agreements with Selexis, OSE Immunotherapeutics agreed to pay Selexis:

- Fixed payments based on the completion of certain milestones, as compensation for the license granted by Selexis;
- Royalties or milestones (optional depending on the level of sales) when products are marketed.

11.3. Commitments in view of sublicensing contracts with INSERM

Two operating agreements were signed with the Nantes Institute of Health and Medical Research (INSERM):

- In October 2011 for the MD707 project, including filing a co-ownership patent; and
- In March 2013 for the FR104 project, including filing a co-ownership patent.

These agreements grant worldwide operating rights on the patent licenses for each of the projects.

For FR104, OSE Immunotherapeutics has signed a sublicensing agreement with Veloxis, which provides for the payment of royalties calculated on the sublicence revenues.

Following the receipt of the up-front, the company will pay royalties amounting to €1.68 million.

11.4. Other off-balance sheet commitments

As part of the initial transaction for the acquisition of Memopi® (including Tedopi®) assets from the pharmaceutical company Takeda, the Company agreed to pay an earn-out when its product was registered, then no more than single-digit royalties on future sales.

The following commitments are transferred to the Company by way of merger-absorption.

Collateral pledged

Interest-bearing bank account pledged to Crédit Mutuel as collateral, amounting to €10 thousand.

Interest-bearing bank account pledged to CIC as collateral, amounting to €146 thousand.

Interest-bearing bank account pledged to CIC as collateral, amounting to €161 thousand.

Guarantees given

€18 thousand lease payment guarantee to CIC.

Guarantees received

The Company received a guarantee from Bpifrance covering 70% of the original amount of its loans from BNP, Crédit Mutuel and CIC, for €375 thousand each.

The Company does not have any other off-balance sheet commitments.

The outstanding capital as of December 31, 2022, amounted to €5,999 thousand.

NOTE 12: EARNINGS PER SHARE

Earnings per share are calculated by dividing consolidated net income by the weighted average number of shares outstanding in the fiscal year.

Result per share	**12/31/2022**	**12/31/2021**
Net Result in €K	**(**17,760)	**(16,850)**
Weighted average number of shares outstanding	18,527,401	18,154,978
Basic earnings per share (€/share)	**(0.96)**	**(0.93)**
Diluted earnings	**12/31/2022**	**12/31/2021**
Net Result in €K	**(17,760)**	**(16,850)**
Weighted average number of shares outstanding	18,527,401	18,154,978
Adjustment for dilutive effect of share subscription warrants, founders' share warrants and free share allocation	1,241,982	1,241,982
Diluted earnings per share (€/share)	**(0.96)**	**(0.93)**

The allocations of subscription share warrants, founders' share warrants and free shares have no dilutive effect on earnings per share.

NOTE 13: FINANCIAL RISK MANAGEMENT

The Group's main financial instruments are in cash. These instruments are managed for the purpose of funding the Company's activities. The Group's policy is not to subscribe for financial instruments for speculative purposes. The Group does not use any financial derivatives.

The main risks to which the Company is exposed are liquidity risk, foreign exchange risk and interest rate and credit risk.

13.1. Liquidity risk

The Company carried out a specific review of its liquidity risk; it considered that its available cash at the date of the Universal Registration Document as well as future cash flows will enable it to finance its clinical trials.

13.2. Foreign exchange risk

The Company's exposure to foreign exchange risk is solely due to trading relations with customers and suppliers outside the euro area (currencies in USD, GBP).

At this stage of its development, the Company has not made any hedging arrangements to protect its business against foreign exchange rate fluctuations. The Company cannot, however, discount the fact that a significant increase in its business would increase its exposure to foreign exchange risk.

The Company then envisages implementing a suitable policy to hedge such risks.

13.3. Credit risk

Credit risk is from cash and deposits with banks and financial institutions, as well as exposures to client credit, particularly outstanding receivables and agreed transactions.

Credit risk associated with cash and current financial instruments was immaterial considering the quality of the co-contracting financial institutions.

13.4. Interest rate risk

Not applicable

NOTE 14: RELATED PARTIES

14.1. Compensation of management and members of the Board of Directors

No post-employment benefits were granted to members of the Board of Directors.

Compensation paid to management and members of the Board of Directors breaks down as follows:

IN €K	12/31/2022	12/31/2021
Salaries and other short-term benefits *	1,712	1,354
Directors' fees	350	231

Share-based payments **	1,329	1,200
Fees	12	16
Total	**3,403**	**2,799**

** Excluding social charges*
*** Relating to the allocation of free shares and share subscription and founders' share warrants*

Methods used to measure the benefit of share-based payments are shown in Note 4.3.

NOTE 15: EVENTS AFTER THE REPORTING PERIOD

15.1 Financing

OSE Immunotherapeutics has secured several financing lines.

On April 27, 2023, the Company has signed an equity financing line with Vester Finance for a maximum volume of up to 15% of its capital. This financing line would materialize through the exercise of 2,800,00 warrants. The exchange ratio is 1 warrant for 1 share with the exercise on Vester Finance's own initiative. However, Vester Finance is obliged to exercise a minimum of 300,000 warrants per quarter with a maximum discount of 6% on the weighted average unit cost of the last two trading days.

Based on the current share price, this would allow to raise a €3.4M amount by December 31, 2023, and an additional €1.7 million amount until April 30, 2024.

The Company has also obtained a support from "La Région Pays de la Loire" through a financing line under a €1.5 million loan with a 2% interest rate, 2 years of differed global capital repayment and 4 annual repayments. This loan is subject to the final validation of the Committee scheduled end of May. The Company's management estimates the finalization of this financing as highly probable.

OSE Immunotherapeutics has also implemented a financing through a banking pool (CIC, Crédit Mutuel, BNP Paribas): a "PGE Resilience" of €1.3 million with an interest rate up to 2% and a repayment *in fine* over 12 months (subject to the completion of "PGE Resilience" formalities related to the impact of the Ukrainian war on the Company's activity); and a €1 million global loan with a 4% interest rate and a repayment over 36 months. The agreement of the banking pool is subject to the fulfillment of several conditions, including the counter guarantee from Bpifrance up to 70% and the loan agreement of "La Région Pays de la Loire" as described above.

15.2 Tedopi®

In February 2023, the Company has provided a regulatory update on Tedopi® with the positive recommendation from the Food & Drug Administration (FDA) on the Type C meeting following the European Medicines Agency (EMA) scientific advice for the confirmatory phase 3 trial in second line treatment**.**

In March 2023, the Company has received a new approval for an early access program for Tedopi® in Spain in lung cancer after failure to immunotherapy. The Spanish Drug Agency (Agencia Espanola de Medicamentos y Productos Sanitarios, AEMPS) has made a new early access program available that will allow access to Tedopi® through a Special Situation Authorization [(1)] in the treatment of advanced or metastatic non-small cell lung cancer (NSCLC) after immune checkpoint inhibitor (ICI) failure. This Special Situation Authorization is based on the positive clinical data from the initial phase 3 trial of Tedopi® (Atalante-1) in third line treatment and the high unmet need for these patients.

[(1)] *The Special Situation Authorization (Real Decreto 1015/2009) is intended to provide early access to medicines for patients with a severe or rare disease with high unmet need and for which no authorized therapeutic alternatives are available.*

15.3 OSE-127

In February 2023, OSE Immunotherapeutics announced the online publication in the peer-reviewed "Journal of Immunology" positive Phase 1 clinical results of OSE-127.

Moreover, the Company provided an update on the product developed in immuno-inflammation in two phase 2 clinical trials in ulcerative colitis (sponsor OSE Immunotherapeutics) and in primary Sjögren syndrome (sponsor Servier).

The Company also presented preclinical efficacy results with OSE-127 in hematology, in acute lymphoblastic leukemia, at the 2023 American Association for Cancer Research (AACR) annual meeting.

15.4 Termination of commercial lease

On January 13, 2023, the Company terminated the commercial lease located 12, rue Ampère – 44240 La Chapelle-sur-Erdre.

18.2 Interim financial information

The reader is referred to the half-year financial report (RFS) including the financial statements as of June 30, 2022, published on September 22, 2022, and incorporated by reference into this Universal Registration Document.

18.3 Auditing of historical annual financial information

18.3.1 Auditing of historical annual financial information

The financial information in this document has been the subject of an independent audit carried out by the statutory auditors, in accordance with Directive 2014/56/EU of the European Parliament and of the Council and Regulation (EU) No 537/2014 of European Parliament and the Council.

18.3.2 Other information audited by statutory auditors

None

18.3.3 Other information non-audited by statutory auditors

None

18.4 Pro forma financial information

None

18.5 Dividend policy

18.5.1 Dividend payment policy

Due to its losses, the Company has never distributed any dividends and does not plan to distribute any dividends over the next three years. For subsequent years, the dividend distribution policy will depend on the results achieved and the assessment of the means necessary to ensure the development of the Company.

18.5.2 Dividends paid in the last three fiscal years

As priority is given to financing the Company's growth and development, and as the Company does not generate any profit, it is reminded that, in accordance with the provisions of article 243 bis of the General Tax Code, no dividend has been distributed since the Company's creation.

18.6 Legal and arbitration proceedings

On the registration date of this Universal Registration Document, there were no governmental, legal or arbitration proceedings, including those of which the Company is aware, which are pending or threatened, that may have, or have had in the last 12 months, materially impacted the Company's financial position, business or results and/or its subsidiaries.

18.7 Significant change in financial position

There has been no material change in the Group's financial position since the publication of the audited financial statements for the fiscal year ended on December 31, 2022.

19 Additional information

19.1 Share capital

19.1.1 Issued capital

As of the date of this Universal Registration Document, the share capital stood at €3,780,220.20.

It was divided into 18,901,101 shares with a nominal value of €0.20 each.

As of January 1, 2022, there were 18,527,401 Company shares outstanding.

Please also refer to Chapter 18 of this Universal Registration Document.

19.1.2 Non-equity shares

There were no non-equity shares.

Please refer to Section 15.2.

19.1.3 Treasury shares

On December 31, 2022, the Company held 70,095 OSE Immunotherapeutics shares, acquired for a total of €468 thousand. Sales of treasury shares generated a net gain on disposal of €112 thousand in 2022.

19.1.4 Potential capital

As of the date of this Universal Registration Document, the Company had:

- Issued and allocated 42,850 **2018 share subscription warrants** to Gérard Tobelem (to replace the 25,000 2016 share subscription warrants) – if all these share subscription warrants were exercised, this would give entitlement to **42,850** new shares;

- Issued and allocated 25,900 **2018 founders's share warrants** to Dominique Costantini (to replace the 12,162 2016 founders' share warrants) – if all these founders' share warrants were exercised, this would give entitlement to **25,900** new shares;

- Issued and allocated 60,000 **2019 founders' share warrants** to each of the non-salaried, non-executive directors in post at June 26, 2019 – if all these founders' share warrants were exercised, this would give entitlement to **60,000** new shares;

- Issued and allocated 70,000 **2020 founders' share warrants** for each of the non-salaried non-executive directors in office as of June 17, 2020 - 10,000 founders' share warrants were exercised in June 2021. If all of the remaining founders' share warrants were exercised, they would give entitlement to **60,000** new shares;

- Issued and allocated 850,000 **share subscription warrants to the EIB**. If all of the EIB share subscription warrants were exercised, they would give entitlement to **850,000** new shares;

- Issued and allocated 80,000 **2021 founders' share warrants** to each of the non-salaried, non-executive directors in post at June 24, 2021 – if all these founders' share warrants were exercised, this would give entitlement to **80,000** new shares;

- Issued and allocated **80,000 2022 founders' share warrants** to each of the non-salaried, non-executive directors in post at June 23, 2022 – if all these founders' share warrants were exercised, this would give entitlement to 80,000 new shares;

- Issued and allocated 550,000 **share subscription warrants** to the EIB. If all of the EIB share subscription warrants were exercised, they would give entitlement to **550,000** new shares.

Details of the various dilutive instruments outstanding are given in paragraph 15.2.1.1 of this Universal Registration Document.

	Number of shares created	**Percentage interest**	**Dilution**
Existing securities	**18,901,101**		-
If only the 2018 share subscription warrants are exercised	42,850	1.00%	0.23%
If only the 2018 founders' share warrants are exercised	25,900	1.00%	0.14%
If only the 2019 founders' share warrants are exercised	60,000	1.00%	0.32%
If only the 2020 founders' share warrants are exercised	60,000	1.00%	0.32%
If only the 2021 founders' share warrants are exercised	80,000	1.00%	0.42%
If only EIB share subscription warrants are exercised (T1)	850,000	0.96%	4.30%
If only EIB 2022 founders' share warrants are exercised	80,000	1,00%	0.42%
If only EIB share subscription warrants are exercised (T2)	**550,000**	0.97%	2.83%
If all dilutive instruments are exercised	**20,649,851**	0.92%	8.97%

On the date of this Universal Registration Document, the total number of shares likely to be created by the exercise, and as the case may be, the vesting of all instruments allocated and outstanding giving access to the Company's equity, stood at 1,748,750 new shares, thus generating a dilution of 8.97% based on existing share capital at date.

In addition, the Company could, in the future, allocate or issue new instruments giving access to equity.

The Company was also authorized by the General Shareholders' Meeting on June 23, 2022, to carry out capital increases by private placement of up to a maximum of 20% of the capital. In this respect, it is recalled that the Company carried out (i) on

November 18, 2020 a capital increase with cancellation of preferential subscription rights through a private placement with 25 French and international qualified investors, and (ii) on February 15, 2021 a financing of €25 million with the EIB to which 850,000 share subscription warrants are attached (under the first tranche drawn on July 8, 2021) and 550,000 share subscription warrants (upon drawing of the second tranche on December 16, 2022).

The exercise of instruments giving access to outstanding capital, any new allocation or issue of such instruments, or any capital increase by private investment, in particular, by the Board of Directors using the authorizations referred to below, would result in a significant dilution for shareholders.

The following table shows the various and still valid financial delegations granted to the Company's Board of Directors in terms of capital increase:

Purpose of the resolution	Resolution	Duration and expiry of the authorization	Methods	Setting the price of the shares issued	Maximum nominal amount in euros	Use
Capital increase, through the issue – with preferential subscription rights – of shares and/or transferable securities giving access to the Company's equity and/or the issue of transferable securities giving entitlement to the allocation of debt securities	17th	26 months from the General Shareholders' Meeting of June 23, 2022, i.e. until August 23, 2024	Delegation of power to the Board of Directors	The price of one share issued will be at least equal to the nominal value of the share on the issue date	1,500,000*	
Capital increase through the issue – without preferential subscription rights – of shares and/or transferable securities giving access to the Company's equity and/or the issue of transferable securities giving entitlement to the allocation of debt securities through an offering, as referred to in Article L. 411-2 II of the French Financial and Monetary Code, in particular, to qualified investors or a restricted circle of investors	18th	26 months from the General Shareholders' Meeting of June 23, 2022, i.e. until August 23, 2024	Delegation of power to the Board of Directors	The price of one share will be at least equal to the average price weighted by volume based on the last three (3) trading sessions prior to the issue price being set, which may be reduced by a maximum discount of five (5)%	1,500,000*	Board meeting of 11/22/2022 Decision of the CEO of 12/02/2022 (550.000 share warrants EIB)
Capital increase, through the issue of shares and/or debt securities and/or transferable securities giving access to equity or giving entitlement to a debt security, without preferential subscription rights, with no indication of beneficiaries and by public offering	19th	26 months from the General Shareholders' Meeting of June 23, 2022, i.e. until August 23, 2024	Delegation of power to the Board of Directors	The price of one share will be at least equal to the average price weighted by volume based on the last three (3) trading sessions prior to the issue price being set, which may be reduced by a maximum discount of five (5)%	10% of the capital 1,500,000*	
Capital increase through the issue of ordinary shares and/or any other transferable securities giving access to equity and/or giving entitlement to the allocation of debt securities – without preferential subscription rights – to	20th	18 months from the General Shareholders' Meeting of June 23, 2022, i.e. until December 23, 2023	Delegation of power to the Board of Directors	The ordinary share issue price will be at least equal to the weighted average price based on the last three trading sessions prior to the issue price being set, which may be reduced by a maximum discount of 20% or increased by a premium at the full discretion of the Board of	1,500,000*	

categories of persons with specific characteristics				Directors depending on the category of person		
Issuance of financial instruments comprising and/or giving entitlement to (upon exercise of subscription warrants) debt securities giving access to the Company's capital, to which equity warrants are attached – without preferential subscription rights – to a single category of person in accordance with Article L. 225-138 of the French Commercial Code	21st	18 months from the General Shareholders' Meeting of June 23, 2022, i.e. until December 23, 2023	Delegation of power to the Board of Directors	The issue price of financial instruments comprising debt securities giving access to Company's capital, to which share subscription warrants are attached, will be determined on the basis of their nominal value, which may be reduced by a discount of no more than 10%. The issue price of the ordinary shares, resulting from the exercise of rights attached to these debt securities or share subscription warrants, will be at least equal to the lowest daily price, weighted by volume, based on the last ten trading sessions prior to the issue price being set, which may be reduced by a discount of no more than 10%	1,500,000*	
Increase in the number of securities to be issued in the event of a capital increase, with or without preferential subscription rights for shareholders, in the event of over-subscription, of up to 15% of the initial issue	23rd	26 months from the General Shareholders' Meeting of June 23, 2022, i.e. until August 23, 2024	Delegation of power to the Board of Directors	Same price as that used for the initial issue and within thirty days of closure of the subscription period	*	
Capital increase through the incorporation of premiums, reserves, profits or other items	24th	26 months from the General Shareholders' Meeting of June 23, 2022, i.e. until August 23, 2024	Delegation of power to the Board of Directors	N/A	1,500,000	
Issuance of ordinary shares and/or transferable securities giving access to Company's capital, as payment in kind comprising equity securities or transferable securities giving access to capital	25th	26 months from the General Shareholders' Meeting of June 23, 2022, i.e. until August 23, 2024	Delegation of power to the Board of Directors	None	*	
Issuance of ordinary shares and/or transferable securities giving access to Company's capital, in the event of a public exchange offer	28th	14 months from the General Shareholders' Meeting of June 23, 2022, i.e. until August 23, 2023	Delegation of power to the Board of Directors	None	1,500,000*	
Allocation of free performance shares to be issued to the Group's salaried members of staff and corporate officers, or some of them, without preferential subscription rights	31ST	38 months from the General Shareholders' Meeting of June 23, 2022, i.e. until	Delegation of power to the Board of Directors	N/A		

		September 23, 2025			Overall cap of 500,000 securities	
Allocation of existing or future free shares to the Group's salaried members of staff and corporate officers, or to some of them	32nd	38 months from the General Shareholders' Meeting of June 23, 2022, i.e. until September 23, 2025	Delegation of power to the Board of Directors	N/A		
Issuance of founders' share warrants under the terms provided for in Article 163 bis G of the French General Tax Code without preferential subscription rights for shareholders, to a single category of person	33rd	18 months from the General Shareholders' Meeting of June 23, 2022, i.e. until December 23, 2023	Delegation of power to the Board of Directors	The price of a share will be at least equal to the average closing price based on the last twenty (20) trading sessions prior to the allocation date without, if the capital increase was carried out through the issue of securities giving entitlement to equivalent rights within the last six months prior to allocation, the price being lower than the issue price of said securities		Board of Directors meeting on 06/23/2022 (80,00 founders' share warrants Directors) CA du 23.06.2022 (80.000 BSPCE administrateurs)
Issuance of share subscription warrants to a category of person**	34TH	18 months from the General Shareholders' Meeting of June 23, 2022, i.e. until December 23, 2023	Delegation of power to the Board of Directors	The issue price of a share subscription warrant will be set by the Board of Directors on the basis of a valuation report prepared by an independent expert in accordance with the requirements of Article 262-1 of the AMF general regulation The subscription price of shares issued as a result of share subscription warrants being exercised will be no less than the average closing price based on the last twenty (20) trading sessions prior to the date on which the share subscription warrants were allocated		
Allocation of existing or future free shares to the Group's salaried members of staff and corporate officers, or to some of them	26th	38 months from the General Shareholders' Meeting of June 23, 2022, i.e. until December 23, 2023	Delegation of power to the Board of Directors	N/A	500,000 shares	

* The overall maximum nominal amount of capital increases that may be carried out under these resolutions is capped at €1,500,000.

** The right to subscribe to the share subscription warrants was allocated to the category of person defined as follows: members of the Board of Directors who are not salaried employees or executive corporate officers subject to the tax regime for employees of the Company; the Company's external consultants, i.e. natural persons or legal entities outside the

Company, who, through their expertise, contribute to the Company's development in particularly technical and specialized areas of scientific, medical, or operational expertise.

19.1.5 Information on requirements governing any acquisition right and/or any obligation attached to authorized, but not issued, capital or on any Company aiming to increase the capital

According to the share warrant subscription contract, the EIB has an anti-dilution clause allowing it to benefit from additional share subscription warrants, in case of capital increase of the Company at a price of less than 20 euros per share, after application of a deductible on the first 1,500,000 shares to be issued. In such a case, the Company should allocate to the EIB additional share warrant subscriptions allowing it to remain at a potential level of capital of 4.44% (corresponding to its percentage of theoretical holding post-attribution of the 850,000 share warrant subscriptions and exercise of the said share warrants subscribed in the first tranche of financing) and 2.97% (corresponding to his percentage of theoretical holding post-attribution of the 550,000 share warrant subscriptions and exercise of the said share warrant subscriptions subscribed within the framework of the second tranche of financing).

In such a case, the Company should allocate to the EIB additional share warrant subscriptions allowing it to maintain a potential level of capital of 4.44% (corresponding to its percentage of theoretical holding post-attribution of the 850,000 share warrant subscriptions and exercise of the said share warrant subscriptions subscribed within the framework of the first tranche of financing) and 2.97% (corresponding to its percentage of theoretical holding post-attribution of the 550,000 share warrant subscriptions and exercise of the said share warrant subscriptions subscribed in the framework of the second tranche of funding).

On 9 July 2026, the EIB will have the option of asking the Company to buy back its share warrant subscriptions at market value (less the exercise price of the share warrant subscriptions) with a ceiling of €15 million, provided that the Company maintains a cash level of at least €10 million euros. Failing this, the EIB's put option will be exercised on a number of share warrant subscriptions allowing the Company to keep cash of €10 million. This put option also applies in the event of a change of control, understood as the holding of more than 33% of the capital or the takeover by a third party (other than the current key managers). The Company may replace an existing shareholder or a third party to redeem these share warrant subscriptions at market value. The Company has a purchase option allowing it to buy back the share warrant subscriptions from the EIB at market value (less the exercise price of the share warrant subscriptions) in the event of a public offer by a third party resulting in an exit of the managing shareholders for a period of one month following said release. The Company also has a right of first refusal allowing it to buy back the share warrant subscriptions from the EIB if the latter wishes to sell them to a third party.

On December 16, 2027, the EIB will have the option to ask the Company to buy back its share warrant subscriptions at market value (less the exercise price of the share warrant subscriptions) with a ceiling of €15 million, provided that the Company maintains a cash level of at least €10 million. Failing this, the EIB's put option will be exercised on a number of share warrant subscriptions allowing the Company to keep cash of €10 million. This put option also applies in the event of a change of control, understood as the holding of more than 33% of the capital or the takeover by a third party (other than the current key managers). The Company may replace an existing shareholder or a third party to buy back these share warrant subscriptions at market value. The Company has a purchase option allowing it to buy back the share warrant subscriptions from the EIB at market value (less the exercise price of the share warrant subscriptions) in the event of a public offer by a third party leading to an exit of the managing shareholders. , for a period of one month following said release. The Company also has a right of first refusal allowing it to buy back the share warrant subscriptions from the EIB if the latter wishes to sell them to a third party.

19.1.6 Information on the share capital of any member of the Group that is subject to an option or conditional or unconditional agreement to place it under option

None

19.1.7 Table of the history of the Company's share capital

Dates	Nature of the transaction	Nominal (in €)	Additional paid-in capital (in €)	Price per share (in €)	Adjusted price per share	Number of shares created/canceled	Total number of shares	Capital after the transaction (in €)
	Creation							
4/27/2012	10 for 1 split	1	0	1		1,000	1,000	1,000
4/27/2012	Increase	1		1		25,500	26,500	26,500
4/27/2012	Increase	1	0	1		500,000	526,000	526,000
4/10/2014	5 for 1 split	0.20	0	0.20			2,632,500	526,500
4/10/2014	Increase	0.20	9.80	10		5,000,000	7,632,500	1,526,500
6/30/2014	Increase	0.20	7.80	8		355,947	7,988,447	1,597,689.40
7/29/2014	Increase	0.20	7.80	8		37,500	8,025,947	1,605,189.40
3/30/2015	Increase	0.20	10.60	10.80		1,955,000	9,980,947	1,996,189.40
6/24/2015	Increase	0.20	7.80	8		31,250	10,012,197	2,002,439.40
9/9/2015	Increase	0.20	7.80	8		36,744	10,048,941	2,009,788.20
5/31/2016	Increase	0.20	-	-	-	4,107,187	14,156,128	2,831,225.60
5/31/2016	Increase	0.20	7.80	8		88,256	14,244,384	2,848,876.80
6/17/2016	Increase	0.20	5.60	5.80		6,369	14,250,753	2,850,150.60
12/6/2016	Increase	0.20	5.60	5.80		39,217	14,289,970	2,857,994
3/28/2017	Increase	0.20	-	-		85,000	14,374,970	2,874,994
12/13/2017	Increase	0.20	-	-		113,851	14,488,821	2,897,764.20
6/13/2018	Increase	0.20	-	-		173,040	14,661,861	2,932,372.20
7/18/2018	Increase	0.20	-	-		40,151	14,702,012	2,940,402.40
12/5/2018	Increase	0.20	0.80	1		115,000	14,817,012	2,963,402.40
6/26/2019	Increase	0.20				150.000	14,967,012	2,993,402.40
12/10/2019	Increase	0.20				38,712	15,005,724	3,001,144.80
3/26/2020	Increase	0.20	-	-		141,800	15,147,524	3,029,504.80
6/27/2020	Increase	0.20	-	-		150.000	15,297,524	3,059,504.80
6/27/2020	Increase	0.20	-	-		145,300	15,442,824	3,088,564.80
11/17/2020	Increase	0.20	7.20	7.40		2,517,589	17,960,413	3,592,082.60
12/18/2020	Increase	0.20	-	-		22,625	17,983,038	3,596,607.60
6/17/2021	Increase	0.20	-	-		100,000		3,616,607.60
6/17/2021	Increase	0.20	-	-		150.000		3,646,607.60
6/17/2021	Increase	0.20	4.45	4.65		42,000		3,655,007.60
6/17/2021	Increase	0.20	-	-		10,000		3,657,007.60
12/18/2021	Increase	0.20	-	-		231,000		3,703,207.60
12/18/2021	Increase	0.20	-	-		11,363		3,705,480.20
03/28/2023	Increase	0.20	-	-		373,700		3,780,220.20

19.2 Company's constitution and bylaws as of the date of this Universal Registration Document

19.2.1 Company's purpose (Article 2)

The Company is registered with the Nantes Trade and Companies Register under number 479 457 715.

The Company's purpose, in France and abroad:

- The design, research and development of healthcare products from creation to obtaining marketing authorization, and all related operations including marketing;
- The acquisition, filing, obtaining, sale or licensing of all patents, brands, licenses and use processes;
- The acquisition of interests in any companies or undertakings already established or to be established, in France or abroad, whether or not they have a similar purpose to that of the Company;
- The provision of services, consultancy in research and development, marketing or commercial consultancy, consultancy on market access (pricing and reimbursement), structural audits in the field of healthcare, pharmaceuticals, cosmetics, nutrition and veterinary;
- And, more generally, all industrial, commercial, financial, civil, intangible property or real estate transactions directly or indirectly related to one of the above purposes or to any similar or related purpose that could be useful to the achievement and development of the Company's business;
- It may carry out any transactions that are compatible with, related to and contribute to achieving this purpose.

19.2.2 Rights attached to shares (Articles 11 to 18)

Article 11 - Rights and obligations attached to shares

I - Common rights attached to common shares

Each common share confers the right to company profits and assets in proportion to the portion of capital that it represents.

Shareholders are only liable for losses up to their contributions.

The rights and obligations attached to common shares follow said shares, regardless of any change of ownership.

Ownership of common shares automatically entails full compliance with the bylaws and decisions taken by General Shareholders' Meetings.

Each common share confers the right to participate, under the terms set by legislation and the bylaws, in General Shareholders' Meetings and vote on resolutions.

Whenever it is necessary to own more than one share in order to exercise any given right, or even in the event of an exchange, grouping or allocation of shares, or as a result of a capital increase or reduction, a merger or any other transaction, owners

of isolated shares or numbers of shares below the required number may only exercise said right on condition that they personally carry out the grouping and, where appropriate, the purchase or sale of the common shares necessary.

II - Rights attached to A Shares

A Shares and the rights of their owners are governed by the French Commercial Code, in particular, by Articles L. 228-11 et seq.

A Shares are subject to all the provisions of the bylaws and decisions taken by general meetings of owners of common shares.

A Shares do not confer distribution rights in the event of any distribution or, where applicable, allocation of assets, decided on for each common share.

A Shares do not have preferential subscription rights for any capital increase or transaction with entitlement to common shares; on the other hand, the conversion ratio will be adjusted to preserve the rights of holders of A Shares, in accordance with legal and regulatory requirements, as shown in Article 12 of these bylaws. With regards to ownership of Company assets, A Shares confer the right to liquidating dividends in proportion to the amount of capital that they represent.

A Shares do not confer voting rights at ordinary and extraordinary meetings of common shareholders, given that they have voting rights at special meetings of A Shareholders. Holders of A Shares shall meet in a special meeting for any proposed modification of the rights attached to the A shares. In addition, in accordance with Article L. 228-17 of the French Commercial Code, any plans for the merger or spin-off of the Company under which A Shares may be exchanged for shares conferring equivalent special rights, will be subject to the approval of any related special meeting.

Decisions taken by special meetings are only valid if the shareholders present or represented by proxy hold, upon first convocation, at least one third, and on second convocation, one fifth, of the preference shares with voting rights. In the event of modification or depreciation of capital, the rights of A Shareholders are adjusted to preserve their rights in accordance with Article L. 228-99 of the French Commercial Code. Given that the other rights attached to A Shares are temporary, these rights are specified in Article 12 of these bylaws.

Article 12 - A Shares

Subject to fulfilling the conditions set out below, A Shares, on their conversion date, will automatically be converted by the Company into common shares.

The Company may inform holders of A Shares that the shares are being converted, by whatever means, before the effective conversion date.

Two years after the A Shares are allocated by the Board of Directors, they will be converted into common shares using a conversion ratio which is dependent on at least one criterion based on changes in the market price of the common share compared with an initial threshold which cannot be lower than the market price of the common share as recognized on the date on which the A Shares were allocated and one criterion relating to the Group's performance.

Subject to adjustment in accordance with legal and regulatory requirements, the conversion ratio will be 100 common shares per A Share where the target objective is met in full, for the criterion based on changes in the market price, with a proportional and linear reduction in the event of failure to meet the criterion in full and, for the performance-based criterion, a reduction in line with the degree of fulfillment of the criterion if it has not been met in full.

Where the total number of common shares due to be received by the holder by applying the conversion ratio to the number of A Shares held is not a whole number, the number of shares received by said holder will be rounded down to the next whole number.

Notwithstanding the above, the conversion may take place prior to the two-year deadline from the date of allocation of the A Shares by the Board of Directors, if the beneficiary becomes disabled (category two or three disability provided for in Article L. 341- 4 of the French Social Security Code), at the beneficiary's request, at any time after said disability is recognized.

The Board of Directors, or by delegation of authority under the terms set out by legal requirements, the Chairman of the Board of Directors, shall recognize the conversion of A Shares into common shares where the conversion is carried out under the conditions set out above.

At intervals which it shall itself determine, the Board of Directors shall acknowledge, where applicable, the number of common shares resulting from the conversion of A Shares in the fiscal year in question and shall make the necessary changes to the bylaws, in particular, with regard to the breakdown of shares by category. This option may be delegated to the Chief Executive Officer in accordance with legal requirements.

Common shares arising from the conversion of A Shares will be identical in all respects to outstanding common shares.

Article 13 - Type of shares

Shares are either registered or bearer shares, at the shareholder's choice. They can only be bearer shares once they are fully paid-up.

Fully paid-up A Shares are registered shares.

The Company is authorized to identify the holders of bearer securities by simple request to the organization in charge of clearing bearer securities, the name or corporate name, nationality, year of birth or year of incorporation, address of the holders of securities as well as the quantity of securities held by each of them.

Article 14 - Payment for shares

In the event of a capital increase, at least one quarter of the nominal value of shares issued for cash and, where necessary, the full issue premium, is paid up at the time of subscription.

The balance may be paid in one or more installations at the Board of Director’s request, within five years of the date on which the transaction becomes final in the case of a capital increase.

Shareholders are notified of calls for funds by individual recorded delivery letters, at least fifteen days prior to the date set for each payment.

Shareholders who fail to make the payments owing for the shares by the due date shall, automatically, and without any formal notification, be liable to pay the Company late payment interest calculated on a daily basis, from the due date, at the legal rate applicable to commercial transactions, plus three points.

In order to secure the payment of these sums, the Company is entitled to apply the sanctions provided for by Articles L. 228-27 et seq. of the French Commercial Code.

Article 15 - Transfer of shares

Shares are freely transferable as soon as they are issued, in accordance with the procedures laid down by law.

They are registered in a share account and transferred between accounts on the basis of instructions signed by the transferor or their qualified representative.

Article 16 - Disclosure thresholds

Pursuant to Article L. 233-7 of the French Commercial Code, any individual or legal entity, acting alone or in concert, within the meaning of Article L. 233-10 of the French Commercial Code, who comes to hold or ceases to hold a number of shares representing a fraction equal to 5%, 10%, 15%, 20%, 25%, 30%, 33.33%, 50%, 66.66%, 90% or 95% of the share capital or voting rights, is required to disclose to the Company no later than the close of trading on the fourth trading day following the date on which the aforementioned shareholding threshold is crossed, the number of shares and voting rights held. The individual required to disclose the above information shall specify the number of securities held giving future access to the share capital and related voting rights.

A shareholder who has not properly made the required disclosures as referred to above shall be stripped of the voting rights attached to the shares in the conditions pursuant to the French Commercial Code.

Article 17 - Indivisibility of shares - Bare ownership - Usufruct

(i) The shares are indivisible in respect of the Company.

Joint owners of undivided shares are represented at General Shareholders' Meetings by one owner or by a single proxy. In the event of a disagreement, the proxy is appointed by the court at the request of the joint owner acting first.

(ii) The beneficial owner has the voting right at Ordinary General Shareholders 'Meetings and the bare owner at Extraordinary General Shareholders' Meetings. Shareholders may, however, agree to any distribution of voting rights at General Shareholders' Meetings. The Company is notified of the agreement by registered letter and is obliged to apply this agreement for any meeting that may be held after one month has lapsed since the letter was sent.

Article 18 - Double voting rights

Each common share and each A Share confers entitlement to one vote. Double voting rights of those conferred by other common shares in terms of the portion of capital that they represent are given to any fully paid-up common shares that can be proven to have been registered for at least two years in the name of the same shareholder.

Should obtaining double voting rights result in the shareholding threshold being crossed, under the requirements of Article 16 of the bylaws, the shareholder in receipt of the double voting rights would be obliged to comply with the provisions of said article.

This double voting right is also conferred on ordinary registered shares, as soon as they are issued, in the event of a capital increase through the incorporation of reserves, profits or issue premiums, allocated free of charge to shareholders who hold old common shares which confer this right.

Common shares transferred as a result of inheritance, the liquidation of community property between spouses or *inter vivos* gifts to a spouse or close relative do not result in the loss of the right acquired and do not interrupt the qualifying periods provided for above.

It is likewise, in the event of transfer of common shares following the merger or spin-off of a corporate shareholder.

In addition, the merger or spin-off of the Company does not affect the double voting rights that may be exercised within one or more beneficiary companies if permitted by their bylaws.

19.2.1 Company bylaws, charters or regulations that may have the effect of delaying, postponing or preventing a change of control.

N/A

20 Important contracts

In the two years prior to the publication of this Universal Registration Document, the Company did not enter into any material contract (it being recalled that the Boehringer Ingelheim contract to develop BI 765063 (OSE-172) was signed on April 4, 2018) but:

- The worldwide licensing agreement with Veloxis Pharmaceuticals Inc., for the development, manufacture and marketing of FR104, a CD28 antagonist, in the organ transplantation market. At the same time, OSE Immunotherapeutics retains all rights to develop FR104 in autoimmune diseases. Through this agreement, Veloxis plans to develop FR104 to provide a new therapeutic option for the prophylaxis of organ rejection in solid organ transplant patients.

  Under this agreement, the Company will receive up to €315 million in potential milestone payments from Veloxis, including a €7 million due on signature, development, registration and marketing milestones, and tiered royalties on potential future sales. Veloxis will assume all production, development and marketing costs of FR104 in transplantation indications.

- The financing agreement for a total amount of €25 million with the EIB.

As of the date of this Universal Registration Document, the Group as a whole is bound by the following contracts, conferring a material obligation or right for the entire group:

- OSE Immunotherapeutics retained the confidential contractual obligations entered into by its subsidiary, OPI, with Takeda, with a milestone payment upon registration of Tedopi® in the United States and in Europe, then additional payments (fees or royalties) corresponding to a percentage of sales of Tedopi® by OSE Pharma, this being no greater than a single-digit percentage.

- OSE Immunotherapeutics signed a licensing agreement with OPI in Switzerland in July 2012 for Tedopi® (OSE-2101). This first contract gives OSE Pharma the commercial rights to market the product in Europe as well as responsibility for international development in Europe and the United States. OSE Immunotherapeutics will set up an international development team and seek to obtain the green light from the two Registration Agencies (EMA and FDA) in both Europe and the United States.

21 Publicly available documents

So long as this Universal Registration Document is valid, the following documents (or copies of them) may be physically viewed at the Company's registered office at 22, Boulevard Benoni Goullin - 44200 Nantes, France:

- The Company's instrument of incorporation and bylaws;
- The 2020 and 2021 Registration Documents;
- any reports, letters and other documents, historical financial information, assessments and statements produced by an expert at the Company's request, some of which are included or referred to in this Universal Registration Document;
- The Company's historical financial information for each of the three fiscal years preceding the publication of this Universal Registration Document.

The regulated information within the meaning of the General Regulation of the AMF is available on the Company's website (www.ose-immuno.com) and the websites of the AMF (www.amf-france.org) and Euronext (www.euronext.com).

22 Glossary

Adjunctive: an antigen mixed for example with a mineral oil (adjunctive), generates an inflammatory reaction at the point of injection and an activation of innate immunity (cells presenting antigens) leading to recognition of those antigens, then co-stimulation signals on the surface of antigen-presenting cells that will be necessary for the activation of T lymphocytes.

Antibodies: these are proteins produced by cells, plasmocytes, resulting from the activation of B lymphocytes (B lymphocyte cells at the origin of antibodies). Antibodies are specifically directed against the tumor antigens. They bind onto these latter to form an immune complex. The existence of this complex triggers several defense mechanisms including the recruitment of innate immunocompetent cells such as macrophages or NK cells.

Checkpoint Inhibitor: specific antibodies of certain cellular signaling channels that intervene in immuno-oncology treatments.

Cytokines: molecules that play a messenger role allowing communication between cells.

These are the regulating principles of the immune response.

Dendritic cells: these are "sentinel" cells present in tissues and migrating in lymphoid tissues. They have the capacity to present tumor antigens to T lymphocytes to activate them. They also secrete substances called cytokines, messengers that stimulate the overall immune response.

Epitope: this fragment of tumor antigen called "antigenic determinant" is the often very small molecular structure that binds to cell receptors and triggers an immune response.

HLA: the human Major Histocompatibility Complex (MHC) is also called HLA (Human Leukocyte Antigens). HLA plays a role in the acceptance or rejection of a transplant. The presentation of the antigen (in reality a small peptide called epitope or antigenic determinant) is provided by the HLA system. Two classes exist: class I and class II.

HLA-A2 (also called HLA-A * 02 or A * 02): HLA serotype (belonging to the class I MHC, is measured by a positive or negative serology test). This receptor is involved in immunosurveillance and in T cell response. It is expressed in approximately 45% of the general population.

Major Histocompatibility Complex (MHC): MHC molecules are on the surface of antigen-presenting cells and ensure the antigen is presented to the T lymphocytes in order to activate them. There are class I and class II MHC molecules. In humans, we speak of HLA antigens. This group of genes is expressed on the surface of cells and has been analyzed internationally for organ transplants. The class I genes are the A, B, C genes; the class II genes are the DP, DQ and DR genes.

MHC I molecules are present on all nucleated cells of the organism and present the antigen to cytotoxic T lymphocytes.

The MHC II molecules are found on the surface of antigen-presenting cells (APC) as dendritic cells, activated B lymphocytes, macrophages, in order to educate the lymphocytes in the non-recognition of self-peptides and the recognition of "foreign" peptides of the non-self.

These two systems take part in immune responses and are the key to cellular immunity and communication between cells providing for the protection of the organism.

Monoclonal antibodies: antibodies that possess the same chemical structure and therefore a unique specificity for an antigen. Produced by recombinant protein technology in bioreactors, they are used as therapeutic agents in many areas of medicine, in particular in cancerology, immunology and inflammation.

Myeloid cells: these are white blood cells that play a major role in the initiation and control of inflammation. Suppressive myeloid cells accumulate in some forms of cancer, where they prevent the T cells from destroying the tumor.

NK Lymphocytes: these innate immunity cells can recognize and kill tumor cells without having been activated. Their mechanism of recognition is non-specific for tumor antigens. In the absence of unique receptors for a particular antigenic target, the NK cells cannot distinguish the self from the non-self.

Regulatory T Lymphocytes (Treg): these cells control the occurrence and the intensity of immune responses made by the T lymphocytes. They are naturally present and their absence leads to autoimmune diseases. Inversely, their accumulation reduces autoimmunity and prevents the rejection of transplants.

T Lymphocytes: these cells provide the specific cellular response. A distinction is made between T-CD8 lymphocytes, activated in cytotoxic lymphocytes that will directly attack the tumor cells and, on the other hand, T-CD4 cells, helper T cells or auxiliary, that mainly provide the functions of stimulation / regulation of the immune response. Initially naive (that is "non-informed") these cells are educated by the dendritic cells that teach them to specifically recognize tumor antigens.

TCR: this is a specific immunoreceptor; the T lymphocytes express this TCR receptor (T-Cell Receptor) on their surface. It only recognizes the epitopes presented by the major histocompatibility system (or HLA system).

Tumor antigens or tumor-associated antigens: these are macromolecules, proteins and protein fragments specific to the tumor. They betray its presence. When they are recognized by the immune system, they produce a response specifically directed against the tumor cells. Sometimes shared with other healthy tissues, they are not recognized since they are considered as "self-antigens".

Tumor escape: the capacity of tumor cells TO escape the surveillance of the immune system and create metastases in other parts of the body.

LIST OF ABBREVIATIONS

ALK	Anaplastic Lymphoma Kinase: genetic abnormality with abnormal activation of the ALK protein, i.e. 4 to 5% of non-small cell lung cancers for which targeted therapies are available
APC	Antigen-Presenting Cells: dendritic, macrophage cells, etc. presenting antigens
APC	Antigen Presenting Cells: or APC see above.
ASCI	Antigen-Specific Cancer Immunotherapeutic: a vaccine targeting a tumor antigen, an antigenic proteinaceous macromolecule
ASCO	American Society Of Clinical Oncology: annual cancer conference in the United States
BRCA1	Breast Cancer Gene 1: mutations of this gene with an increased risk of cancer
CD4 T	CD4 T Lymphocytes: helper or auxiliary T cells are "amplifying cells" of the immune response. They carry a CD4 marker on their surface.
CD8 T	Cytotoxic T Lymphocytes (CD8 T or killer T cells) destroy the infected or "foreign" cells, and are able to destroy target cells that present specific antigens through the MHC class I. They carry a CD8 marker on their surface.
CEA	Carcino Embryogenic Antigen: tumor antigen very frequently expressed on the surface of tumor cells
CMC	Chemistry Manufacturing Control: part of a drug's pharmaceutical dossier
CMO	Contract Manufacturing Organization: organization for production of industrial batches
CRO	Contract Research Organization: organization subcontracting trials
CTLA-4	Cytotoxic T Lymphocyte-Associated Protein 4: checkpoint blocking T responses
EBV	Epstein Barr Virus: an oncogenic virus at the origin of some cancers
ECOG	Eastern Cooperative Oncology Group Performance Status: index of patient's condition
EGFR	Epidermal Growth Factor Receptor: transfers of tea EGFR gene in some cancers, overexpression of the EGFR protein, therapies targeted on that target, the frequency of EGFR mutations is 5 to 20%
ELISPOT	Enzyme-Linked Immunosorbent Spot assay: measures specific responses of T lymphocytes

EMA	European Medicines Agency: European drug agency
EP-2101	Former code of OSE2101:
ER	Estrogen receptor: a marker in breast cancer influencing the therapeutic options
ErbB	Family of epidermal growth factors EGFR and HER / neu belong to this family of receptors, involved in many cancers.
EU	European Union
FDA	Food And Drug Administration: American drug agency
FIGO	International Federation of Gynecology and Obstetrics
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GLP, GMP, GCP	Good Laboratory Practices, Good Manufacturing Practices, Good Clinical Practices
GMP	Good Manufacturing Practice
HER-2/neu	Human Epidermal Receptor-2 / Neurological: Tumor antigen
HLA	Human Leukocytes Antigens: molecules on the surface of cells that allow identification by the immune system. These proteins are called " Major Histocompatibility Complex " (MHC) molecules.
ICH	International Conference on Harmonization (of Technical Requirements for Registration of Pharmaceuticals for Human Use) International Pharmaceutical Standards
IFN	Interferon: a cytokine produced by the cells of the immune system
IL	Interleukin cytokine produced by cells to communicate between themselves
IND - United States IMPD – Europe	Investigational New Drug Application: complete documentation of a pharmaceutical dossier in the United States Investigational Medicinal Product Dossier: complete documentation of a pharmaceutical dossier in Europe
Ligand	A molecule able to bind itself to a specific protein
MAGE 2/MAGE 3	Melanoma Antigen type 2 / type 3: tumor antigens expressed in many cancers
MHC	Major Histocompatibility Complex
MHC class I	Major Histocompatibility Complex or HLA system: the MHC class I molecules enable presentation of the peptide (or antigenic determinant = epitope) to the CD8 T-lymphocytes - the most important are the HLA-A, HLA-B and HLA-C molecules.
MHC class II	The MHC class II molecules enable the presentation of the antigenic peptide to the CD4 T-lymphocytes. The most important are the HLA-DP, HLA-DQ and HLA-DR molecules.
MUC	Tumor antigen associated with many cancers
NK	Natural Killer: these natural killer cells are immunity cells.
NSCLC	Non-Small Cell Lung Carcinoma: non-small cell lung cancer or non-small cell bronchial carcinoma NSCLC, the most common form of lung cancer
ORR	Overall Response Rate: tumor response rate

OSE-2101	Product code of the multiepitopes targeting 5 tumor antigens - Tedopi® trademark, from the optimized multiepitope technology - Memopi® trademark
p53	A Nuclear Regulatory Protein Oncogene: The gene coding for the p53 protein is disabled in half of human cancers. This protein is a tumor antigen.
PARP	Poly ADP Ribose Polymerase enzyme, targeted cancer therapies targeting that enzyme
PCT	Patent Cooperation Treaty: treaty for cooperation on patents (PCT) at the international level
PD-L1	P-1 Ligand 1: checkpoints blocking T responses
PDCD1	Programmed Cell Death 1: checkpoints blocking T responses
PR	Progesterone Receptors: a breast cancer marker influencing therapeutic options
QP	Qualified Person: person qualified for pharmaceutical responsibility in Europe
RCC	Renal Cell Carcinoma: kidney cancer
RECIST	Response Evaluation Criteria In Solid Tumor: RECIST criteria are used to evaluate and measure the tumor response.
TCR	T-Cell Receptor: the TCR receptor, expressed on the surface of T cells, recognizes a peptide presented in a molecule of the Major Histocompatibility Complex (MHC)
TIL	Tumor Infiltrating Lymphocytes: intra-tumoral lymphocytic infiltrate
TKI	Tyrosine Kinase Inhibitors: therapies targeted on certain mutations or molecular alterations of the cancerous cell (for example, erlotinib and gefitinib)
TNBC	Triple Negative Breast Cancer: triple negative breast cancer, tumor cells negative for three prognostic markers (estrogen receptors (ER), progesterone receptors (PR), overexpression of the HER2 protein)
VEGF	Vascular Endothelial Growth Factor plays a role in tumor growth. Bevacizumab is the first monoclonal antibody directed against the VEGF and marketed for treatment against some cancers in 2004.

Appendix A – Board of Directors' Management Report

OSE IMMUNOTHERAPEUTICS

Limited company (*Société anonyme*) with a Board of Directors

With share capital of €3,780,220.20

Registered office: 22 Boulevard Benoni Goullin 44200 Nantes

479 457 715 Nantes Trade and Companies Register

MANAGEMENT REPORT OF THE BOARD OF DIRECTORS TO THE COMBINED GENERAL SHAREHOLDERS' MEETING OF JUNE 22, 2023

Fiscal year ended December 31, 2022

Dear Shareholders,

In accordance with legal and regulatory provisions, we have convened this Combined General Shareholders' Meeting (Ordinary and Extraordinary), in order to report to you on the Company's position and activity as well as the results achieved during the fiscal year ended December 31, 2022.

The Statutory Auditors will provide you, in their report on the separate financial statements, with all information concerning the regularity and fairness of the financial statements presented to you.

We will give you all additional clarifications and information concerning the material and documentation provided for by the regulations in force and which were made available to you within the legal deadlines.

In accordance with the provisions of Article L. 225-100 of the French Commercial Code, please note that the various information provided in this report constitute our objective and thorough analysis of the business development, results and financial position of the Company for the fiscal year ended on December 31, 2022.

1. ACTIVITY OF THE COMPANY DURING FISCAL YEAR 2022

1.1 Position and development of the Company's business over the fiscal year

1.1.1 *Capital structure at December 31, 2022*

See Section 16.1 of the Universal Registration Document.

1.1.2 *Development of the Company's business*

During 2022, the Company continued to develop.

JANUARY 2022

- Appointment of Dominique Costantini as Interim Chief Executive Officer following the departure of Alexis Peyroles.

Dominique Costantini, current Chairwoman of OSE Immunotherapeutics' Board of Directors, and previously CEO from 2012 to 2018, has been appointed interim Chief Executive Officer, effective immediately.

Alexis Peyroles resigned for health reasons, and he remains committed to OSE's success. He will continue to support the company in a consulting capacity for the upcoming months to ensure a smooth transition.

- Notice of allowance received from the Japanese Patent Office for a new patent covering Tedopi®, a combination of neoepitopes, for use after failure with PD1 or PD-L1 immune checkpoint inhibitor treatment in HLA-A2 positive cancer patients. This patent, which will further strengthen Tedopi®'s global intellectual property portfolio in immuno-oncology, will provide the product with a new protection until 2037.

- Acceptance of the IND obtained by Veloxis Pharmaceuticals, Inc. from the Food & Drug Administration (FDA) for VEL-101/FR104. As part of the global license agreement signed in April 2021, this first step triggers a €5 million from Veloxis Pharmaceuticals, Inc. to OSE Immunotherapeutics.

FEBRUARY 2022

- OSE Immunotherapeutics' shares have been transferred from compartment C to compartment B of Euronext Paris, taking effect from January 31, 2022.

- Veloxis Pharmaceuticals, Inc., the Company's partner in Transplantation, has obtainedFDA Fast-Track Designation for CD28 Antagonist VEL-101/FR104.

- Appointment by cooptation of Alexandre Lebeaut as an independent Director of the Company; he replaces Alexis Peyroles who resigned as Board member.

MARCH 2022

- Early biomarker analyses from the Phase 1 clinical trial with SIRPα inhibitor BI 765063 in patients with advanced solid tumors selected for presentation in an in-person poster session at the American Association Cancer for Research (AACR) annual meeting to be held on April 8 – 13, 2022 in New Orleans, Louisiana.

- Positive Long Term Memory Responses obtained with CoVepiT, its T Lymphocyte Multi-Target Anti-COVID Vaccine:
  - Positive long term immunological results at 6 months in healthy volunteers with strong T cell memory responses against virus proteins.
  - CoVepiT, based on 13 peptides, elicits durable T-cell immunity against a wide range of structural and non-structural viral proteins.
  - The vaccine remains independent of mutations identified in current and emerging variants.

- First notice of allowance received from the United States Patent and Trademark Office (USPTO) for a patent application covering OSE-279, an anti-PD1 monoclonal antibody, and its use in cancer treatment. This patent will strengthen the global intellectual property of OSE-279 and will provide the product a protection until 2039.

- On March 30, 2022, OSE Immunotherapeutics reports its 2021 annual results: major progress on its clinical programs and a solid cash position to support its activities.

APRIL 2022

- The Company is invited to present the latest progress on its bispecific antibody checkpoint inhibitor BiCKI® platform, and in particular on its bifunctional therapy targeting PD1 and the Interleukin-7 (IL-7) cytokine, BiCKI®-IL-7, during a plenary oral presentation in an educational session dedicated to immunocytokines at the American Association Cancer for Research (AACR) annual meeting to be held on April 8 – 13, 2022 in New Orleans, Louisiana.

MAY 2022

- Grant of a new patent from the European Patent Office (EPO) strengthening the protection covering the novel myeloid cell immune checkpoint target, CLEC-1 (a C-type lectin receptor), and its use in cancer treatment. This patent provides a protection until 2037.

- Initiation of the expansion Phase 1 clinical trial of BI 765063 in endometrium and colorectal cancer and payment of a €10 million milestone from Boehringer Ingelheim to OSE Immunotherapeutics.

- Achievement of a new step through the global collaboration and license agreement under which Boehringer Ingelheim obtained from OSE Immunotherapeutics exclusive rights to BI 765063, a first-in-class SIRPα inhibitor on the SIRPα/ CD47 myeloid pathway. Dosing of the first patient in the Phase 1 expansion trial conducted by Boehringer Ingelheim triggered a €10 million payment from Boehringer Ingelheim to OSE Immunotherapeutics.

- OSE Immunotherapeutics has been invited to provide an update on its R&D programs in immuno-oncology at two dedicated international conferences in May and June.

- First participant dosed in a Phase 1 study of VEL-101/FR104 evaluated in renal transplantation, a study sponsored and conducted by OSE Immunotherapeutics' partner, Veloxis Pharmaceuticals, Inc.

JUNE 2022

- OSE Immunotherapeutics and its clinical partners GERCOR, ARCAGY-GINECO and the FoRT Foundation (Fondazione Ricerca Traslazionale), presented four posters featuring neoepitope specific immunotherapy Tedopi® in various cancer indications at the American Society of Clinical Oncology (ASCO) Annual Meeting held June 4 – 7.

- Creation of an Advisory Board (SAB) composed of six leading international experts to guide the Company in its next phases of growth and scientific orientations. The SAB members include Pr. Wolf-Hervé Fridman (Université de Paris), Dr. Sophie Brouard (CRTI, Nantes), Dr. Bernard Malissen (CIML, Marseille), Pr. Miriam Merad (Mount Sinai, New-York), Pr. Charles Serhan (Harvard, Boston) and Dr. Jennifer Wargo (MD Anderson Cancer Center, Houston).

- Collaboration agreement with Microsoft giving OSE Immunotherapeutics the opportunity to further develop its digital tools and infrastructures, particularly in terms of Artificial Intelligence and algorithmic approaches applied to the development of innovative first-in-class immunotherapies.

- The Combined General Shareholders' meeting of June 23, 2022, approved all the resolutions as proposed by OSE Immunotherapeutics' Board of Directors.

JULY 2022

- Appointment of Alexis Vandier as Chief Executive Officer.

SEPTEMBER 2022

- Presentation of two new analyses from the Phase 3 Atalante-1 study of immunotherapy Tedopi®, in patients with advanced non-small cell lung cancer (NSCLC) in secondary resistance after failure of previous checkpoint inhibitor treatments, at the 2022 European Society for Medical Oncology (ESMO) Congress, being held September 9-13, in Paris.

- OSE Immunotherapeutics provides updates on key milestones achieved during H1 2022 and reports its consolidated half-year financial results as of June 30, 2022.

OCTOBER 2022

- Appointment of Nicolas Poirier as new Chief Executive Officer following the decision of the Board of Directors to terminate the mandate of Alexis Vandier.
- Update on Tedopi® with authorizations for compassionate use in non-small cell lung cancer (NSCLC) by Health agencies in Europe. Regulatory meetings planned with the regulatory Agencies to validate the new confirmatory Phase 3 clinical trial in NSCLC.

NOVEMBER 2022

- Servier and OSE Immunotherapeutics announced the completion of patient enrollment in the Phase 2a clinical trial evaluating the efficacy and safety of monoclonal antibody OSE-127/S95011 in primary Sjögren's syndrome (sponsor Servier).

- Presentations of scientific updates in oral and poster presentations selected for international conferences: the Society for Immunotherapy of Cancer (SITC) 37th Annual Meeting in Boston, MA, November 8 – 12 and the Protein & Antibody Engineering Summit (PEGS) Europe 14th Annual Meeting in Barcelona, Spain, November 14 – 16. The communications feature the latest research on pre-IND programs from the pioneering Myeloid and BiCKI® platforms, namely presentations on OSE-230 (first pro-resolutive monoclonal antibody) in chronic inflammation, CLEC-1 (new myeloid immune checkpoint) and BiCKI®-IL-7 (new bifunctional therapy targeting PD1 and IL-7) in immuno-oncology.

- Publication of data in the peer-reviewed journal Science Advances on a first-in-class preclinical program with CLEC-1, its novel myeloid immune checkpoint target for cancer immunotherapy.

DECEMBER 2022

- Presentation of the latest preclinical data on the use of its anti-IL-7 receptor (IL-7R) antagonist OSE-127 for the treatment of B- and T-Cell Acute Lymphoblastic Leukemia (B- and T-ALL) at the American Society of Hematology (ASH) annual meeting (1) on December 11, 2022 (New Orleans, Louisiana). This oral presentation has received the merit-based "Abstract Achievement Award" from the peer-review committee.

- OSE Immunotherapeutics receives a €10 million payment corresponding to the second tranche of the financing granted by the European Investment Bank. This financing aims at further supporting the progress and expansion of OSE Immunotherapeutics' lead clinical development programs in therapeutic areas with high unmet medical needs.

- First patient dosed in the Phase 1/2 clinical trial evaluation OSE-279, a high affinity anti-PD1 blocking monoclonal antibody in patients with advanced solid tumors or lymphomas.

Issue of subscription share warrants (BSA), founders' share warrants (BSPCE) and free shares

See Section 19.1.4 of the Universal Registration Document.

1.2 Progress made and difficulties encountered

PROPRIETARY PRODUCTS IN CLINICAL DEVELOPMENT

- TEDOPI®: PHASE 3 FINAL POSITIVE RESULTS IN NON-SMALL CELL LUNG CANCER (NSCLC) IN SECONDARY RESISTANCE TO A CHECKPOINT INHIBITOR TREATMENT

The international Phase 3 clinical trial of Tedopi®, Atalante-1, was designed to evaluate the benefits of Tedopi®, a T specific immunotherapy in HLA-A2 positive patients in second- or third-line therapy versus second- or third-line chemotherapy (docetaxel or pemetrexed) in invasive stage IIIB or metastatic stage IV non-small cell lung cancer after failure of treatment with checkpoint inhibitors. The main assessment endpoint was overall survival.

Tedopi® has shown a favourable benefit/risk ratio versus the standard treatment (docetaxel or pemetrexed) in HLA-A2 postivie patients with NSCLC in secondary resistance to immune checkpoint inhibitors.

In 2022, based on these Phase 3 positive results, the Company has prepared upcoming discussions with the regulatory agencies on the best development / regulatory strategic options to register Tedopi® in NSCLC in secondary resistance to checkpoint inhibitors.

In parallel, the significant medical need for new therapeutic options in NSCLC patients post-ICI failure associated with promising efficacy, safety and quality of life data resulted in authorizations for compassionate use of Tedopi® from Health Agencies in Europe - in France, Italy and Spain - in third line post-chemotherapy and immunotherapy.

- TEDOPI®, IN PHASE 2 CLINICAL TRIAL IN ADVANCED PANCREATIC CANCER: CONTINUATION OF PATIENT ENROLLMENT UNDER AN AMENDED STUDY PROTOCOL

The Phase 2 clinical trial TEDOPaM is conducted under the sponsorship of the cooperative oncology group GERCOR in HLA-A2 positive patients with advanced or metastatic pancreatic adenocarcinoma.

Due to the COVID-19 pandemic, the screening and enrollment of new patients in TEDOPaM, evaluating Tedopi® in pancreatic cancer in monotherapy and in combination with nivolumab (Opdivo®, BMS) had been temporarily suspended in March 2020. After data analysis on the first 29 patients included in the trial, the Independent Data Monitoring Committee (IDMC) of the trial recommended stopping the assessment the treatment with Opdivo® and proposed to introduce a treatment arm of Tedopi® + chemotherapy. GERCOR modified the protocol accordingly and in the second quarter of 2021, the first patients

have been randomized in two treatment arms : Tedopi® in combination with FOLFIRI chemotherapy versus FOLFIRI. The main endpoint of the trial remains the one-year survival rate.

An interimary analysis performed on the 29 first patients has shown interesting results for Tedopi® in monotherapy versus FOLFIRI. These results were presented by the GERCOR at the ASCO annual meeting in June 2022.

Patient enrollment resumed in 2021 and is continuing since then.

- **TEDOPI® : TWO PHASE 2 CLINICAL TRIALS ONGOING IN COMBINATION WITH A CHECKPOINT INHIBITOR IN NON-SMALL CELL LUNG CANCER AND IN OVARIAN CANCER, IN COLLABORATION WITH COOPERATIVE GROUPS IN ONCOLOGY**

- A Phase 2 clinical trial, sponsored and conducted by FoRT, an Italian foundation in oncology, is ongoing in non-small cell lung cancer. This trial aims at evaluating Tedopi® in combination with a checkpoint inhibitor, Opdivo® (nivolumab) versus Tedopi® combined with a chemotherapy versus a chemotherapy alone in second-line treatment in patients with NSCLC after a first line of chemo-immunotherapy. The first patient was randomized in November 2021 and the recruitment is continuing since then.
- Another Phase 2 clinical trial, 'TEDOVA', sponsored and conducted by ARCAGY-GINECO, has been initiated in the ovarian cancer. This trial aims at evaluating Tedopi® as a maintenance treatment, alone or combined with an anti-PD1 immune checkpoint inhibitor, Keytruda® (pembrolizumab) versus the standard treatment in patients with platinum-sensitive recurrent ovarian cancer and whose disease is controlled after platinum-based chemotherapy. The first patient was randomized in August 2021 and the recruitment is continuing since then.

The design of both studies was presented at the ASCO annual meeting in June 2022.

The Atalante-1 Phase 3 clinical results in lung cancer have boosted the clinical development of Tedopi® with 3 additional Phase 2 ongoing studies.

In January 2022, the Japanese Patent Office has issued the notice of allowance for a new patent covering Tedopi® for use after failure with PD1 or PD-L1 immune checkpoint inhibitor treatment in HLA-A2 positive cancer patients. This patent, which further strengthens Tedopi®'s global intellectual property portfolio in immuno-oncology, will provide the product with a new protection until 2037.

- **OSE-279, AN ANTI-PD1 HUMANIZED MONOCLONAL ANTIBODY, INITIATION OF THE PHASE 1/2 CLINICAL TRIAL**

OSE-279, the key backbone component of bifunctional checkpoint inhibitor BiCKI® platform, is a humanized monoclonal antibody that is targeting PD1. OSE-279 entered Phase 1/2 clinical phase in December 2022 in advanced solid tumors and lymphomas. Thus, the Company has its own proprietary anti-PD1.

This first clinical study will also allow the Company, at a later stage, to explore OSE-279 in combination with other OSE drug candidates or with external assets accessed through potential new partnerships with biotech or pharmaceutical companies.

In 2022, the Company has pursued the product's manufacturing to start the clinical phase at the end of the year. In March 2022, it has received a first notice of allowance for a patent application in the United States covering OSE-279 and its use in cancer treatment.

CLINICAL PRODUCTS DEVELOPED IN PARTNERSHIP

- OSE-127/S95011, CONTINUATION OF THE PHASE 2 CLINICAL TRIAL IN ULCERATIVE COLITIS FOLLOWING THE REVUE OF THE FUTILITY ANALYSIS RESULTS

OSE-127/S95011, an immunomodulatory monoclonal antibody targeting the CD127 receptor, the alpha chain of the Interleukin 7 receptor, is being developed under a two-step licensing option agreement granted to Servier for its development and marketing in autoimmune diseases.

The Phase 2 trial in ulcerative colitis, an autoimmune bowel disease started in December 2020, sponsored by OSE Immunotherapeutics.

An interim futility analysis has been conducted according to the protocol on the first 50 patients (i.e., 33% of the total patient enrollment in the study) having completed the Induction Phase. The primary endpoint of the futility analysis was the efficacy of OSE-127/S95011 versus placebo assessed according to the reduction in the modified Mayo Score (an index used to assess the activity of ulcerative colitis).

In December 2021, based on the efficacy and tolerability results of this analysis, the Independent Data Monitoring Committee (IDMC) of the trial recommended the continuation of the study evaluating OSE-127/S95011, an Il-7 receptor antagonist, in patients with ulcerative colitis.

Moreover OSE-127/S95011 has shown a good safety and tolerability profile in the whole patient population as already demonstrated in healthy volunteers in the Phase 1 study.

Based on the recommendation of the trial's IDMC, OSE Immunotherapeutics is continuing the study.

- END OF PATIENT ENROLLMENT IN THE PHASE 2 CLINICAL TRIAL OF OSE-127/S95011 IN PRIMARY SJÖGREN'S SYNDROME

In parallel, another phase 2 in primary Sjögren's Syndrome, a systemic autoimmune disease characterized by damage to the exocrine glands, in particular the lacrimal and salivary glands, has started in August 2021 sponsored by Servier. This trial aims at evaluating the efficacy and tolerance of OSE-127/S95011 in primary Sjögren syndrome. As stipulated in the licensing option agreement, inclusion of the first patient in this trial has triggered a €5 million milestone payment from Servier to OSE Immunotherapeutics. .

In November 2022, the last patient has been enrolled this clinical trial and the results are expected in 2023.

A second payment of €15 million is expected if Servier exercises the option at the end of the two Phase 2 trials.

- FR104, CONTINUATION OF THE WORLDWIDE LICENSE AGREEMENT WITH VELOXIS PHARMACEUTICALS INC. IN ALL TRANSPLANT INDICATIONS

FR104 is an immunomodulator consisting of an optimized monoclonal antibody fragment targeting the CD28 receptor, a key component of the destruction function of effector T lymphocytes which are deleterious in autoimmune diseases and transplantation.

In April 2021, a worldwide licensing agreement was agreed with Veloxis Pharmaceuticals Inc. Under the terms of the agreement, OSE Immunotherapeutics has granted it worldwide rights to develop, manufacture, register and market FR104 in all transplant indications. At the same time, OSE Immunotherapeutics retains all rights to develop FR104 in autoimmune diseases. Through this agreement, Veloxis plans to develop FR104 to provide a potential therapeutic alternative for the prophylaxis of organ rejection in solid organ transplant patients.

Under this agreement, OSE Immunotherapeutics will be able to receive up to €315 million in potential milestone payments, including a payment of €7 million paid at signature and royalties on sales.

At the end of January 2022, Veloxis Pharmaceuticals, Inc. received acceptance of the New Investigational Drug (IND) application in the United States for VEL-101/FR104. As part of the worldwide licensing agreement signed in April 2021, this first step triggered a €5 million payment from Veloxis Pharmaceuticals, Inc. to OSE Immunotherapeutics.

In May 2022, Veloxis started a new clinical trial assessing the safety, tolerance, pharmacokinetics and pharmacodynamics of single ascending doses of FR104/VEL-101 or placebo when administered subcutaneously (SC) or intravenously (IV). Approximately 56 healthy participants will be enrolled and will undergo monitoring for 50 days.

In parallel, a Phase 1/2 study evaluating FR104, administered for the first time in patients who have received a renal transplant, is underway as part of a clinical collaboration agreement between OSE Immunotherapeutics and the Centre Hospitalier Universitaire de Nantes as sponsor. This Phase 1/2 clinical trial aims to assess the safety, tolerability, pharmacokinetics, pharmacodynamics and efficacy of FR104 in patients who have received a renal transplant.

- **BI 765063 (OSE-172), IN PHASE 1 CLINICAL TRIAL IN ADVANCED SOLID TUMORS: PROMISING DATA FOR THE DOSE ESCALATION PHASE AND START-UP OF THE EXPANSION PHASE**

BI 765063, a checkpoint inhibitor targeting the SIRPa receptor on the SIPRa/CD47 axis, is being developed as part of a partnership with Boehringer Ingelheim, which acquired the worldwide rights in April 2018 for the development, registration and marketing of the product.

Since March 2019, BI 765063 is in a Phase 1 clinical trial This first-in-human Phase 1 trial is a dose finding study of BI 765063 administered as a single agent and in combination with Boehringer Ingelheim's monoclonal antibody PD1 antagonist BI 754091, a T-lymphocyte checkpoint inhibitor. The trial aims to characterize safety, pharmacokinetics, pharmacodynamics and preliminary efficacy of the immunotherapy in patients with advanced solid tumors.

The dose escalation part (Sep 1) of the Phase 1 trial has shown positive results with a good tolerance of BI 765063 in monotherapy and in combination with Ezabenlimab and promising efficacy signals in patients with solid tumors and heavily pretreated (data presented at the 2021 ASCO and ESMO meetings).

In May 2022, the initiation of the Phase 1 clinical expansion trial with BI 765063 sponsored and conducted by Boehringer Ingelheim triggered a €10 million milestone payment from Boehringer Ingelheim to OSE Immunotherapeutics.

A new Phase 1 clinical trial was set up by Boehringer Ingelheim, in combination with their anti-PD1 in recurrent or metastatic hepatocellular carcinoma (HCC) and head and neck cancer patients in combination.

MYELOID PLATFORM

- **OSE-230, NEW PRECLINICAL DATA ON THE FIRST PRORESOLUTIVE MONOCLONAL ANTIBODY IN CHRONIC INFLAMMATION**

OSE-230 is an agonist antibody against ChemR23, also known as chemerin chemokine-like receptor 1 (CMKLR1), a G-protein coupled receptor (GPCR) expressed on myeloid immune cells known to modulate inflammation.

Most anti-inflammatory agents act using a mechanism that blocks pro-inflammation pathways. In contrast, OSE Immunotherapeutics is developing OSE-230 as a first-in-class therapeutic agent with the potential to resolve chronic inflammation by driving affected tissues to complete the inflammation program and restore tissue integrity.

New preclinical advances were presented au the 2022 PEGS congrès (*Protein & Antibody Engineering Summit Europe*). Resolution of inflammation is triggered by pro-resolving lipids activating GPCRs (G-Protein Coupled Receptor) targets. The ChemR23 GPCR is expressed on inflammatory myeloid immune cells, such as macrophages and neutrophils, and is over-expressed in tissues affected by chronic inflammatory diseases, such as lung inflammatory diseases or severe IBD (Inflammatory Bowel Disease) unresponsive to anti-TNF or anti-integrin therapies. ChemR23's over-expression is associated with chronic neutrophil accumulation in damaged tissues. OSE-230 is the first monoclonal antibody (mAb) to activate a pro-resolutive GPCR target (ChemR23). Its innovative mechanism of action drives inflammatory neutrophil tissue clearance through apoptosis and inhibition of the pathogenic NETosis* process. This mAb triggered resolution demonstrated positive preclinical efficacy in chronic colitis or chronic arthritis models with significant decrease in tissue fibrosis and restoration of tissue healing.

** NETosis is a program for formation of neutrophil extracellular traps (NETs), which consists of modified chromatin decorated with bactericidal proteins from granules and cytoplasm. Recent research has highlighted that neutrophils, and in particular NETs that can be released upon activation, have central roles in the initiation and perpetuation of systemic autoimmune disorders and trigger complex and chronic inflammatory responses that lead to organ damage and fibrosis.*

This breakthrough discovery opens the development pathway of OSE-230 in various chronic inflammations such as inflammatory bowel diseases, lung or kidney inflammatory diseases, arthritis or type 1 diabetes.

In 2023, the OSE Immunotherapeutics' teams actively pursue their preclinical research.

- **CLEC-1, NEW PRECLINICAL EFFICACY DATA ON THE NOVEL MYELOID IMMUNE CHECKPOINT IN IMMUNO-ONCOLOGY**

The OSE Immunotherapeutics teams have characterized a new CLEC-1 myeloid checkpoint target (among CLR receptors - C-type lectin receptors) and have identified monoclonal antibody antagonists that block this new signal "Don't Eat Me". They increase both the phagocytosis of tumor cells by macrophages and the uptake of antigens by dendritic cells.

The identification of CLEC-1 and its antagonists constitute an exciting innovative step in cancer immunotherapy.

A scientific article (*CLEC-1 is a death sensor that limits antigen cross-presentation by dendritic cells and represents a target for cancer immunotherapy*), published in the peer-reviewed journal « *Science Advances* » of November 2022, reports on the latest data of the preclinical program conducted with CLEC-1 :

- Overall, CLEC-1 genetic deletion leads to a profound reinvigoration of the tumor immune microenvironment by enhancing infiltrates of dendritic cell (antigen presenting cells), increasing memory and activated T lymphocyte infiltrates, decreasing infiltrates of exhaustion marker PD1-expressing T lymphocytes and limiting the recruitment of immunosuppressive cells such as myeloid derived suppressor cells (MDSCs).
- Importantly, CLEC-1 blockade using monoclonal antibody treatment demonstrates robust anti-tumor activity, also by reinvigorating the tumor immune microenvironment in several preclinical oncology models, thereby faithfully recapitulating the effect of CLEC-1 genetic deletion in the context of human CLEC-1-expressing mice. Proprietary anti-CLEC-1 mAbs increase survival in monotherapy in orthotopic model of hepatocellular carcinoma while combination with chemotherapy increases preclinical tumor eradication in colon carcinoma model.

In 2023, the OSE Immunotherapeutics' teams are continuing their research and their strategy to protect the inventions as shown by the delivery of a new European patent on CLEC-1 granted in May 2022.

BICKI® PLATFORM

- BiCKI®, PRECLINICAL ADVANCES ON THE BIFUNCTIONAL THERAPY TARGETING PD1 AND IL-7 IN CANCER IMMUNOTHERAPY

BiCKI®-IL-7 is an innovative bispecific therapy targeting PD1 and at the same time delivering the IL-7 cytokine PD1-expressing T-cells to restore the function of exhausted T cells, to disarm the suppressive activity of effector T cells and to increase stem-like T cells able to reconstitute memory T cells and effector T cells. This immunotherapy has potential to address the high medical need of patients with cancers with primary or secondary resistance or that are refractory to immune checkpoint inhibitor treatments.

The latest preclinical progress on BiCKI®-IL-7 : *« Anti-PD1/IL7v immunocytokine promotes durable T-cell responses and overcomes anti-PD1 resistance »* were presented at the 2022 *American Association for Cancer Research* (AACR) congress.

The BiCKI®-IL-7v immunocytokine significantly improves the quality and durability of memory T lymphocytes in the tumor microenvironment (with T lymphocyte stem cells without immune exhaustion). BiCKI®-IL-7 could potentially adress the medical need of a patient population in immune escape after checkpoint inhibitor treatment.

The BiCKI® platform, and in particular the bifunctional therapy BiCKI®-IL-7v, preferentially delivers the IL-7 cytokine at the heart of the tumor microenvironment (TME) where T PD1+ lymphocytes accumulate in response to immunotherapy. This TME-driven IL-7 immunocytokine has a well differentiated biodistribution compared to other cytokines being currently developed.

COVEPIT, A PROPHYLACTIC VACCINE AGAINST COVID-19 : POSITIVE PRECLINICAL AND *EX VIVO* RESULTS – IN CLINICAL PHASE, POSITIVE LONG-TERM IMMUNOLOGICAL RESULTS AT SIX MONTHS IN HEALTHY VOLUNTEERS WITH STRONGT CELL RESPONSES AGAINST VIRUS PROTEINS

In May 2020, OSE Immunotherapeutics committed to the fight against COVID-19 and announced the launch of a research program on the development of a prophylactic vaccine called CoVepiT.

The Phase 1 clinical trial started in April 2021 to evaluate the tolerance, reactogenicity and immunogenicity of CoVepiT in healthy adult volunteers.

In July 2021, the Company announced a voluntary, out of an abundance of caution, the recrutment and dosing of CoVepiT in this trial due to a limited number of grade 1 and one grade 2 (in one participant) adverse events (nodules around injection points). Then the data have been regularly assessed with the independant Safety Monitoring Committee and the investigator center of Ghent (Belgium). The indurations have bee resolved in a few weeks in most of the participants (without system reaction, no fever, no inflammation, no local ulceration). The follow up continued, showing a good tolerance profile. This profile with frequent indurations is close to that of the vaccines inducing a T cell response and it is regularly linked to this mecanism of action.

In March 2022, OSE Immunotherapeutics announced the positive analysis of the long term immune T response of CoVepiT with immunological results at six months on T cell memory response in the vaccinated subjects. In parallel, the resolution of local indurations related to T cell mechanism of action and the good safety profile were confirmed.

OSE Immunotherapeutics has validated the concept and paradigm that long-term immunity against coronavirus could be achieved in human with its T-cell vaccine platform inducing durable memory T lymphocytes, with additional properties as T cells resident in the lung already described in preclinical studies.

New treatments like monoclonal antibodies or anti-viral treatments are available for immunocompromised patients. Additional booster shots of registered vaccines are also recommended for this fragile population with a poor antibody response.

Given the new therapeutics and multiple boosters recommended in these patients, additional clinical development of CoVepiT is difficult under the current circumstances. The strategy for OSE is now to leverage these long-term T cell response positive results and to select the most relevant peptides allowing an easier industrial scale-up to be ready for any new pandemic crisis with a novel variant of concern.

1.3 FORESEEABLE changes and future outlook

PROPRIETARY PRODUCTS IN CLINICAL DEVELOPMENT

- TEDOPI®: STRATEGY AND NEXT STEPS

The international Phase 3 clinical trial of Tedopi®, Atalante-1, was designed to evaluate the benefits of the product in HLA-A2 positive patients in second- or third-line therapy versus second- or third-line chemotherapy (docetaxel or pemetrexed) in invasive stage IIIB or metastatic stage IV non-small cell lung cancer after failure of treatment with anti-PD1 and anti-PD-L1 checkpoint inhibitors. The main assessment endpoint is overall survival.

The results of the Phase 3 Tedopi® trial have shown significant survival benefits with Tedopi® versus a standard chemotherapy treatment (docetaxel or permetrexed) in positive HLA-A2 positive patients with NSCLC and in secondary resistance after immune checkpoint inhibitors. Importantly, the non-NSCLC patients included in this trial had failed second-line checkpoint inhibitor treatments and represent a hard-to-treat patient population with high medical need.

Based on positive recommendations from the US Food and Drug Administration (FDA) “Type C” meeting following the European Medicines Agency (EMA) scientific advice, OSE Immunotherapeutics is preparing a new pivotal Phase 3 clinical study to support the regulatory registration of Tedopi® in second line. This confirmatory trial will evaluate Tedopi® versus the standard treatment in second line in HLA-A2 positive patients with advanced non-small cell lung cancer.

The Company will also continue the three Phase 2 clinical trials presented at the 2022 ASCO meeting :

- The TEDOPaM study in pancreatic cancer conducted under the oncology group GERCOR sponsorship ;
- The TEDOVA study in ovarian cancer conducted under the oncology group ARCAGY-GINECO sponsorship ;
- The study in non-small cell lung cancer of Tedopi® in combination conducted under the Italian foundation FoRT sponsorship.

At the same time, given that the positive Phase 3 results significantly strengthened the value of Tedopi®, the Company is continuing to explore potential partnering opportunities for the product.

- OSE-279, A HUMANIZED ANTI-PD1 MONOCLONAL ANTIBODY: CONTINUATION OF THE PHASE 1/2 CLINICAL TRIAL

OSE-279, the key backbone of the bispecific fusion protein BiCKI® platform, is a humanized anti-PD1 monoclonal antibody. OSE-279 entered in Phase 1 /2 clinical trial in December 2022 in advanced solid tumors and lymphomas. Hence, the Company owns its proprietary anti-PD1.

This first clinical study will also allow the Company, at a later stage, to explore OSE-279 in combination with other OSE Immunotherapeutics' drug candidates or with external assets accessed through potential new partnerships with biotech or pharmaceutical companies.

PARTNERED PRODUCTS IN CLINICAL DEVELOPMENT

- OSE-127/S95011: TWO ONGOING PHASE 2 CLINICAL TRIALS AND RESULTS EXPECTED FROM THE TRIAL SPONSORED BY SERVIER IN PRIMARY SJÖGREN SYNDROME

- OSE-127/S95011 is developed as part of a two-step licensing option granted to Servier for its development and marketing in autoimmune diseases. This licensing option will allow the product to be developed until the completion of a Phase 2 clinical trial.
- After positive Phase 1 clinical results of OSE-127/S95011 and the exercise of option 1 in February 2019, a Phase 2 trIn parallel, another Phase 2 in Sjögren's Syndrome started in August 2021 sponsored by Servier. As provided in the license option agreement, the inclusion of the first patient in this Phase 2 study triggered a €5 million milestone payment from Servier to OSE Immunotherapeutics.
- In November 2022, the last patient has been enrolled in this Phase 2 trial sponsored by Servier. The results are expected in 2023.
- Option 2 is expected to be exercised upon completion of these two Phase 2 studies, with priority being given to the study in Sjögren's syndrome. Further development beyond Phase 2, if Phase 2 of this licensing option is validated, will be carried out by Servier.

  Product development will also continue until the Phase 2 clinical trial as part of the EFFIMab consortium (with public and private partners and with OSE Immunotherapeutics as leader).

- FR104, TWO CLINICAL TRIALS ONGOING

Since December 2020, FR104 is undergoing a Phase 1/2 clinical trial in patients who have received a renal transplant. This Phase 1/2 clinical trial aims to assess the safety, tolerability, pharmacokinetics, pharmacodynamics and efficacy of FR104 in patients who have received a renal transplant. It is being carried out under a clinical collaboration agreement between OSE Immunotherapeutics and *the Centre Hospitalier Universitaire de Nantes*, which is the sponsor.

At the end of January 2022, Veloxis Pharmaceuticals, Inc. the Company's partner in transplantation, received acceptance of the New Investigational Drug (IND) application in the United States for VEL-101/FR104. As part of the worldwide licensing agreement signed in April 2021, this first step triggered a €5 million payment from Veloxis Pharmaceuticals, Inc. to OSE Immunotherapeutics. This Phase 1 study, evaluating VEL-101/FR104 in renal transplant immunosuppression, is continuing in 2023.

- BI 765063 (OSE-172), IN PHASE 1 CLINICAL TRIAL IN ADVANCED SOLID TUMORS: THE INNOVATIVE APPROACH OF A COMBINATION OF PD1 ANTAGONIST TREATMENTS

BI 765063, a checkpoint inhibitor targeting the SIRPa receptor on the SIRPa/CD47 axis, is being developed as part of a partnership with Boehringer Ingelheim, which acquired the worldwide rights in April 2018 for the development, registration and marketing of the product.

Based on promising initial results from the Phase 1 clinical trial of BI 765063 in monotherapy and in combination, the Company is progressing in 2023 on the Phase 1 expansion step in different cancer cohorts, colorectal cancer and advanced endometrial cancer, as well as in an additional cohort of hepatocellular carcinoma and head and neck cancer to explore the potential of a combination approach of BI 765063 and ezabenlimab as a relevant therapeutic strategy in solid tumors.

COVEPIT: POSITIVE LONG-TERM IMMUNOLOGICAL RESULTS AT SIX MONTHS IN HEALTHY VOLUNTEERS WITH STRONGT CELL RESPONSES AGAINST VIRUS PROTEINS ; A STRATEGY BASED ON INDUSTRIAL SCALE-UP TO BE READY FOR ANY NEW PANDEMIC CRISIS WITH A NOVEL VARIANT OF CONCERN

The positive analysis of the long term immune T response of CoVepiT has shown immunological results at six months on T cell memory response in the vaccinated subjects (results announced on March 16, 2022).

OSE Immunotherapeutics has validated the concept and paradigm that long-term immunity against coronavirus could be achieved in human with its T-cell vaccine platform inducing durable memory T lymphocytes, with additional properties as T cells resident in the lung already described in preclinical studies.

New treatments like monoclonal antibodies or anti-viral treatments are available for immunocompromised patients. Additional booster shots of registered vaccines are also recommended for this fragile population with a poor antibody response.

Given the new therapeutics and multiple boosters recommended in these patients, additional clinical development of CoVepiT is difficult under the current circumstances.

MYELOID AND BICKI® PLATFORMS

The Company is pursuing the preclinical development of its other products from its myeloid and BiCKI® platforms:

- OSE-230, an agonist ChemR23 antagonist in the resolution of chronic inflammation,
- CLEC-1, new immune myeloid checkpoint regulating the antitumor response,
- BiCKI®, a platform of bispecific anti-PD1 checkpoint inhibitors and BiCKI®-IL-7, a bifunctional program targeting PD1 and IL-7 in cancer immunotherapy.

PARTNERSHIPS – VALUE CREATION

The Company continues to seek new collaboration or license agreements that could be initiated at various stages of product development, with industry players involved in the field of activation and regulation immunology and in therapeutic combinations of high clinical interest.

Significant events since the end of the fiscal year

FINANCING

The Company implemented several financial lines.

On April 27, 2023, the Company signed a financing contract with the Company Vester Finance in the form of an equity financing line (commonly called equity line) for a maximum volume representing up to 15% of the Company's capital. This line of financing materializes through the exercise of 2,800,000 BSA. The parity is 1 warrant for 1 share, the exercise of which is carried out by Vester Finance, which has, however, the obligation to exercise a minimum number of 300,000 warrants per

quarter, with a maximum discount of 6% on the lowest average daily price weighted by volumes over the period of the two trading sessions preceding each issue.

Based on the current price, this would raise an amount of €3.4 million by December 31, 2023, and an additional €1.7 million until April 30, 2024.

The Company has also received support from the "Pays de la Loire" Region through a line of financing in the form of a Redeployment loan in the amount of €1.5 million, with an interest rate of 2%, with two years of deferred global capital repayment and 4 annual repayments. This loan is subject to final approval by the Commission, scheduled for the end of May. Management considers the finalization of this financing as highly probable.

The Company has also set up financing through a banking pool (CIC, Crédit Mutuel, BNP Paribas): a Resilience "Prêt Garanti par l'Etat", PGE (loan agreement guaranteed by the French State)in the amount of €1.3 million with an interest rate of up to 2%, with a repayment *in fine* at 12 months (subject to completing the formalities related to the PGE Resilience relating to the impact of the Ukrainian conflict on the activity of the company); and a global loan of €1 million, with an interest rate of 4%, with repayment over 36 months. This banking pool agreement is subject to the lifting of several conditions, namely the 70% counter-guarantee from Bpifrance and the loan agreement from the Pays de la Loire Region detailed above.

TEDOPI®

In February 2023, the Company has provided a regulatory update on Tedopi® with the positive recommendation from the Food & Drug Administration (FDA) on the Type C meeting following the European Medicines Agency (EMA) scientific advice for the confirmatory phase 3 trial in second line treatment**.**

In March 2023, the Company has received a new approval for an early access program for Tedopi® in Spain in lung cancer after failure to immunotherapy. The Spanish Drug Agency (Agencia Espanola de Medicamentos y Productos Sanitarios, AEMPS) has made a new early access program available that will allow access to Tedopi® through a Special Situation Authorization [(1)] in the treatment of advanced or metastatic non-small cell lung cancer (NSCLC) after immune checkpoint inhibitor (ICI) failure. This Special Situation Authorization is based on the positive clinical data from the initial phase 3 trial of Tedopi® (Atalante-1) in third line treatment and the high unmet need for these patients.

[(2)] *The Special Situation Authorization (Real Decreto 1015/2009) is intended to provide early access to medicines for patients with a severe or rare disease with high unmet need and for which no authorized therapeutic alternatives are available.*

OSE-127

In February 2023, OSE Immunotherapeutics announced the online publication in the peer-reviewed "Journal of Immunology" positive Phase 1 clinical results of OSE-127.

Moreover, the Company provided an update on the product developed in immuno-inflammation in two phase 2 clinical trials in ulcerative colitis (sponsor OSE Immunotherapeutics) and in primary Sjögren syndrome (sponsor Servier).

The Company also presented preclinical efficacy results with OSE-127 in hematology, in acute lymphoblastic leukemia, at the 2023 American Association for Cancer Research (AACR) annual meeting.

1.4 Research and development activities

Readers are invited to refer to Section 1.2 of this management report.

1.5 Main risks and uncertainties to which the Company is exposed

See Section 3 of the Universal Registration Document.

1.6 Use of financial instruments by the Company

The Company used financial instruments during the past fiscal year (see Note 3 to the financial statements, Section 18.1.6 of the Universal Registration Document).

1.7 Transactions with related parties

See Section 17.1.2 of the Universal Registration Document.

2. FINANCIAL STATEMENTS FOR THE FISCAL YEAR ENDING DECEMBER 31, 2022

2.1 Presentation of the Company's statutory financial statements

Please note that the presentation rules regarding and the valuation methods used to prepare the statutory financial statements for the fiscal year ended comply with the regulations in force.

General accounting policies have been applied in accordance with the prudence principle, in line with the following basic assumptions:

- Going concern;
- Consistency of accounting rules from one fiscal year to another;
- Independence of fiscal years

and in accordance with the general rules for preparing and presenting the separate financial statements as described in the opinion of the French National Accounting Council (Article R. 123-180 of the French Commercial Code and Art. 531-1 § 1 of the French General Tax Code).

For more information on the accounting rules and methods, please see the notes to the statutory financial statements.

2.1.1 Balance sheet

The Company's overall balance sheet at December 31, 2022, was €133,386 thousand versus €140,484 thousand the previous fiscal year.

Assets include €51,074 thousand in equity interests, €42,901 thousand in intangible assets, €743 thousand in tangible assets, €743 thousand in trade receivables and €9,006 thousand in other receivables, €25,607 thousand in net cash and cash equivalents and marketable securities and €3,452 thousand in prepaid expenses.

Apart from share capital of €3,705 thousand, liabilities include €132,327 thousand in share premiums, -€42,667 thousand in retained earnings, €1,113 thousand in provisions for risks and expenses, €14,425 thousand in conditional advances, €26,768 thousand in borrowings from credit institutions, €8,493 thousand in trade payables, €2,535 thousand in social security and tax liabilities, €33 thousand in other liabilities and €8,588 thousand in deferred income.

2.1.2 Income statement

In 2022, the Company generated revenue of €3,303 thousand, mainly consisting of the reinvoicing to Boehringer Ingelheim of the development costs incurred by OSE for BI 765063 (OSE-172) and the sale of vials to Veloxis for completing their Phase 1 study in transplantation.

Other income for 2022 amounted to €17,074 thousand and consisted of license income (milestone payments) reached as part of the partnerships signed with Boehringer Ingelheim and Veloxis.

In 2021, the Company generated revenue of €6,147 thousand, mainly consisting of the reinvoicing to Boehringer Ingelheim of the development costs incurred by OSE for BI 765063 (OSE-172) and the sale of vials to Veloxis for the completion of their Phase 1 study in transplantation.

Other income for 2021 amounted to €21,427 thousand and consisted of license income (milestone payments) obtained under the partnerships signed with Boehringer Ingelheim, Servier and Veloxis.

2022 operating expenses totaled €39,077 thousand versus €43,756 thousand in 2021.

Operating expenses by type – in €k	2022	2021	Change	Change %
Purchases and external expenses	26,980	31,178	- 4,198	-13%
Taxes and similar payments	153	164	- 11	-7%
Employee benefits expense	8,476	9,471	- 995	-11%
Allocation to depreciation, amortization and provisions	1,614	869	745	86%
Other expenses	1,854	2,074	- 220	-11%
Total	**39,077**	**43,756**	**- 4,679**	**-11%**

The "external expenses" item in 2022 broke down in particular as follows:

- €18,308 thousand for subcontracting: completion of phase 3 clinical trials for Tedopi®, completion and validation of GMP batches for OSE-127/S95011, COVEPIT and OSE-279, Phase 1 clinical trials for COVEPIT and BI 765063 (OSE-172), Phase 2 clinical trials for OSE127/S95011, consulting international clinical experts on the pivotal Phase 3 trial with Tedopi®, for OSE-127/S95011 and BI 765063 (OSE-172);
- €4,315 thousand in fees: fees relating to the Company's status as a listed company and legal transactions, fees particularly for industrial property;
- €4,357 thousand: cost of premises, insurance premiums, travel expenses, consumables and others.

Employee benefits expense in 2022 totaled €8,476 thousand versus €9,471 thousand in 2021.

Average headcount was 61 in 2022 versus 53 in 2021.

The operating profit for fiscal year 2022 was -€18,700 thousand.

With a net financial loss of -€676 thousand, extraordinary income of - €198 thousand and tax income of €5,432 thousand (research tax credit), the net loss for fiscal year 2022 was €14,139 thousand.

2.2 Presentation of the Company's consolidated financial statements

The consolidated financial statements of OSE Immunotherapeutics and its subsidiaries (the Group) are presented in euros and are drawn up in accordance with IFRS standards (International Financial Reporting Standard) as adopted by the European Union.

2.2.1 Consolidated balance sheet

The Company's consolidated statement of financial position at December 31, 2022, was €91,781 thousand versus €101,876 thousand the previous fiscal year.

2.2.2 Consolidated income statement

The Group recognized €18,302 in revenue in 2022 versus €26,306 thousand in revenue generated in 2021.

Operating expenses by function in €K	2022 (consolidated)	2021 (consolidated)
R&D expenses	26,893	30,550
Overhead expenses	6,672	8,608
Expenses related to share-based payments	3,130	3,773
Total	**36,695**	**42,932**

R&D expenses in 2022 mainly comprised:

- €20,850 thousand in subcontracting and fees, before recording the research tax credit of €5,432 thousand and subsidies received in the amount of €399 thousand;

- €5,844 thousand in employee benefits expense allocated to research and development;

- €1,250 thousand in royalties under the sub-license agreement with INSERM;

- €2,813 thousand in allowance for depreciation and provisions;

- €1,967 thousand: seminars, insurance premium, storage costs and others.

Overhead expenses in 2022 mainly comprised:

- €2,388 thousand in fees: accounting, legal, consultancy, stock-market listing and advertising costs;

- €1,953 thousand in employee benefits expense allocated to operations management, finance, communication and Corporate secretariat;

- €350 thousand in Directors' fees;

- €1,981 thousand: cost of premises, insurance premiums, travel expenses, and others;

Operating income for fiscal year 2022 was -€18,476 thousand;

Net income for fiscal year 2021 was -€17,760 thousand.

2.3 Indebtedness (statutory financial statements and consolidated financial statements)

Statutory financial statements

Other receivables amount to €9,006 thousand, of which €7,173 thousand in tax receivables, €1,281 thousand in current account advances granted to its subsidiary OPI, €424 thousand in accrued revenue (subsidies and miscellaneous).

The cash available to OSE Immunotherapeutics stood at €25,608 thousand at December 31, 2022, of which €18,501 thousand in cash and cash equivalents and €7,107 thousand in term deposits and other short-term investments.

The total amount of the Company's operating liabilities is €11,028 thousand (comprising €8,493 thousand in trade payables and €2,535 thousand in tax and social security liabilities).

The amount of loans with financial institutions is €26,263 thousand (French State-Guaranteed loan and EIB) and the amount of repayable advances is €14,425 thousand.

Consolidated financial statements

Other receivables amount to €11,177 thousand and correspond to tax receivables, prepaid income and accrued income (prepaid expenses).

Funds available to the Group stood at €25,617 thousand in net cash at December 31, 2022.

The total amount of the Company's operating liabilities is €11,455 thousand (comprising €8,539 thousand in trade payables and €2,916 thousand in tax and social security liabilities).

The amount of loans with financial institutions is €25,063 thousand (French State-Guaranteed loan) and the amount of repayable advances is €15,258 thousand.

Other liabilities amount to €816 thousand and correspond to deferred income.

2.4 Expenses mentioned in Article 39-4 of the French General Tax Code

In accordance with Article 223 quarter of the French General Tax Code, please note that for the fiscal year ended on December 31, 2022, there were no expenditure or costs of the type qualifying as "extravagant expenditure" under point 4 of Article 39 of the General Tax Code, or excessive amortization as referred to in the same point 4.

2.5 Information on payment terms for suppliers and customers

We hereby inform you that the Company's financial statements as submitted show trade payables in the amount of €4,551 thousand at December 31, 2022.

In accordance with the provisions of Articles L. 441-6-1 and D. 441-4 of the French Commercial Code, we hereby provide you with the following information relating to the breakdown of the balance of trade payables at the end of the last two fiscal years by due date:

Balance of trade payables and receivables at December 31, 2022, by due date (in €k):

Invoices received and not paid on the reporting date							
Maturities	**1 to 30 days**	**31 to 60 days**	**61 to 90 days**	**91 days and over**	**Total**	**Invoices not yet due**	**Total #411**
Number of invoices	103	21	1	11	136	498	634
Amount incl. VAT in €K	692	72	1	1,216	1,980	2,571	4,551
% of amount incl. VAT of purchases during the fiscal year	2%	0%	0%	4%	6%	8%	13%
Invoices issued and not paid on the reporting date which are past due							
Maturities	**1 to 30 days**	**31 to 60 days**	**61 to 90 days**	**91 days and over**	**Total**	**Invoices not yet due**	**Total #411**
Number of invoices		2		1	3	7	10
Amount incl. VAT in €K		37		113	77	194	118
% of amount incl. VAT of purchases during the fiscal year		0%		-1%	0%	1%	1%

For an amount (VAT included) of purchases evaluated at €33,886 for 2022

Balance of trade payables and receivables at December 31, 2021, by due date (in €k):

Invoices received and not paid on the reporting date							
Maturities	**1 to 30 days**	**31 to 60 days**	**61 to 90 days**	**91 days and over**	**Total**	**Invoices not yet due**	**Total #411**
Number of invoices	18	3	-	6	27	217	244
Amount incl. VAT in €K	393	50	-	506	949	1,994	2,943
% of amount incl. VAT of purchases during the fiscal year	1%	0%	0%	1%	3%	5%	8%
Invoices issued and not paid on the reporting date which are past due							
Maturities	**1 to 30 days**	**31 to 60 days**	**61 to 90 days**	**91 days and over**	**Total**	**Invoices not yet due**	**Total #411**
Number of invoices	-	-	1	-	1	3	4
Amount incl. VAT in €K	-	-	2	-	2	167	169
% of amount incl. VAT of purchases during the fiscal year			0%			2%	2%

2.6 The Company's results over the last five fiscal years

In accordance with the provisions of Article R. 225-102 of the French Commercial Code, the Company's results over the last five fiscal years can be found in Note 1.

2.7 Proposed appropriation of net income for the fiscal year

The annual financial statements the fiscal year ended on December 31, 2022, show a loss of €14,139,435, which we propose to appropriate to retained earnings, which, as a result, will stand at -€56,805,994.

In order to comply with the provisions of Article 243 bis of the French General Tax Code, please note that no dividends have been distributed over the last three fiscal years.

3. SUBSIDIARIES AND EQUITY INTERESTS – INVESTMENT SECURITIES

3.1. Activity of subsidiaries

The activity of our subsidiary OPI is limited to managing the industrial property of our OSE-2101 technology.
The activity of our subsidiary OSE Immunotherapeutics Inc. remains limited at the current time. Over the medium term, it will be used to support international scientific or pharmaceutical collaborations.

3.2 Equity holdings or takeovers

None

3.3 Controlled company

Since March 25, 2014, the Company has held all of the share capital and voting rights of OPI and OSE Immunotherapeutics Inc., created in Delaware in 2017.

EMPLOYEE SHAREHOLDING

In accordance with the provisions of Article L. 225-102 of the French Commercial Code, please note that there were thirty-nine employee shareholders in the Company on the last day of the fiscal year, i.e. December 31, 2022, the most important of which (in terms of share ownership on the basis of 18,527,401 shares) were as follows:

- Dominique Costantini, whose employment agreement dates from July 1, 2014, as Director of Development, holding 2,007,163 shares, representing 10.83% of share capital at December 31, 2022.
-

- Nicolas Poirier, whose employment agreement dates from May 31, 2016, as Chief Scientific Officer, holding 192,802 shares, representing 1.04% of share capital at December 31, 2022.

On December 5, 2018, the Board of Directors approved in principle the issue and allocation of 150,000 free shares to employees who are not corporate officers of the Company and gave all powers to the CEO to issue and allocate said shares. As such, on March 12, 2019, the Chief Executive Officer decided to issue and allocate 149,200 free shares to employees who are not corporate officers of the Company (leading to the acquisition of 141,800 free shares recognized by the Board of Directors on March 26, 2020).

On June 26, 2019, the Board of Directors approved in principle the issue and allocation of 150,000 free shares to employees who are not corporate officers of the Company and gave all powers to the CEO to issue and allocate said shares. As such, on June 26, 2019, the Chief Executive Officer decided to issue and allocate 148,400 free shares to employees who are not corporate officers of the Company (leading to the acquisition of 145,300 free shares by the Chief Executive Officer on June 27, 2020).

On June 17, 2020, the Board of Directors approved in principle the issue and allocation of 250,000 free shares to employees who are not corporate officers of the Company and gave all powers to the Chief Executive Officer to issue and allocate said shares. Thus, on December 18, 2020, the Chief Executive Officer decided to issue and allocate 244,500 free shares to employees who are not corporate officers of the Company.

On December 7, 2021, the Board of Directors approved in principle the issue and allocation of 250,000 free shares to employees who are not corporate officers of the Company and gave all powers to the Chief Executive Officer to issue and allocate said shares. Thus, on March 28, 2022, the Chief Executive Officer decided to issue and allocate 228,700 free shares to employees who are not corporate officers of the Company.

However, the Company does not have any employee shareholder whose shares are subject to collective management as per the above-mentioned article (i.e. as part of an employee savings scheme or company mutual fund).

4. INFORMATION ON THE FINANCIAL RISKS RELATING TO THE EFFECTS OF CLIMATE CHANGE

Given the nature of its business, the Group is not significantly exposed to environmental risks and has not identified any financial risks relating to the effects of climate change. The risks of climate change are limited due to the fact that the Company is not involved in any industrial activity, marketing or research and development.

5. CONTROL MECHANISM

Article 18 of the bylaws gives double voting rights to all fully paid-up shares that have been registered in the name of the same shareholder for at least two years.

Apart from these double voting rights, there are no other special rights attached to the shares.

There are also no control mechanisms in employee shareholding arrangements or agreements between shareholders of which the Company is aware and which could lead to restrictions on share transfers.

6. GENERAL INFORMATION ON THE COMPANY AND ITS SHARE CAPITAL

6.1 Identity of the Company

(i) Name

The name of the Company is OSE Immunotherapeutics.

(ii) Registered office

The registered office of the Company is: 22 boulevard Benoni Goullin, 44200 Nantes.

(iii) Legal form

OSE Immunotherapeutics is a limited company (*société anonyme*) with a Board of Directors, whose shares have been listed in compartment C of Euronext Paris under ISIN code FR0012127173 since March 30, 2015.
On January 31, 2023, the Company's shares have been transferred from compartment B to compartment C of Euronext Paris which includes listed companies with a market capitalization under 150 million.

(iv) Capital

The share capital of OSE Immunotherapeutics currently stands at three million, seven hundred and five thousand, two hundred and twenty euros and twenty cents (3,705,220.20). It is composed of eighteen million nine hundred and oneand one hundred and one (18,901,101) shares of twenty (20) euro cents nominal value each, all of the same category.

(v) Company's buyback of its own shares

The Combined General Shareholders' Meeting of June 23, 2022, authorized the Board of Directors to implement a share buyback program in the conditions described in Section 18.1.6 (Note 4.4 to the consolidated financial statements) of this Universal Registration Document.

In this respect, the Company carried out the following transactions in fiscal year 2022:

Number of shares purchased	239,254 shares
Average purchase price	€7.02
Number of shares sold	200,529 shares
Average sale price	€6.98
Total trading expenses	N/A
Number of shares registered in the name of the Company at fiscal year end and percentage of share capital	70,095 shares (i.e. 0.39%)
Value measured at average purchase price	€467,884
Total nominal value	€14,019

All of these purchases were made under the liquidity agreement with Invest Securities covering the Company's shares. Due to technical constraints, the number of Treasury shares held by the Company at the date of the Board of directors meeting of April 27, 2023, is not available. However, at the date of the Audit committee meeting of April 25, 2023, the number of

Treasury shares held by the Company stood at 81,999 shares, representing 0.43% of share capital.

(vi) Term

The Company was incorporated for a term of 99 years from the date of its registration with the Trade and Companies Register.

(vii) Incorporation details

The Company is registered with the Nantes Trade and Companies Register under number 479,457,715.

(viii) APE code

The APE code of OSE Immunotherapeutics is as follows: 7211Z.

(ix) Consultation of legal documentation

At the registered office of OSE Immunotherapeutics, at the register of the Nantes Commercial Court and on the Company's website: http://ose-immuno.com/

(x) Company's purpose

The purpose of OSE Immunotherapeutics in France and abroad is:

- The design, research and development of healthcare products from creation to obtaining marketing authorization, and all related operations including marketing;
- The acquisition, filing, obtaining, sale or licensing of all patents, brands, licenses and use processes;
- The acquisition of interests in any companies or undertakings already established or to be established, in France or abroad, whether or not they have a similar purpose to that of the Company;
- The provision of services, consultancy in research and development, marketing or commercial consultancy, consultancy on market access (pricing and reimbursement), structural audits in the field of healthcare, pharmaceuticals, cosmetics, nutrition and veterinary;
- And, more generally, all industrial, commercial, financial, civil, intangible property or real estate transactions directly or indirectly related to one of the above purposes or to any similar or related purpose that could be useful to the achievement and development of the Company's business;
- It may carry out any transactions that are compatible with, related to and contribute to achieving this purpose.

(xi) Fiscal year

The fiscal year of OSE Immunotherapeutics begins on January 1 and ends on December 31 of each year.

(xii) General Shareholders' Meetings

See Section 19.2.2 of the Universal Registration Document and Articles 29–35 of the Company's bylaws.

(xiii) Shareholding disclosure thresholds

The Company's bylaws provide that the crossing of thresholds will be subject to the following disclosures:

ARTICLE 16 – DISCLOSURE THRESHOLDS

Pursuant to Article L. 233-7 of the French Commercial Code, any individual or legal entity, acting alone or in concert, within the meaning of Article L. 233-10 of the French Commercial Code, who comes to hold or ceases to hold a number of shares representing a fraction equal to 5%, 10%, 15%, 20%, 25%, 30%, 33.33%, 50%, 66.66%, 90% or 95% of the share capital or voting rights, is required to disclose to the Company no later than the close of trading on the fourth trading day following the date on which the aforementioned shareholding threshold is crossed, the number of shares and voting rights held. The individual required to disclose the above information shall specify the number of securities held giving future access to the share capital and related voting rights.

If they have not been declared according to the above conditions, the shares exceeding the fraction that should have been declared shall be stripped of voting rights under the conditions pursuant to the French Commercial Code.

(xiv) Identification of bearer securities

Please refer to Chapter 16 related to the main shareholders.

ARTICLE 13 – TYPE OF SHARES

Shares are either registered or bearer shares, at the shareholder's choice. They can only be bearer shares once they are fully paid-up.

The Company is authorized to identify the holders of bearer securities by simple request to the organization in charge of clearing bearer securities, the name or corporate name, nationality, year of birth or year of incorporation, address of the holders of securities as well as the quantity of securities held by each of them.

(xv) Distribution of profits

ARTICLE 39 - APPROPRIATION AND DISTRIBUTION OF EARNINGS

The difference between income and expenses for the fiscal year constitutes the profit or loss for the fiscal year.

At least 20% of profit, less any prior losses, are appropriated to the statutory reserve. This appropriation is no longer mandatory once the reserve equals one-tenth of the share capital. It becomes mandatory again if, for any reason, the reserve falls below this one-tenth percentage.

The profit available for distribution is made up of the profit for the fiscal year less any prior losses and the appropriation referred to above, and plus any retained earnings.

This profit is available to shareholders who, on the proposal of the Board of Directors, can decide to carry it forward in full or in part, to allocate it to general or special reserve funds, or to distribute it to shareholders as dividends. The dividend can be in the form of Company shares.

The General Shareholders' Meeting may also decide to distribute amounts deducted from reserves, in which case, the resolution must expressly indicate the reserve items from which the deductions are made. However, dividends must be taken as a priority from the distributable profit for the fiscal year.

Losses carried forward by resolution of the General Shareholders' Meeting are registered in a special account on the liabilities side of the statement of financial position, to be charged to the profits of subsequent years until extinction or posted as a deduction of reserves.

ARTICLE 40 – PAYMENT OF DIVIDENDS

Dividends are paid annually at the times and places determined by the General Shareholders' Meeting or the Board of Directors within a maximum period of nine months from fiscal year end. An extension of this deadline may be granted by court order.

If shareholders wish to receive their dividend in the form of shares, they must make a request to this effect within a deadline set by the General Shareholders' Meeting no more than three months after the date of the meeting. This deadline may be suspended for a period not exceeding three months by decision of the Board of Directors in the event of a capital increase.

6.2 Company activity

OSE Immunotherapeutics is a biotechnology company specializing in immune response activation and regulation with agonist and antagonist biotherapies developed in immuno-oncology and in autoimmune diseases.

(i) Intellectual property

See Section 5.5 of the Universal Registration Document.

(ii) Important contracts

See Section 20 of the Universal Registration Document.

7. INTERNAL AND RISK MANAGEMENT CONTROL PROCEDURES RELATING TO THE PREPARATION AND PROCESSING OF ACCOUNTING AND FINANCIAL INFORMATION

This presentation of the internal control and risk management procedures implemented by the Company is based on the reference framework implementation guide published by the AMF and applicable to financial market mid-cap and small-cap stocks.

In view of the Company's headcount (57 people at December 31, 2022), OSE Immunotherapeutics considers that the internal control procedures are not relevant overall in order to assess its reliability. Nevertheless, OSE Immunotherapeutics has implemented measures proportionate to its specific organizational structure, and plans to develop assignments focused on these elements, and to improve them gradually as its operational and financial position progresses. In particular, the Company has implemented a new « expenditure commitment » software effectively launched on January 1st, 2022. These items are presented below.

OBJECTIVES OF INTERNAL CONTROL

OSE Immunotherapeutics has implemented an internal control organization, in order to guarantee optimization of control within the Company, taking particular care to ensure that there are no material elements capable of jeopardizing the reliability of the statutory and consolidated financial statements presented to shareholders.

The aim of this organization is to ensure:

- Compliance with applicable legislation and regulations,
- Safeguarding and protection of assets,
- Reliability of financial information,
- Prevention and control of risks, and implementation of process optimization.

This internal control mechanism contributes to prevention and control of risks from the Company's activity, including those linked to risks of error and fraud. Like any control system, it cannot, however, provide an absolute guarantee that these risks will be completely eliminated.

ORGANIZATION OF INTERNAL CONTROL

Internal control is also based on a specific organizational structure.

Therefore, in order to liaise with every level of OSE Immunotherapeutics, internal control is based on three internal control lines, and is based on the recommendations formulated by the external auditors, as presented below:

1st control line: compliance with procedures

Each Company employee contributes to the efficiency and smooth operation of the internal control mechanism, by complying with the procedures in place in their field of activity. The existence and application of the procedures, supervised by the Financial Director, is thus the first level of control.

2nd control line: support services and tools

This level of control is provided by specific control, monitoring and steering functions and tools, providing key decision support to the Board of Directors.

- **An expenditure commitment software**, locked at several hierarchical levels to validate all expenditures upstream.
- **Budgetary control** carried out by the Chief Financial Officer and her team. This provides monthly and quarterly monitoring of the budgetary commitments made by the Company and its subsidiaries OPI and OSE Immunotherapeutics Inc. and is given to the Board of Directors every quarter. This reporting also contains non-financial and prospective information to optimize steering of its subsidiary.

- An outsourced **accounting department**, guaranteeing financial information reliability, and liaising with the Finance Department. The Company's tax statements are prepared by an outsourced chartered accountant and verified by the Chief Financial Officer of OSE Immunotherapeutics. These statements are in addition regularly reviewed by external consultants.
- **The legal status of OSE Pharma International (OPI),** a Swiss law-subsidiary, enables OSE Immunotherapeutics to carry out controls based on the information and management by its single director.
- **The legal status of OSE Immunotherapeutics, Inc.,** a US law-subsidiary, enables OSE Immunotherapeutics to carry out control based on the information and management by its CEO who is also Chief Executive Officer of the French parent Company.
- **Centralized cash reporting to monitor legal operations** (contract, legal secretariat, dispute management, internal restructuring and external growth operations), making occasional use of advice from external consultants.
- **Consolidation** is carried out by an outsourced accountancy firm and reviewed by the Chief Financial Officer, in order to guarantee consistency of consolidation restatements, and ensure they comply with the Company's rules and procedures. Reporting data are reconciled with the prepared consolidated financial statements and published semi-annually.

3rd control line: compliance and optimization audits

Due to the Company's size, it does not have an internal audit department.

However, following creation of an Audit Committee at the meeting of the Board of Directors on March 27, 2015, this Committee also has the mission to monitor issues relating to the preparation and control of accounting and financial information. It is responsible for continuous assessment of the existence and efficiency of the Company's financial control and risk control procedures, in particular concerning internal control (see Section 1.1.2.1 of the Universal Registration Document).

External recommendations: legal audits

In addition to the control lines presented above, as part of their work, the Statutory Auditors assess the internal control procedures, and may issue recommendations, which are taken into account to improve reliability and timeliness when preparing financial information, as well as in risk management.

IMPLEMENTATION OF INTERNAL CONTROL

Main actions in the 2022 fiscal year

OSE Immunotherapeutics implemented a number of procedures in 2016, which were renewed in the subsequent fiscal years.

These procedures are as follows:

- Control of document standards
- Personnel training
- Organization of the Pharmacovigilance system
- Management of product quality claims
- Selection of GLP, GMP, GCP suppliers
- Management of discrepancies, preventive and corrective actions
- Management of internal and external audits / inspections
- Management of products for clinical trial
- Management of clinical trials
- Batch recall
- Filing and archiving

- Administrative and financial management
- Human resources management
- Management of inventions and inventors
- Pre-study site visit
- Site initiation visit
- Monitoring visits
- Close out visit
- Management of privileged information
- Medical review
- Change control
- Personal data protection

In particular in 2022, following the implementation of SAP ByDesign on January 1, 2022, financial and administrative management procedures have been reviewed. Similarly, following the arrival of an Human Resources Manager to support the Head of Human Resources, the human resources management procedure was overhauled.

2023-2024 areas of work

Focus areas for the fiscal year 2023-2024 will concern in particular the continuous improvement of the main procedures implemented as well as the implementation of procedures directly related to clinical studies, and the work initiated in 2022 on the Company's Environmental and Social Responsibility will be closely monitored.

MAIN CHANGES

As a continuation of the efforts devoted by the Company during fiscal year 2022, the Company will continue its work on internal control to achieve its internal governance goals. Accordingly, the Company plans to double its efforts to implement its policy to improve internal control mechanisms during fiscal year 2023. Therefore, the Company will strive to put into practice the risk management system and to focus on tracking the identified action plans by preparing a more detailed mapping of the risks encountered. The Company will also continue to update its internal control mechanism by taking into account the changes in its internal organization and its activity, as well as real time changes to its risk management process.

8. SERVICES OTHER THAN THE CERTIFICATION OF THE FINANCIAL STATEMENTS PROVIDED BY THE STATUTORY AUDITORS

- On December 2, 2022 EY verified the claim statement established as part of the issue of 550,000 share subscription warrants to the EIB to be subscribed as compensation for a claim and established in this context a note resulting from agreed procedures relating to the payment of the said warrants and a certificate of the depositary.

9. POWERS TO CARRY OUT FORMALITIES

We propose that you confer full powers on the bearer of copies or extracts of these minutes in order to perform all legal formalities.

The Board of Directors
Chairwoman

Appendix to the management report: Summary of transactions by management and persons mentioned in Article L. 621-18-2 of the French Monetary and Financial Code

A summary of the transactions mentioned in Article L.681-18-2 of the French Monetary and Financial Code during the 2022 fiscal year relating to the Company's shares is presented below:

Category (1)	Person concerned	Nature of the transaction (2)	Transaction date	Transaction amount (€)	Average unit price (€)	Number of shares
None						

(1) Categories:

a: the members of the Board of Directors, the Management Board, the Supervisory Board, the Chief Executive Officer, the Deputy Chief Executive Officer;

b: any other person who, under the conditions defined by the general regulation of the AMF, has the power to make management decisions concerning its development and strategy within the issuer, and also has regular access to inside information directly or indirectly concerning this issuer;

c: persons having, under conditions defined by decree of the Council of State, close personal ties with the persons mentioned in a and b.

(2) Nature of the transaction: A: Acquisition; C: disposal; S: Subscription; E: Exchange.

Appendix B - The Company's results over the last five years

Nature of the indications	2022 fiscal year	2021 fiscal year	2020 fiscal year	2019 fiscal year	2018 fiscal year
I. Share capital at year-end					
Share capital	€3,705,480.20	€3,705,480.20	€3,596,607.60	€3,001,144.80	€2,963,402.40
Number of existing common shares	18,527,401	18,527,401	17,983,038	15,005,724	14,817,012
Number of bonds convertible into shares	0	0	0	0	0
Number of existing common shares	18,527,401	18,527,401	17,983,038	15,005,724	14,817,012
II. Transactions and profit/(loss) for the period					
Revenue excluding tax	€3,302,807	€6,146,699	€9,742,877	€10,601,683	€9,600,963
Profit/(loss) before tax, depreciation, amortization and provisions	-€19,043,616	-€15,976,594	-€22,024,907	-€1,960,524	€1,170,394
Income tax (tax credit)	-€5,432,461	-€4,344,393	-€5,070,367	-€2,988,795	-€4,485,807
Profit (loss) after tax, depreciation, amortization and provisions	-€14,139,435	-€12,166,418	-€17,398,439	€125,113	€5,501,174
Amount of profit distributed	-€	- €	- €	- €	- €
III Operating earnings per share					
Profit/(loss) after tax, but before depreciation, amortization and provisions	-€0.73	-€0.63	-€0.94	€0.20	€0.07
Profit/(loss) after tax, depreciation, amortization and provisions	-€0.76	-€0.66	-€0.97	€0.01	€0.38
Dividend paid per share	-€	- €	- €	- €	- €
IV Personnel					
Number of average annual employees	57	53	45	35	29
Payroll	€5,723,674	€6,208,643	€4,359,307	€3,745,399	€3,011,508
Amounts paid in respect of social benefits	€2,752,820	€3,262,794	€2,247,621	€1,817,092	€1,354,951

Appendix C - Corporate governance report

In accordance with Article L. 225-37 of the French Commercial Code, the corporate governance report for fiscal year 2021 comprises information concerning the Board's composition, and the application of the principle of gender balance on the Board, the conditions for preparation and organization of the work of the Board of Directors, as well as information concerning the corporate officers. This report also specifies that the Company voluntarily applies a corporate governance code, indicates the specific arrangements concerning participation of shareholders in the General Shareholder's Meeting and presents the principles and rules adopted by the Board of Directors to determine the compensation and benefits in kind granted to the corporate officers. Finally, it mentions disclosure of the information pursuant to Article L. 225-100-3 of the French Commercial Code.

This report was reviewed by the Audit Committee at its meeting on April 25, 2023, in the presence of representatives of the OSE Immunotherapeutics' Statutory Auditors and was then approved by the Board of Directors at its meeting on April 27, 2023, in the presence of representatives of the OSE Immunotherapeutics' Statutory Auditors.

This report is presented as part of the Ordinary and Extraordinary General Shareholders' Meeting of OSE Immunotherapeutics to be held on June 22, 2023.

1. Supervisory and management bodies

Since the IPO of the Company, the Board of Directors has decided that the role of Chairman of the Board of Directors should be separate from that of Chief Executive Officer. The Board of Directors is chaired by Dominique Costantini. The Executive Management of the Company is assumed by Nicolas Poirier since October 7, 2022.

1.1. Board of Directors

1.1.1. Composition of the Board of Directors

These provisions are pursuant to Article 1 of the Board of Directors Internal Rules.

No one over the age of 70 may be appointed director if their appointment meant that more than one-third of the members of the Board of Directors would be over 70.

If this proportion is exceeded, the oldest director is deemed to have resigned automatically at the end of the Ordinary General Shareholders' Meeting called to approve the financial statements of the fiscal year during which this threshold was crossed.

The Board discussed the desired balance in its composition and in that of its committees, in particular concerning balanced gender representation, representation of nationalities and the diversity of skills, and the provisions capable of providing guarantees to shareholders and the market that its missions are accomplished with the necessary independence and objectivity.

The Company's directors originate from different backgrounds and have a variety of experience and skills thereby reflecting the goals of the Board of Directors. The Company complies with Law No. 2011-103 of January 27, 2011, which stipulates that the Board must include at least 40% of each gender.

The details of the corporate offices held by members of the Board of Directors in office on the date of this Universal Registration Document are given in the following table:

First name – Last name or corporate name of the member	Other corporate offices currently held In other companies	Other offices and positions held in other companies during the last five years and not held as of the date of this Universal Registration Document:
Dominique Costantini	- Director of Smart Immune	- Director of Abivax - Director of Theradiag SA - Director of Carthera SAS - Director of Sensorion - Director of Theranexus SAS
Maryvonne Hiance	- Vice Chairman of the Atlanpole Biotherapies cluster - Chairman of HealthTech For Care - Chairman of Olgram - Director of Pherecydes Pharma	- Chairwoman and Vice-Chairwoman of France Biotech
Elsy Boglioli	- Founder and Chief Executive Officer of Bio-Up - Independent Director of Gensight - Independent Director of Laverock Therapeutics - Member of the Supervisory Board of Inova Software, Metafora Biosystems, Womed	- None
Jean-Patrick Demonsang	- Chairman of Demonsang Consulting SAS	- Chairman of Parexi SAS - Chief Executive Officer of Genode Partners SAS - Chairman of the Supervisory Board of G1J Ile-de-France
Brigitte Dréno	- Consulting Firms: BMS, Fabre Oncology	- Deputy Vice-President for Scientific and Technical Culture at the University of Nantes - RHU SUccESS coordinator
Didier Hoch	- President of the Board of Directors of Pherecydes Pharma - Director of the University of the Underground Charity Foundation - Strategic Advisor for Goliver Therapeutics	- Chief Executive Officer of Pherecydes Pharma (2022) - Independent Director of DBV Technology, Genticel, Germitech - Member of the Strategic Board - Advisory Committee of Myastérix, Curavac, Director of the Fondation pour l'Université Grenoble Alpes
Nicolas Poirier	- Member of the Scientific Board of MabDesign and MAbSillico	- None
Alexandre Lebeaut	- Immunorx Pharma Inc., Director - Object Pharma Inc., Director - Calypso Biotech, Director	- I-ACT for Children, Chief Executive Officer - Vifor Pharma, Director
Gérard Tobelem	- Director of Dendrogenix	- Director of SupBiotech - Director of the Louis Dreyfus business foundation - Chairman of Théradiag SA

1.1.2 Composition of the operational management team

- Presentation of each member of the Board of Directors

The nine current members of the Board of Directors, whose current composition is detailed in Section 14.1 of this Universal Registration Document, combine international expertise in development of drugs, marketing, industry and finance, as well as experience with listed biotechnology companies.

DOMINIQUE COSTANTINI (68 YEARS OLD, FRENCH)	**286 BOULEVARD RASPAIL** **75014 PARIS**	**2,007,163 SHARES**
DIRECTOR, CHAIRWOMAN OF THE BOARD OF DIRECTORS, DIRECTOR OF THE DEVELOPMENT		
Professional experience / Areas of expertise		
Since co-founding OSE in 2012, Dominique Costantini has raised private equity funds in 2014, completed the Company's IPO in 2015, acquired Effimune in 2016 to lead the Company's development programs and contributed to the partnership agreements implemented in 2016 and 2018. She is the founder and former Chief Executive Officer of BioAlliance Pharma (1997–2011), which was renamed Oxneo in 2014 and is listed on Euronext Paris. Dominique has designed, developed and secured approval for innovative cancer therapies. She raised funds from 1999 to 2005 and completed an IPO for BioAlliance Pharma on Euronext in late 2005. Three successful stock market fundraisings were then based on product development benchmarks: two innovative products were approved in Europe and the United States. She has established international industrial partnerships, signing contracts worth more than €130 million. BioAlliance Pharma is the only French biotech company to have had two products registered with the FDA. Dominique gained more than 15 years of operational management experience in the pharmaceutical industry while working at HMR (now Sanofi). She led R&D and drug marketing activities from research to market in fields including immunology, endocrinology, inflammation, infection and oncology. Dominique Costantini is a medical doctor and immunologist (Université René Descartes Paris V).		
Duration of term of office		
April 27, 2012	Term of office in progress	
List of corporate offices and other positions held with French and foreign companies		
Offices and positions held within OSE Immunotherapeutics	**Other corporate offices and positions held outside the Group** **OSE Immunotherapeutics**	
Director and Director of Development	- Director of Smart Immune	

MARYVONNE HIANCE (74 YEARS OLD, FRENCH)	**35, RUE EDISON** **44000 NANTES**	**424,084 SHARES**

DIRECTOR, VICE-CHAIRMAN OF THE BOARD OF DIRECTORS

Professional experience / Areas of expertise

Maryvonne Hiance, who was previously the Chairman and co-founder of Effimune, is an engineer who specializes in nuclear science. For 14 years she managed a neutron studies program at FRAMATOME (Areva). Over the past 20 years, she has led several innovative biotechnology companies including SangStat Atlantic (whose parent company, SangStat Medical Corporation, was acquired by Genzyme in 2003 for its product portfolio in immunosuppression and transplantation), DrugAbuse Sciences and TcLand. Maryvonne also founded and managed Strategic Ventures, a consulting firm for technology companies. She has been a member of the French Strategic Council for Innovation and has served as advisor to the French SMEs and Industry Ministry. Maryvonne is Vice-Chairman of France Biotech.

Duration of term of office

May 31, 2016	Term of office in progress

List of corporate offices and other positions held with French and foreign companies

Offices and positions held within OSE Immunotherapeutics	**Offices and positions held outside OSE Immunotherapeutics**
Director and Director of Public Relations	- Director of Pherecydes Pharma - Vice Chairman of Atlanpole Biotherapies - Chairman of HealthTech For Care - Chairman of Olgram

ELSY BOGLIOLI (41 YEARS OLD, FRENCH)	**35, RUE DE BELLECHASSE** **75007 PARIS**	**0 SHARE**

DIRECTOR

Professional experience / Areas of expertise

Elsy Boglioli is the founder and Chief Executive Officer of Bio-Up, a healthcare consulting company that supports companies in their high growth or transformation phases, mainly in the field of cellular and gene therapies. She has extensive expertise and an large network in pharma and medtech companies.

Elsy is a graduate of the École Polytechnique de Paris and holds a master's degree in economics and management from the Pompeu Fabra University in Barcelona (Spain). She also holds a degree in immuno-oncology from the Institut Gustave Roussy in Paris.

Duration of term of office

6/24/2021	Term of office in progress

List of corporate offices and other positions held with French and foreign companies	
Offices and positions held within OSE Immunotherapeutics	**Offices and positions held outside OSE Immunotherapeutics**
Director	- Founder and Chief Executive Officer of Bio-Up - Independent Director of Gensight - Member of the Supervisory Board of Inova Software, Metafora Biosystems, Womed - Independent Director of Laverock Therapeutics

JEAN-PATRICK DEMONSANG (70 YEARS OLD, FRENCH)	**14, RUE DES ÉTANGS 44117 SAINT-ANDRE DES EAUX**	**30,000 SHARES**
DIRECTOR		
Professional experience / Areas of expertise		
Chairman and Chief Executive Officer of Seventure Partners until 2013, Jean-Patrick Demonsang supported the activities of more than 150 companies in the information technology and life sciences sectors. A great entrepreneur, having to his credit the creation and management of several SMEs, he is also started the first club for start-ups. Jean-Patrick Demonsang holds an MBA from HEC and a degree in physics.		
Duration of term of office		
April 10, 2014	Term of office in progress	

List of corporate offices and other positions held with French and foreign companies	
Offices and positions held within OSE Immunotherapeutics	**Offices and positions held outside OSE Immunotherapeutics**
Director, President of the Audit Committee	- Chairman of Demonsang Consulting SAS

BRIGITTE DRÉNO (70 YEARS OLD, FRENCH)	**10 RUE VOLTAIRE 44000 NANTES**	**0 SHARES**
DIRECTOR		
Professional experience / Areas of expertise		

Professor Brigitte Dréno is head of the Dermatology Department at the Nantes University Hospital Center, which develops research expertise and groundbreaking treatments in skin oncology. Brigitte Dréno is also the Director of the Biotherapy Clinical Investigation Center and Director of the Unit of Cell and Gene Therapy, and as such closely oversees all immuno-oncology advances. She is Vice Dean of the Medical School. In collaboration with the academic leadership, she supports OSE Immunotherapeutics' R&D initiatives on the Nantes University campus.

Duration of term of office

June 14, 2017	Term of office expiring at the GSM scheduled for June 22, 2023. It is proposed to renew her term of office.

List of corporate offices and other positions held with French and foreign companies

Offices and positions held within OSE Immunotherapeutics	Offices and positions held outside OSE Immunotherapeutics
Director	Consulting Firms: BMS, Fabre Oncology

DIDIER HOCH **(67 YEARS OLD, FRENCH)**	**1508 ROUTE DE BELLEGARDE** **LA SAUZEE** **42210 SAINT CYR LES VIGNES**	**7,334 SHARES**

DIRECTOR

Professional experience / Areas of expertise

Didier Hoch has more than 25 years of experience in the pharmaceutical industry. From 2000 to 2010, he was Chairman of Sanofi-Pasteur-MSD, a joint venture between Sanofi and Merck dedicated to vaccines. He also held various managerial positions at Rhône Poulenc Rorer, then Aventis (Vice-President Middle East, Africa). Previously, from 2002 to 2010, Didier Hoch was Vice-President and President of the association of vaccine manufacturers "Vaccine Europe" and Chairman of the LEEM Biotechnology Committee (2006-2012).

In 2014, Didier Hoch co-founded and managed the "Big Booster" start-up accelerator. He currently holds offices in healthcare companies including Pherecydes, Goliver Therapeutics and the University of the Underground Charity Foundation (Netherlands).

Didier Hoch is a medical doctor.

Duration of term of office

May 31, 2016	Term of office in progress

List of corporate offices and other positions held with French and foreign companies

Offices and positions held within OSE Immunotherapeutics	Offices and positions held outside OSE Immunotherapeutics
	- President of the Supervisory Board of Pherecydes Pharma

Director	- Director of the University of the Underground Charity Foundation - Strategic Advisor for Goliver Therapeutics

NICOLAS POIRIER (41 YEARS OLD, FRENCH)	**4, IMPASSE DE LA ROCHÈRE 44119 GRANDCHAMPS DES FONTAINES**	**192,802 SHARES**
DIRECTOR		
Professional experience / Areas of expertise		
Nicolas Poirier has been chief scientific officer of OSE Immunotherapeutics since 2016. He joined the company in 2009 as project leader and then as director of scientific programs. Nicolas Poirier holds a Ph.D. in immunology and has a strong expertise in the development of immunotherapies. His role has been to implement innovative therapeutic strategies on new targets and pathways in immunology addressing severe pathologies with high therapeutic need, thus making a robust contribution to the Company's growth. Along with his R&D team, he continues pursuing the identification of novel preclinical targets and translating them into first-class clinical-stage immunotherapies. He is the author of several high-level international publications in the area of immunotherapy. Nicolas Poirier holds a Doctorate of Sciences in Immunology.		
Duration of term of office		
June 26, 2019	Resignation from his mandate as Director representing the Companu's employee shareholders following his appointment as Chief Executive Officer, proposal for appointment as Director at the next GSM	
List of corporate offices and other positions held with French and foreign companies		
Offices and positions held within OSE Immunotherapeutics	**Offices and positions held outside OSE Immunotherapeutics**	
Director, Chief Executive Officer, Chief Scientific Officer	Member of the Scientific Board of MabDesign and MAbSillico	

ALEXANDRE LEBEAUT 66 YEARS OLD, FRENCH AND AMERICAN	8001 Woodmont Avenue Apt # 417 Bethesda, Maryland 20814 United States	**0 SHARE**
DIRECTOR		
Professional experience / Areas of expertise		

Alexandre Lebeaut has more than 25 years of relevant experience and leadership in innovation, research and development, ranging from preclinical to market, with successes particularly in the fields of immunology, oncology, immuno-inflammation and infectious diseases. He has held various international positions, mainly in the United States and in particular within Bluebird Bio, Sanofi, Novartis and Schering Plow Research Institute. More recently, Alexandre Lebeaut was "Executive Vice-President R&D and Chief Scientific Officer" at Ipsen in the United States. Alexandre Lebeaut holds a doctorate in medicine (Université de Paris Diderot Paris VII) and a pediatrician (Université Paris Descartes).		
Duration of term of office		
February 18, 2022 (by co-option)		Term of office in progress
List of corporate offices and other positions held with French and foreign companies		
Offices and positions held within OSE Immunotherapeutics		**Offices and positions held outside OSE Immunotherapeutics**
Independent director		- Immunorx Pharma Inc., Director - Object Pharma Inc., Director - Calypso Biotech, Director
GÉRARD TOBELEM **(75 YEARS OLD, FRENCH)**	**113, RUE MONGE** **75005 PARIS**	**31,250 SHARES**
DIRECTOR		
Professional experience / Areas of expertise		
Former professor of Hematology at the University of Paris 7 and Head of the Blood Diseases Department at the Lariboisière Hospital in Paris, Gérard Tobelem was Executive Chairman of the French Blood Establishment (L'Etablissement Français du Sang). He was awarded the first Diderot Innovation Prize in 2006 and has held strategic positions within the French Ministry of Higher Education and Research. He has also advised various international pharmaceutical companies on their R&D strategy.		
Duration of term of office		
16/06/2020		Term of office expiring at the GSM scheduled for June 22, 2023. It is proposed to renew his term of office.
List of corporate offices and other positions held with French and foreign companies		
Offices and positions held within OSE Immunotherapeutics		**Offices and positions held outside OSE Immunotherapeutics**
Director, President of the Company's Appointment and Compensation Committee		Director of Dendrogenix

- Changes in composition of the Board of Directors

The terms of office of Gérard Tobelem, Brigitte Dréno and Jean-Patrick Demonsang were renewed by the Shareholders' Meeting of June 16, 2020, for a term of three years expiring at the end of the Ordinary General Shareholders' Meeting to be called to approve the financial statements for the fiscal year ended December 31, 2022, i.e. the General Shareholders' Meeting scheduled on June 22, 2023.

The term of office of Dominique Costantini was renewed by the General Shareholders' Meeting of June 24, 2021 for a period of three years expiring at the end of the Ordinary General Shareholders' Meeting called to approve the financial statements for the fiscal year ended December 31, 2023.

Elsy Boglioli was appointed Director by the General Shareholders' Meeting of June 24, 2021 for a period of three years expiring at the end of the Ordinary General Shareholders' Meeting called to approve the financial statements for the fiscal year ended December 31, 2023.

The terms of office of Maryvonne Hiance, Didier Hoch, Nicolas Poirier and Alexandre Lebeaut were renewed by the General Shareholders' Meeting of June 23, 2022, for a period of three years expiring at the end of the Ordinary General Shareholders' Meeting called to approve the financial statements for the fiscal year ended December 31, 2024.

The term of office of Sophie Brouard expired at the General Shareholders' Meeting of June 23, 2022.

Moreover, following his appointment as Chief Executive Officer, Nicolas Poirier resigned from his mandate as Director representing the employee shareholders, effective at the next General Shareholders' Meeting scheduled on June 22, 2023.

You will be asked to decide on:
- The renewal of the terms of office of Gérard Tobelem and Brigitte Dréno;
- The appointment of Nicolas Poirier as a director;
- The appointment of Eric Leire as a a director;
- The appointment of Anne-Laure Autret-Cornet as a director representing the employee shareholders following the election by the employee shareholders.

Jean-Patrick Demonsang indicated that he would not be presenting himself for renewal of his term of office.

- Independence

These provisions are pursuant to Articles 1 and 11 of the Board of Directors Internal Rules.

As of December 31, 2022, the Company had five independent directors: Gérard Tobelem, Jean-Patrick Demonsang, Didier Hoch, Brigitte Dréno and Elsy Boglioli. Independent directors must fulfill the following criteria of the December 2008 AFEP-MEDEF code adopted as the Middlenext corporate governance code of December 2008, and revised in September 2021:

• not have been, during the last five years, and not be an employee or executive corporate officer of the Company or of a company in its group;

• not to have had, during the last two years, and not to be in a significant business relationship with the company or its group (customer, supplier, competitor, service provider, creditor, banker, etc.);

• not be a reference shareholder of the Company or hold a significant percentage of voting rights;

• have no close relationship or close family ties with a corporate officer or reference shareholder;

• have not been a Statutory Auditor of the Company in the last six years.

The Board of Directors discusses and reviews the qualification of independent directors every year prior to publication of the annual report. Subject to justifying its position, the Board may consider as independent one of its members who does not fulfill all these criteria, and vice versa; it may also consider that one of its members who fulfills all these criteria is not independent.

In the event that the permanent representative of a legal entity director qualified as independent ceases its position, this director will be deemed to have resigned.

Each of the independent directors fulfills the above-mentioned criteria.

- Representation of women and men

To date, the Company has 50% of women, in compliance with the regulations applicable to listed companies since January 1, 2017.

1.1.3 Functioning of the Board of Directors

These provisions are pursuant to Articles 2 and 3 of the Board of Directors Internal Rules.

- Missions of the Board of Directors

In compliance with Article 22 of the Company's Bylaws, the Board of Directors determines the Company's business strategies and ensures that they are implemented. Subject to the powers expressly granted by law to shareholders' meetings and to the extent of the corporate purpose, it examines any issue affecting the proper functioning of the Company and through its proceedings resolves matters that concern it.

The Board of Directors determines the Company's business strategies, validates them and ensures that they are implemented. Subject to the powers expressly granted to General Shareholders' Meetings and to the extent of the corporate purpose, it examines any issue affecting the proper functioning of the Company and through its proceedings resolves matters that concern it.

In this context, the Board of Directors approves the Company's significant transactions prior to their implementation, and in particular:

Regarding control:

- Adoption of the annual and semi-annual statutory and consolidated financial statements, and preparation of the Group management report and the semi-annual financial report;

- Verification of the relevance and consistency of the accounting rules adopted to prepare the Company's consolidated and statutory financial statements;

- Review of the means implemented by the Company, the Statutory Auditors and the internal audit to ensure that the statutory and consolidated financial statements are true and fair;

- Review of the financial position, cash position and commitments of the Company, adoption of the forward planning documents and corresponding reports;

- Review and approval of the budget;

- Monitoring of the effectiveness of the internal control and risk management systems and adoption of the corresponding report;

- Authorization of the related-party agreements, and in particular the agreements concluded to the benefit of the Chairman, the Chief Executive Officer or the Chief Operating Officers, corresponding to components of compensation, indemnities or benefits due or likely to be due as a result of the termination or change of their positions or subsequently;

- Prior authorization of decisions by Executive Management described in Chapter II of these regulations below:

Regarding appointments and compensation;

- Appointment and dismissal of the Statutory Auditors;

- Determination of the methods used to carry out Executive Management of the Company;

- Appointment and dismissal of the Chief Executive Officer and setting of his compensation;

- Appointment and dismissal of the Chief Operating Officers following proposal by the Chief Executive Officer, setting of their compensation, where appropriate;

- Selection and dismissal of the Chairman of the Board of Directors;

- Co-opting of directors in the event of resignation or death;

- Distribution of directors' fees;

- Notice of meeting for General Shareholders' Meetings, setting the agenda, preparation of the corresponding reports.

In relations with third parties, the Company is bound even for actions by the Board of Directors that do not fall within the corporate purpose unless it proves that the third party knew that the action in question exceeded this purpose or that it could not be unaware of this given the circumstances, it being stated that the mere publication of the bylaws is not sufficient to constitute this proof.

The Board of Directors may at any time perform the audits and verifications it deems appropriate. All directors must receive the information required for completing their assignments and they may obtain all documents they consider necessary from

the Executive Management. The Board of Directors may give any agent of its choice any delegation of authority within the bounds of its powers under the law and these bylaws.

It may decide to create working committees tasked with studying the issues the Board or the Chairman of the Board submits to it. The Board of Directors is not qualified to vote on or authorize a bond issue; these bylaws reserve that power for the General Shareholders' Meeting.

- Information for Directors

The Board of Directors carries out the verifications and controls that it deems appropriate, at any period during the year. For this purpose, each director must receive the information necessary to accomplish their mission.

In this context, the Chief Executive Officer shall provide each director with all the documents and information that it judges necessary to carry out their control mission.

The Chief Executive Officer, the Chairman of the Board of Directors, as well as the Chairman of each of the Committees, prior to each meeting of the Board of Directors, shall provide the directors with the information and documents necessary for them to fully carry out their mission. In particular, the Chairman of each Committee shall provide the directors with the reports, assessments or consultations prepared as part of their mission.

Directors who judge that they are not in a position to deliberate in full possession of the facts have a duty to inform the Board of this situation, and to demand the necessary information. Outside the sessions of the Board of Directors, the directors receive from the Chief Executive Officer the appropriate information required at any stage in the life of the Company or Group, if warranted by the importance or urgency of the information.

They receive the press releases issued by the Company, as well as a review of press articles and financial analysis recommendations concerning the Company.

- Notices of meetings, meetings and proceedings

The Board of Directors meets as often as is required in the interests of the Company, and at least once every quarter, by notice of meeting from its Chairman or on request from the Chief Executive Officer or from at least one third of the directors if it has not met for at least two months. The meetings are held either at the registered office, or at any other place specified by the sender of the notice of meeting.

The notices of meetings are issued by any written means, in particular by letter, electronic means or by facsimile, within a period of three business days except in the case of an emergency.

The Board of Directors may invite external persons to attend the Board meetings.

- Representation

Any director can give another director power of attorney to represent them and to vote on his/her behalf at a specific Board session.

The Board is the sole judge of the validity of the power of attorney which may be given by any written means, in particular by simple letter, by facsimile and including by electronic power of attorney.

Each director may only represent one other director.

The provisions of the two paragraphs above are applicable to the permanent representative of a legal entity director.

- Quorum and majority

The proceedings of the Board of Directors are only valid if at least half of its members are present.

In compliance with the bylaws, decisions are taken by the majority of the directors present or represented. In the event of a tied vote, the Chairman of the session has the casting vote.

An attendance register signed by all the members participating in each Board session is kept at the registered office. However, the names of directors participating remotely in the Board meeting are simply recorded on the attendance register.

- Video conference and other means of telecommunication

The Board of Directors can opt to allow its members to participate in the proceedings (discussions and votes) by video conference (which entails a combination of sound and vision), or by a means of telecommunication such as a telephone conference call enabling them to be identified by voice transmission by each participant, and guaranteeing their effective participation in accordance with the requirements of the applicable regulations.

Videoconferencing or telephone conference calls, or other means of telecommunication must meet the technical requirements guaranteeing effective participation in the meeting of the Board of Directors, the proceedings of which are transmitted, that is, transmission of voice and picture, or at least the voices of all the participants simultaneously and continuously.

If these requirements are met, the directors participating in the meeting by video conference or telephone conference call or other means of telecommunication are deemed to be present for calculation of the quorum and majority.

A director participating in the meeting by video conference, telephone conference call or other means of telecommunication can represent another director, provided that on the day of the meeting the Chairman is in possession of a power of attorney from the director thereby represented.

Recourse to videoconferencing, telephone conference calls or other means of telecommunication is prohibited when the Board of Directors is called to approve and control the separate financial statements and the consolidated/combined financial statements, preparation of the management report and the report on management of the Group, and on appointment or dismissal of the Chairman of the Board of Directors, the Chief Executive Officer and the Chief Operating Officers.

The register of attendance at Board of Directors' sessions must indicate, if necessary, that the relevant directors are participating by video conference or by means of telecommunication.

The minutes of the Board of Directors' meeting must indicate the names of the directors participating in the meeting via video conference or by means of telecommunication.

They must also report any technical incident that may occur concerning a video conference, telephone conference call or other means of telecommunication if this incident disrupted the proceedings of the session, including the interruption and restoration of remote participation.

If malfunctioning of the video conference or telephone conference call system or the means of telecommunication is noted by the Chairman of the session, the Board of Directors is entitled to deliberate and/or to continue with only the members that are physically present, or for whom transmission of voices and/or picture remains continuous and simultaneous, provided that the quorum requirements are met.

A director participating remotely in the Board meeting that cannot be deemed present due to a malfunction may then give power of attorney, provided it meets the requirements stipulated in Articles 1316 to 1316-4 of the French Civil Code (written document, e-mail, facsimile, etc.), to a director who is physically present, provided this power of attorney is known to the Chairman. Directors may also communicate a power of attorney in advance, stipulating that it will only take effect in the event of a malfunction preventing them from being deemed present.

- Participation of third parties and non-voting members at the sessions of the Board of Directors

Invitations

Depending on the items included on the agenda, the Chairman of the Board of Directors may decide, in particular following a proposal by a member of the Board of Directors, to invite any person they believe useful, whether or not a Company employee, to give a presentation or to clarify the discussions in preparation for the proceedings.

Statutory Auditors

The Statutory Auditors are given notice to attend all meetings of the Board of Directors during which the separate or interim financial statements are reviewed or adopted, consolidated/combined or not.

The Statutory Auditors are given notices of meetings at the same time as the members of the Board of Directors, but their notice is sent by registered letter with a request for acknowledgement of receipt.

Non-voting members

Non-voting members are given notice to attend all meetings of the Board of Directors.
They take part in the proceedings in an advisory capacity.
In particular, their mission is to ensure the bylaws are strictly enforced. In particular, their role is to provide information, advice and supervision to the Board of Directors.

- Confidentiality obligation

If third parties who are not members of the Board of Directors are invited to a session of the Board of Directors or to the preparatory session for such a meeting, the Chairman of the Board of Directors reminds them of their confidentiality obligations concerning the information received during the meeting of the Board of Directors or in advance of such a meeting.

- Board of Directors Internal Rules

The applicable Internal Rules are the Rules as adopted by the decision of the Board of Directors on March 27, 2015, amended on June 14, 2017 and on March 30, 2022. The complete version of the Board of Directors Internal Rules can be consulted, following a prior written request, and the Company's registered office.

- Presentation of the main provisions

The Internal Rules of the Company contain all of the provisions relating to the methods for assigning corporate governance duties to the different Company bodies. Accordingly, it gives details of all the powers of the Board of Directors and of all the advisory committees, as well as those of the Chairman of the Board of Directors and of the Chief Executive Officer. The Rules also contain the rules concerning ethics, detailing all the principles that the Company directors must uphold, in particular relating to insider trading and market transactions.

- Assessment of the Board of Directors

Upon the initiative of the Chairman, the members of the Board of Directors were invited, at the meeting of April 27, 2023, to give their opinion regarding the functioning of the Board, the Audit Committee and the Appointments and Compensation Committee, and on the preparation of its work for fiscal year 2022.

This self-assessment by the members of the Board of Directors of the Board's performance was carried out on the basis of precise criteria such as the operating methods and the effective contribution of its members.

The results of this assessment were discussed in an overall and open manner by the directors, who consistently work to improve internal communication.

1.1.4. Work of the Board of Directors in 2022

- Number of meetings

In 2022, the functioning of the Board was governed by the provisions of the bylaws. In addition to the obligatory Board meetings (approval of the separate and semi-annual financial statements), meetings were held as justified by the course of business.

During 2022, the Company's Board of Directors met nine times:

- January 14, February 18, July 13 and October 7, 2022 (changes in the governance).
- March 30, 2022 (2021 financial statements, organization of the Combined General Shareholders' Meeting).
- June 23, 2022 (update on the Company’s development strategy, allocation of 80,000 founders’ share warrants to the directors).
- September 22, 2022 (consolidated financial statements for the first half of 2022).
- November 22, 2022 (approval of the European Investment Bank loan and issuance of EIB founders’ share warrants).
- December 6, 2022 (update on the Company’s development strategy, determination of the achievement of the 2022 variable objectives of the management and setting of 2023 objectives).

The average attendance rate of the Board members was 91.67%.

- Main subjects discussed

During fiscal year 2022, the Board took a certain number of decisions relating in particular to the review of financial statements, and approval of the annual financial statements. It decided on the issue of financial instruments (free shares, share subscription warrants, founders' share warrants) and monitored the progress of Research & Development projects in T-cell-based vaccines (Tedopi®), in immuno-oncology (BI 765063, BiCKI® platform, CLEC-1, OSE-279), and in autoimmunity (FR104, OSE-127/S95011) and inflammation (OSE-230), on its own or in partnership. It also carried out strategic reviews of the Company's assets in order to align the Company's portfolio with the required needs (in terms of financial, human and organizational resources, etc.). The Board of Directors also worked on changes in the Company's governance following the departure of its previous Chief Executive Officer in 2022.

1.1.5. Limitations placed on the powers of the Chief Executive Officer by the Board of Directors

These provisions are stipulated in Chapter II of the Board of Directors' Internal Rules.

The position of Chief Executive Officer has been assumed by Nicolas Poirier since October 7, 2022, who is invested with the most extensive powers to take action in any circumstances in the name of the Company, within the limits nevertheless of the provisions of Article 10 of the Internal Rules of the Board of Directors.

Accordingly, the Chief Executive Officer cannot adopt certain decisions or conclude certain acts, commitments or contracts if these have not been authorized in advance by the Board of Directors.

As an internal measure not binding on third parties, the Chief Executive Officer may not take the following decisions outside the limits set by the annual budget adopted and approved by the Board of Directors without the prior agreement of the Board:

- Decisions relating to acquisition or sale in any form, in return for payment or not, rental, lease, of any real estate asset or intangible non-current assets;
- Any proposal to create subsidiaries or to acquire Companies (or a business) including any project to acquire a holding in any entity, any project to sell, liquidate or dissolve subsidiaries, to start new business activities, or to take under lease management all or part of any business;
- Taking out a loan for an amount greater than €400,000 excluding the annual budget with the exception of bank overdrafts according to the authorization of the overdraft authorized by the banks, or deposits granted by partners:
- Conclude contracts or investments relating to the Company's activity corresponding to an income or expense greater than €400,000 excluding the annual budget per fiscal year;
- Constitute sureties, grant guarantees, endorsements greater than €500,000;
- Grant loans;
- Conclude agreements with shareholders;
- Any decision relating to initiation of a dispute, conduct of legal proceedings and any decision concerning any transactional settlement of the dispute;
- Pronounce the early dissolution of a subsidiary in which the Company holds all or more than the majority of the equity securities and voting rights.
- Any project to grant licenses, to sell or acquire licenses, for any intellectual property right that the Company holds such as, for example, patents, know-how or brands not identified in the annual budget, with the exception of that pertaining to the ordinary course of business of the Company.

Similarly, as an internal measure not binding on third parties, the Chief Executive Officer cannot without the prior agreement of the Extraordinary General Shareholder's Meeting:

- Liquidate, dissolve or close down the Company, including any closure concerning all or part of the Company's activity, or any event deemed to constitute a liquidation (including its methods and conditions);
- Carry out any substantial modification in the type or nature of the Company's activity;
- Acquire significant shares or assets from another company or any other economic entity or conclude any transaction outside the normal sphere of business;
- Any decision concerning a project for merger, demerger or contribution concerning the Company;
- Any decision relating to a proposal to issue securities, to increase or reduce the share capital and any decision relating to a proposal to reorganize the share capital (share buyback, reduction in number of shares, etc.), except for share capital increases resulting from the exercise of share subscription warrants or founders' warrants;
- Any decision relating to a proposal to distribute dividends, interim dividends or reserves of any kind whatsoever;
- Any decision relating to a proposal to issue or allocate founders' warrants, share subscription warrants or any other security; setting of methods for exercise or subscription of these securities.

For all intents and purposes, it is specified that these limitations are applicable to the function of Chief Executive Officer, regardless of the person performing this duty.

1.1.6. Combination of employment contract and duties as corporate officers

Dominique Costantini, Chairwoman of the Board of Directors, has held an open-ended employment agreement since July 1, 2014 as Director of Development. Her gross annual compensation is €302,500 with variable compensation of up to three months' salary depending on the achievement of objectives.

These activities are thus significantly different from those of the Chairman of the Board of Directors (Article 20 of the bylaws) and Chief Executive Officer (Article 25 of the bylaws). They are above all essential so that the Company can continue to advance its preclinical and clinical programs and seek new targets of therapeutic interest for patients. Lastly, they are part of the continuity and stability that the Company needs in this period of managerial transition, due to her length of service and the distinct technical roles that Dominique Costantini exercises in drug development. At its meeting of January 14, 2022, the Board of Directors confirmed the hierarchical relationship of the functional organization in place within the Company. The scope of her employment contract includes the implementation of strategies to define and achieve proofs of concept and explore mechanisms of action.

Dominique Costantini receives no compensation as Chairwoman of the Board of Directors.

Nicolas Poirier, Chief Executive Officer since October 7, 2022, signed an open-ended employment agreement as Chief Scientific Officer on May 31, 2016, with a gross annual compensation of €250,000 since July 1st, 2021, and a variable compensation of up to 3 months' salary depending to the achievement of objectives.

When he was appointed as Chief Executive Officer, the Board of Directors confirmed the maintenance of this contract due to his seniority and the distinct technical functions that Nicolas Poirier performs in terms of Research, and in particular with the supervision of all of immunological research and that of the Company's industrial property. He is placed under the authority of the Board of Directors from whom he takes his instructions and to whom he reports. The characteristics of his employment contract are linked to the scientific management.

Nicolas Poirier receives no compensation as Chief Executive Officer.

1.1.7. Delegations of authority and powers granted to the Board of Directors for capital increases

See Section 19.1.4 of the Universal Registration Document.

1.1.8. Board of Directors Committees

1.1.8.1. Audit Committee

- Composition

The Audit Committee consists of Jean-Patrick Demonsang (Committee Chairman) and Didier Hoch, appointed for a two-year term at the Board of Directors' meeting on June 24, 2021.

The independent members are Jean-Patrick Demonsang and Didier Hoch. Jean-Patrick Demonsang also has specific financial, accounting and auditing skills.

- Operating procedures

  - Duties

The Audit Committee is responsible for overseeing issues relating to the preparation and audit of accounting and financial information. It is responsible for continually assessing the existence and effectiveness of the Company's financial control and risk control procedures, and has as its duties:

Internal control

- Ensuring that the internal control and risk management systems are effective;
- Verifying the smooth operation with assistance from the Finance Department;
- Reviewing the schedule of internal and external audits;
- Ensuring that the Statutory Auditors conduct the statutory audit of the separate financial statements and, where applicable, the consolidated financial statements;

Statutory financial statements and financial information

After regularly reviewing the financial position, the cash position and the commitments appearing in the Company's separate financial statements:

- Reviewing the accounting and financial documents, annual and interim financial statements;
- Overseeing the process of issuing the statutory and consolidated/combined financial statements and the process of preparing the financial information;
- Reviewing the internal control measures;
- Reviewing the material risks for the Company, particularly off-balance sheet risks and commitments;
- Validating the relevance of accounting rules and choices;
- Verifying the relevance of the financial information reported by the Company.

Risk management

- Reviewing any item likely to have material, financial and accounting impacts;
- Reviewing the status of major litigation;
- Reviewing off-balance sheet risks and commitments;
- Reviewing the relevance of the risk monitoring procedures;
- Reviewing any related-party agreements.

Statutory Auditors

- Leading the selection of the Statutory Auditors, managing their compensation and ensuring their independence;
- Ensuring the proper implementation of their assignment;
- Monitoring the statutory audit of the separate financial statements and, where applicable, the consolidated financial statements by the Statutory Auditors;
- Establishing the rules for using the Statutory Auditors for tasks other than the audit of the financial statements and ensuring the proper implementation of their assignment;
- Issuing a recommendation on the proposals for the appointment and potential reappointment of the Statutory Auditors presented to the General Shareholders' Meeting, their fees and any issues related to their independence.

- Internal Rules

The operating procedures of the Audit Committee are governed by Article 7 of the Internal Rules of the Board of Directors. These Internal Rules may be viewed at the Company's registered office upon prior written request.

- Work in 2022

The Audit Committee met twice in 2022, to review and approve the statutory and consolidated financial statements for fiscal year 2021 (March 28, 2022) and to review and approve the consolidated financial statements for first-half 2022 (September 20, 2022).

1.1.8.2. Appointments and Compensation Committee

- Composition

The Appointments and Compensation Committee consists of Gérard Tobelem (Committee Chairman), Maryvonne Hiance and Elsy Boglioli, appointed for a two-year term at the Board of Directors' meeting on June 24, 2021.

The independent members are Gérard Tobelem and Elsy Boglioli.

- Operating procedures

- Duties

The Appointments and Compensation Committee issues recommendations to the Board of Directors on the following topics:

- Advice and assistance regarding compensation, the pension and welfare benefit plan, supplementary pensions, benefits in kind, various cash entitlements of the executive corporate officers, allocations of free or performance shares, stock subscriptions or purchase options;

- The determination of the procedures for setting the variable portion of the compensation of the executive corporate officers, and overseeing the enforcement of these procedures;

- The distribution of the directors' fees, where necessary, to the directors taking into account their attendance record and tasks accomplished on the Board of Directors;

- Any extraordinary compensation of the directors for specific assignments or duties given to them by the Board;

- Any changes to the composition of the Board of Directors or the Executive Management;

- Prevention of conflicts of interest on the Board of Directors;

- Oversight of the establishment of structures and procedures making it possible to apply proper governing practices within the Company;

- Ensuring compliance with ethical principles within the Company and in its relations with third parties;

- Discussions on the classification of independent director for each director when the director is first appointed and every year before the publication of the Universal Registration Document, and presentation of the report of its recommendations to the Board of Directors.

In addition, the Executive Management proposes to it the various stock subscriptions or purchase option plans, equity warrant plans, founders' warrant allocation plans or free share allocation plans.

- Internal Rules

The operating procedures of the Appointments and Compensation Committee are governed by Article 6 of the Board of Directors' Internal Rules. These Internal Rules may be viewed at the Company's registered office upon prior written request.

- Work in 2022

The Appointments and Compensation Committee met five times in 2022.

1.1.9. Statements relating to the Board of Directors

In the last five years, none of the members of the Company's Board of Directors have been:

– Convicted of fraud or subject to an incrimination or official public sanction by the statutory or regulatory authorities;

– Involved in any bankruptcies, receiverships or liquidations as a manager or corporate officer;

- Prevented from acting as a member of an administrative, management or supervisory body or from participating in the management or conduct of business of an issuer;

- Subject to any incrimination and/or official public sanction by the statutory or regulatory authorities (including designated professional organizations).

There are no family ties between directors.

1.1.10. Conflicts of interest

- Describe arrangements for preventing and managing conflicts of interest

Each director strives to avoid any potential conflict between their moral and material interests and those of the companies. He or she notifies the Board of Directors in advance and in full of any actual or potential conflicts of interest between him or herself (or any other legal or natural person with whom he or she has business dealings) and the Company or any of the companies in which the Company has an investment or any of the companies with which the Company is planning on entering into an agreement of any type in which he or she may be directly or indirectly involved.
Directors must notify the Board of Directors of any conflict of interest that arises after taking office as soon as they become aware of it. They must not take part in any discussions and decision-making related to the issues in question and, where appropriate, must resign.

If a member of the Board of Directors has a doubt as to the existence of a conflict of interest or potential conflict of interest, he/she must immediately notify the Chairman of the Board of Directors who must independently decide whether there are grounds for notifying the Board of Directors.

If the Board member referred to in the previous paragraph is also the Chairman of the Board of Directors, he/she should notify the Board of Directors.

An absence of information amounts to the acknowledgement that no conflict of interests exists.

Where the agreement in question is not an agreement entered into under normal conditions, the relevant Board member shall not take part in the vote on entering into the agreement in question nor in the discussion prior to this vote.

Moreover, the Chairman of the Board of Directors, members of the Board of Directors, Chief Executive Officer and any Chief Operating Officers will not be required to disclose to any Board members of whom they have good reason to believe has a conflict of interest within the meaning of this article, information or documents relating to the agreement or transaction giving rise to the conflict of interest, and will inform the Board of Directors of this lack of such disclosure.

- List potential conflicts of interest and state the opinion of the Board of Directors

To the Company's knowledge, as of the date of this Universal Registration Document, there are no existing or potential conflicts of interest between the duties towards the Company and the private interests and/or duties of the individuals that comprise the administrative, management and executive management bodies.

- Agreements between the members of the Board of Directors and the companies of the OSE Immunotherapeutics group

As indicated in Section 1.1.5, Ms. Costantini has an open-ended employment agreement since July 1, 2014, as Head of Development, for gross annual compensation of €302,500 and a variable compensation up to 3 months of salary depending on the achievement of objectives.

As indicated in Section 1.1.5, Nicolas Poirier, Chief Executive Officer, signed an open-ended employment agreement as Chief Scientific Officer on May 31, 2016, for gross annual compensation of €250,000 since July 1st, 2021, and variable compensation of 3 months of salary depending on the achievement of objectives.

1.2. Application of the Middlenext Corporate Government Code for listed companies.

Through a decision dated March 27, 2015, the Board of Directors wished to establish Internal Rules in order to specify, supplement and implement the rules for its organization and operation that apply to it under the law (and to its committees), the Company's regulations and bylaws, and the ethical rules that apply to all the directors and the corporate governance principles by which it refers (Middlenext Corporate Governance Code revised in September 2021).

In accordance with the law of July 3, 2008, the disclosures presented herein are established by referring to the corporate governance code and additional recommendations regarding communication on the compensation of executive corporate officers of listed companies as defined by Middlenext. The Middlenext Code used as a reference by the Company can be consulted at: https://www.middlenext.com/IMG/pdf/c17_cahier_14_middlenext_code_de_gouvernance_2021-2.pdf.

The Reference Code contains key areas of vigilance to ensure proper governance of French companies with reminders of the questions the Board of Directors must ask itself to promote effective governance. The Company's Board of Directors acknowledged these areas of vigilance at its meeting on April 27, 2023.

The Reference Code contains recommendations relating more specifically to corporate officers and the Board of Directors. The Company complies with all recommendations in the Reference Code.

1.3. Compensation and benefits of any kind paid or allocated for the last fiscal year ended to management

In accordance with Article L. 22-10-34 I and II of the French Commercial Code, the Ordinary General Shareholders' Meeting called to approve the financial statements closed on December 31, 2022, will approve:

(a) information relating to the compensation of executive corporate officers referred to in I of Article L. 22-10-9 of the French Commercial Code (general ex post vote); and on

(b) the fixed, variable and exceptional items making up the total compensation and benefits of any kind paid or allocated in respect of the previous fiscal year by separate resolutions for the executive corporate officers.

The General Shareholders' Meeting must explicitly approve the payment of variable or exceptional compensation items (specific ex post vote). It is specified, concerning the executive corporate officers (i.e. the Chairman of the Board of Directors and the Chief Executive Officer), that the payment of variable and exceptional compensation is subject to approval by the General Shareholders' Meeting of the components of compensation of the relevant officer. Only the resolutions relating to the compensation of Dominique Costantini for the fiscal year ended December 31, 2022, will be submitted to a specific ex post vote at the next General Shareholders' Meeting, as Nicolas Poirier is not compensated for his corporate office but under his employment agreement (as Chief Scientific Officer).

The payment of the sum allocated to the directors will be suspended if the information relating to the compensation of the corporate officers mentioned in I of Article L. 22-10-9 of the French Commercial Code is not approved by the General Shareholders' Meeting, until a revised compensation policy submitted by the Board of Directors is approved at a future General Shareholders' Meeting.

1.3.1. Compensation of executive corporate officers

The work of the Appointments and Compensation Committee is based on review meetings through the course of the year and interim preparatory meetings chaired by the Committee Chairman. The principles and criteria for setting, distributing and allocating the components of total compensation and benefits in kind of executive corporate officers of OSE Immunotherapeutics for the 2022 fiscal year were thus reviewed by the Appointments and Compensation Committee before being proposed to and approved by the Board of Directors.

The Board will present the components of compensation due or allocated to each of the executive corporate officers in respect of the fiscal year ended to the Ordinary Annual General Shareholders' Meeting for approval. This presentation is to be followed by a mandatory shareholder vote. Should the Ordinary General Shareholders' Meeting reject the proposal, following the recommendation of the Appointments and Compensation Committee, the Board shall vote on the changes to be made to the compensation due or allocated in respect of the fiscal year ended or the future compensation policy. It will immediately post a statement on the Company's website setting how it intends to act on the vote by the Ordinary General Shareholders' Meeting and submits a report at the following meeting.

The Appointments and Compensation Committee submits a proposal to the Board of Directors on the compensation of executive corporate officers consistent with the rules for setting such compensation in view of the medium-term outlook and Company's results.

The Committee draws on market practices of comparable Companies in particular in order to determine the structure of this compensation. These surveys are conducted with reference to a panel of French companies with similar characteristics, selected according to the following criteria: market capitalization, industrial activity, revenue, total workforce.

It ensures that none of the components of compensation are disproportionate and analyzes compensation as a whole, taking into account all components.

In fiscal year 2022, Dominique Costantini and Nicolas Poirier (from October 7, 2022) were the only executive corporate officers. No compensation was paid to executive corporate officers during 2022 in respect of their corporate offices (other than directors' fees paid to all directors present).

- Components of the compensation paid in 2022 or allocated in respect of the same fiscal year to the Chairman of the Board of Directors subject to the approval of the next General Shareholders' Meeting (specific "ex post" vote).

In accordance with the provisions of Article L. 22-10-34 II of the French Commercial Code, the next Ordinary General Shareholders' Meeting will be asked to vote on a draft resolution relating to the components of compensation allocated in 2022 to the Chairman of the Board of Directors, Ms. Dominique Costantini:

Dominique Costantini has held an open-ended employment contract since July 1, 2014, for her position as Director of Development. The compensation under this employment agreement is calculated on the basis of €302,500 in gross annual salary. This compensation was confirmed at the meeting of the Board of Directors on June 23, 2022, in accordance with the

compensation criteria set out in Article 2 of the Board of Director's Internal Rules (comprehensiveness, balance between the different components of compensation, consistency, legibility of rules, balance, transparency), and on the basis of the benchmark for compensation of equivalent biotech management.

Variable compensation equal to up to three months' salary is provided for based on the achievement of certain targets.

At its meeting of December 7, 2021, the Board of Directors set the following objectives for Dominique Costantini in respect of the 2022 fiscal year under her contract as Director of Early Development: continue to develop the clinical portfolio; anticipate the future with new Research projects to bring to the Clinic. These objectives were met in the 2022 fiscal year. The variable compensation of three months' salary was paid in cash up to 80%.

The Board of Directors meeting of June 23, 2022 granted 10,000 founders' share warrants to each director (excluded to Nicolas Poirier).

- Components of the compensation paid in 2022 or allocated in respect of the same fiscal year to the Chief Executive Officer subject to the approval of the next General Shareholders' Meeting (specific "ex post" vote).

In accordance with the provisions of Article L. 22-10-34 II of the French Commercial Code, the next Ordinary General Shareholders' Meeting will be asked to vote on a draft resolution relating to the components of compensation allocated in 2022 to the Chief Executive Officer, Mr. Nicolas Poirier:

Since Nicolas Poirier is only remunerated under his employment contract, the elements making up his remuneration as well as the benefits in kind granted to him are presented here for information only:

Nicolas Poirier, elected director representing employee shareholders on June 26, 2019, is employed as Chief Scientific Officer under an employment contract dated May 31, 2016. The annual gross compensation under this employment contract is of €250,000 since July 1, 2021, with a variable compensation of three months of salary based on the achievement of objectives. His pre-existing employee mandate and being precisely the basis of his appointment as director representing employee shareholders, it was considered that Nicolas Poirier's employment contract constituted a current agreement entered into under normal conditions.

Nicolas Poirier was appointed Chief Executive Officer on October 7, 2022. He does not receive any compensation for this.

- Components of the compensation paid in 2022 or allocated in respect of the same fiscal year to the other corporate officers (for information purposes only).

None

1.3.2. Information on the compensation granted during the fiscal year ended on December 31, 2022, to corporate officers and submitted to the approval of the General Shareholders' Meeting in accordance with article L. 22-10-34-i of the French Commercial Code (general "ex post" vote)

This section presents, for each corporate officer of the Company, all the information mentioned in Article L. 22-10-9 I of the French Commercial Code relating to their compensation for the fiscal year 2022.

In accordance with the provisions of Article L. 22-10-34 I of the French Commercial Code, the shareholders of the Company will be asked to vote on this information in a resolution submitted to the next General Shareholders' Meeting.

- Information on the compensation granted to executive corporate officers for the fiscal year ended December 31, 2022.

  The total compensation and benefits in kind owed to the Chairman of the Board of Directors and the Chief Executive Officer during the past fiscal year are presented in Tables 1 and 2 using the AMF nomenclature in the 2022 Universal Registration Document (Section 13.1), which distinguishes between fixed, variable and exceptional components of this compensation.

  The relative proportion of fixed and variable compensation in the total compensation due to executive corporate officers during fiscal year 2022 is approximately as follows:

  For Dominique Costantini, Chairwoman of the Board of Directors, fixed compensation represents 80% and variable compensation represents 20% of total compensation.

  The payment of variable and exceptional components of compensation will be subject to and suspended until the General Shareholders' Meeting approves the components of compensation components of the relevant executive corporate officer. Consequently, the Company does not foresee the option of requesting the return of variable compensation.

  The last General Shareholder's Meeting on June 23, 2022, in its 10th and 11th resolutions, in accordance with the law in force at the time, approved the principles and criteria for setting, distributing and allocating the fixed, variable and exceptional components of the total compensation and benefits of any kind attributable to the executive corporate officers in respect of the fiscal year ended December 31, 2021.

  The Company has not deviated from the procedure for implementing the compensation policy or made any exceptions to the policy.

- Breakdown of compensation and benefits in kind for each executive corporate officer

None

- Summary of compensation and benefits in kind of executive corporate officers

None

- Summary of employment contracts, specific retirement benefits, severance payments and non-compete clauses of executive corporate officers

The Company has not provisioned sums for the purpose of payment of pensions, retirement and other benefits for the benefit of corporate officers and/or executive corporate officers who do not benefit elsewhere (or have not benefited) from severance or a hiring bonus within the Company.

- Information on the compensation granted to the directors for the fiscal year ended December 31, 2022

  All compensation received by directors for their term of office during the past fiscal year is presented in table 3 in Section 13.1. of the 2022 Universal Registration Document.

If, following a change in its current composition, the Board of Directors was no longer composed in accordance with the first paragraph of Article L. 225-18-1 of the French Commercial Code, the payment of compensation to the Directors for their participation in the work of the Board would be suspended. The payment would be reinstated when the composition of the Board of Directors is legally restored, including the arrears since the suspension.

- Equity ratios between the level of management compensation and the average and median compensation of the Company's employees and annual change in compensation, Company performance and equity ratios.

This presentation is in accordance with the terms of Article L.22-10-9 of the French Commercial Code.

It sets out the level of compensation of the Chairman of the Board of Directors and the Chief Executive Officer as a ratio of both the mean compensation of employees and the median compensation of employees (excluding corporate officers) of the Company, as well as how these ratios have changed over the previous two fiscal years.

The ratios below were calculated on the basis of fixed and variable annualized compensation paid in the relevant fiscal years as well as free shares and founders' warrants allocated in the same periods at fair value. The scope of this information is based on the workforce of OSE Immunotherapeutics.

	2018 fiscal year	**2019 fiscal year**	**2020 fiscal year**	**2021 fiscal year**	**2022 fiscal year**
Chairman of the Board of Directors *					
Ratio with average employee compensation	597%	470%	596%	655%	468%
Ratio with median employee compensation	799%	622%	861%	866%	640%
Chief Executive Officer **					
Ratio with average employee compensation	1351%	1514%	2441%	799%	1238%
Ratio with median employee compensation	1809%	2004%	3525%	1057%	1694%

* Ms. Dominique Costantini was Chief Executive Officer between 2014 and March 2018 and has been Chairwoman of the Board of Directors since that date. The ratios were calculated on the basis of aggregate compensation paid to Ms. Costantini for her office and employment contract. Free share allocations were also factored in when calculating these ratios.
**The ratios were calculated on the basis of aggregate compensation paid to the successive chief executive officers over 2022 (Mr. Alexis Peyroles from January 1st to January 14th, 2022, including his severance pay, Mr. Alexis Vandier from July 13th to October 7th, 2022, Mr Nicolas Poirier from October 7th to December 31st, 2022) for their respective term of office and employment contract. Free share allocations were also factored in when calculating these ratios.

Given its activity, the Company believes that no financial information is relevant to qualify its performance over the last five years.

1.4. Compensation policy for corporate officers for the fiscal year 2023 (principles and criteria for setting, distributing and allocating components of compensation for executive corporate officers for the purposes of the ex-ante vote).

In accordance with Article L. 22-10-8 of the French Commercial Code, this report sets out the compensation policy

for corporate officers, which is the subject of a draft resolution submitted to the approval of the General Shareholders' Meeting held to approve on the financial statements for the fiscal year 2022.

If the General Shareholders' Meeting does not approve the resolution(s) for this purpose, the compensation will be determined in accordance with the compensation allocated for the previous fiscal year.

As of the date of this Universal Reference Document, OSE Immunotherapeutics has two executive corporate officers: Dominique Costantini, Chairwoman of the Board of Directors and Nicolas Poirier, Chief Executive Officer since October 7th, 2022, and 9 directors including Dominique Costantini and Nicolas Poirier.

Dominique Costantini and Nicolas Poirier are paid by the Company under her employment agreement and not under their term of office. The Company's directors are compensated for an activity remuneration corresponding to a fix amount for each participation to the Board of Directors and granted by the Board of Directors.

1.4.1. Compensation policy for all corporate officers

- General principles

In accordance with the provisions of Article L. 22-10-8 of the French Commercial Code, this section sets out the principles and criteria for setting the fixed, variable and exceptional components of the total compensation and benefits in kind of executive corporate officers: Chairman of the Board of Directors and Chief Executive Officer of OSE Immunotherapeutics for the 2023 fiscal year.

On the basis of a report issued by the Board of Directors, a proposal will be submitted to the Combined General Shareholders' Meeting on June 22, 2023, to approve the compensation policy of executive corporate officers for the next fiscal year.

In the event that the Combined General Shareholders' Meeting of June 22, 2023, does not approve the resolution adopting the compensation policy for executive corporate officers, compensation will be set in line with the compensation allocated in the previous fiscal year or, if no such compensation was allocated in respect of the previous fiscal year, in line with current Company practice.

In accordance with Article L. 22-10-8 of the French Commercial Code, the payment of variable and exceptional components of compensation will be subject to the approval by the General Shareholders' Meeting of the components of the compensation of the relevant individuals under the conditions set out in Article L. 225-100 of the French Commercial Code.

In accordance with the law of July 3, 2008, the disclosures presented herein are established by referring to the corporate governance code and additional recommendations regarding communication on the compensation of executive corporate officers of listed companies as defined by Middlenext.

In accordance with Article 2 of the Internal Rules of the Board of Directors, in order to determine the level of compensation of its management as well as the information disclosed in this respect, the Board of Directors will draw on the following seven principles.

- Comprehensiveness: determining the compensation of executive corporate officers must be comprehensive: fixed part, variable part (bonuses), stock-options, free shares, attendance fees, retirement conditions and personal benefits must be factored in when assessing overall compensation.

- Balance between the different components of compensation: reasons must be given for each component of compensation which must be in the Company's general interest.
- Benchmark: insofar as possible, this compensation must be assessed based in the context of a given role and reference market and proportionate to the Company's position, while paying attention to its inflationary impact.
- Consistency: the compensation of the executive corporate officer must be consistent with that of other managers and employees within the Company.
- Legibility of rules: rules must be simple and transparent; performance criteria used to calculate the variable part of compensation or, where relevant, to allocate options or free shares, must be consistent with the business's objectives, be stringent, explicable and, where possible, long-term.
- Balanced: when determining compensation and the allocation of options or free shares, the right balance must be struck between the general interest of the Company, market practices and the performance of management.
- Transparency: annual information is provided to shareholders on the compensation received by management in accordance with applicable regulations.

- Policy on the distribution of directors' fees

All compensation received by directors for their term of office during the past fiscal year is presented in table 3 in Section 13.1. of the 2022 Universal Registration Document.

If, following a change in its current composition, the Board of Directors was no longer composed in accordance with the first paragraph of Article L. 225-18-1 of the French Commercial Code, the payment of compensation to the Directors for their participation in the work of the Board would be suspended. The payment would be reinstated when the composition of the Board of Directors is legally restored, including the arrears since the suspension.

The Board of Directors may receive fixed annual compensation in the form of directors' fees, set by the General Shareholders' Meeting, the amount of which is charged to operating expenses.

The Board of Directors decides on the distribution of directors' fees among directors following a proposal by the Appointments and Compensation Committee. This distribution may take into account directors' specific experience, their actual participation at Board meetings or their actual participation at Committee meetings.

Under Article L. 225-46 of the French Commercial Code, they may also receive exceptional compensation for specific assignments or offices assigned by the Board.

Directors' fees remain set at €300,000 per year.

1.4.2. Compensation policy for executive corporate officers

The overall compensation of executive corporate officers is composed of the following:
• a portion of fixed compensation under their employment contract;
• variable compensation components under their employment contract.

These components are precisely defined by the Board of Directors but are not made public in full for reasons of confidentiality.

1.4.2.1 Description of the principles and criteria on which the Chairman of the Board of Directors' compensation is based

a) No fixed or variable compensation

According to the Company's bylaws, the compensation of the Chairman of the Board of Directors of OSE Immunotherapeutics is set by the Board for the duration of his three-year term. However, the Chairman of the Board of Directors does not receive any fixed compensation in respect of his office, nor variable compensation.

For fiscal year 2023, Ms. Costantini will receive her salary as Director of Development on the basis of a gross annual compensation of €302,500.

For the fiscal year 2023, her objectives were set as follows: to obtain an additional financing, to successfully continue the clinical development of the Company's portfolio, drive R&D and scientific recognition. Variable compensation equivalent to no more than three months' salary would be paid in cash.

b) No exceptional compensation

Other than her compensation in respect of her unemployment contract (see a) above), the Chairman of the Board of Directors is not entitled to severance pay or to any compensation in respect of a non-compete clause.

c) Allocation of directors' fees

The Chairwoman of the Board of Directors, like the other directors, receives compensation.
As a reminder, Dominique Costantini received a net compensation of €25,988 as a director in 2022.

d) No other benefits

She receives no other benefits.

1.4.2.2 Description of the principles and criteria on which the Chief Executive Officer's compensation is based

According to the Company's bylaws, the compensation of the Chief Executive Officer of OSE Immunotherapeutics is set by the Board.

a) No fixed or variable compensation

The Chief Executive Officer does not receive any compensation in respect of his corporate office.

For the fiscal year 2023, Nicolas Poirier will receive his salary as Chief Scientific Officer based on a gross annual compensation of €250,000.

For the fiscal year 2023, his objectives were set as follows: to obtain an additional financing, to successfully continue the clinical development of the Company's portfolio, drive R&D and scientific recognition. Variable compensation equivalent to no more than three months' salary would be paid in cash.

b) No exceptional compensation

Other than compensation in respect of his employment contract (see a) above), the Chief Executive Officer is not entitled to severance pay nor to compensation in respect of a non-compete clause.

c) Allocation of securities giving access to capital

In 2023, Nicolas Poirier was definitively granted 150,000 free shares at the end of the vesting period (March 28, 2023). He received other allocations in respect of previous years as described in the annual financial report included in the Universal Registration Document.

In accordance with Article L. 225-197-1 II of the French Commercial Code and standard Company practice in terms of the allocation of free shares to management, Nicolas Poirier has committed to holding 5% of the free shares allocated to him as registered shares until the end of his corporate office within the Company.

d) Allocation of directors' fees

The Chief Executive Officer, like the other directors, receives compensation like any other director.
As a reminder, Nicolas Poirier received a net compensation of €27,146 as a director in 2022.

e) No other benefits

Nicolas Poirier receives no other benefits.

1.4.3. Directors' compensation policy

The General Shareholders' Meeting of June 24, 2021 set the total amount of directors' fees at three hundred thousand euros (€300,000) net for the 2021 fiscal year and for subsequent fiscal years, pending any subsequent resolution passed by the Ordinary General Shareholders' Meeting.
This compensation is granted to all directors (including the Chairman of the Board of Directors and the Chief Executive Officer) as follows:

- €2,500 per meeting attended in person (one meeting is scheduled per quarter);
- €1,500 per meeting attended by video conference or other means of telecommunication subject to the internal rules;
- Travel and lodging costs incurred by each Committee participant for meetings of the Board of Directors held outside of Europe will be covered for an amount of €3,000 per meeting, while costs incurred for meetings in Europe will be covered for an amount of €500 per meeting.

Since March 2020, the participation of Directors who have attended Board meetings by audio or video conference is remunerated in the same way as those who participated in person, and this rule also applies to all meetings of the Board and its committees.
Members of the Board of Directors received a total of €221,500 net in directors' fees from the Company for fiscal year 2022.

A breakdown of the compensation awarded to corporate officers is presented in summary form in Section 13.1 "Overall gross compensation for members of the Board of Directors and Executive Management."

1.4.4 Pensions and other benefits

1.4.4.1 Compensation, payments and benefits due or likely to become due as a result of taking or leaving a corporate office or a change in duties

The Company has not provisioned sums for the purpose of payment of pensions, retirement and other benefits for the benefit of corporate officers and/or executive corporate officers who do not benefit elsewhere (or have not benefited) from severance or a hiring bonus within the Company.

1.4.4.2 Other benefits

At December 31, 2022, the Company provisioned for retirement benefits as well as for bonuses for corporate officers and/or executive corporate officers who are not otherwise entitled (or have not previously been entitled) to severance or a hiring bonus.

1.5 Information on corporate officers

Agreements covered by Articles L. 225-38 et seq. of the French Commercial Code

See Section 17.1.2 of the Universal Registration Document.

1.6 Governance and list of offices and positions held by each corporate officer

See Section 12 (Governing, management, supervisory bodies and executive management) and 13 (Compensation and benefits) of the Universal Registration Document.

4 Items likely to have an impact in the event of a public offering

In accordance with Article L. 22-10-11 of the French Commercial Code, the following items may have an impact in the event of a takeover bid:

The Company's capital structure	See Note to the Financial Statements Number 4: Capital, Section 18.1.6 of the Universal Registration Document
The restrictions contained in the bylaws on exercising voting rights and share transfers or agreement clauses brought to the attention of the Company in accordance with Article L. 233-11 of the French Commercial Code.	See (iv) Shareholding disclosure thresholds (Article 16 of bylaws)
Any direct or indirect investments in the Company's share capital of which it is aware under Articles L. 233-7 and L. 233-12 of the French Commercial Code.	None
The list of holders of any securities conferring special control rights and description of these securities.	None
The control mechanisms provided for in any employee shareholding plan when control rights are not held by employees.	None
Shareholder agreements of which the Company is aware and which may include restrictions on share transfers and on exercising voting rights.	None

Rules governing the appointment and replacement of members of the Board of Directors as well as changes to the Company's bylaws.	See Report on corporate governance and legal and statutory provisions
The powers of the Board of Directors, in particular issuing or buying back shares.	See Appendix C - Corporate governance report, Sections 1.1.2 (Functioning of the Board of Directors) and 1.1.4 (Restrictions on the powers of the Chief Executive Officer and Board of Directors)
Any agreements entered into by the Company that are amended or terminated in the event of a change of control of the Company, unless this disclosure would seriously harm its interests, notwithstanding any legal disclosure duty.	See Note 4 to the consolidated financial statements: Capital (Section 18.1.6 of the Universal Registration Document)
Agreements providing for severance payments for the Board of Directors or employees should they resign or be dismissed without proper cause or if their employment is terminated as a result of a public offering.	None

The Board of Directors

Appendix D – Corporate Social Responsability (CSE) Charter

OSE Immunotherapeutics is a biotechnology company engaged in the development of first-in-class immunotherapies aimed at controlling the immune system in the fields of immuno-oncology and immuno-inflammation.

Our goal is to develop innovative treatment options for patients suffering from severely debilitating diseases with a high medical need, and to provide physicians with new, effective and life-saving treatments for their patients.

The Company benefits from the expertise of a leading team committed to the research, optimization, pharmaceutical development and registration of innovative immunotherapy drugs. And because immunology is a history of collaborations, our strategy is based on global pharmaceutical, clinical and academic partnerships to make a difference in the fields of immuno-oncology and autoimmune diseases for the benefit of patients. Moreover, partnerships represent a strong element of the Company's business model by generating non-dilutive revenues that allow us to finance our research and development programs on new therapeutic targets and entities.

The Company's ambition is to become a fast-growing biotech company, combining a portfolio of first-in-class clinical assets in immuno-oncology and immuno-inflammation with a unique and highly promising innovation platform engine, with a commitment to strengthen our societal and environmental contribution.

To this end, OSE Immunotherapeutics is committed to optimizing and structuring its existing Corporate Social and Environmental Responsibility (CSR) approach.

The company has decided to evaluate the actions already taken and the expectations according to the ISO26000 standard "Social Responsibility" published in November 2010, promulgated by the International Organization for Standardization: ISO. It contains a set of guidelines for deploying a complete and ambitious CSR approach. OSE is planning an evaluation by the Ecovadis label as confirmation of the deployment of its approach.

The 5 main principles of the CSR approach at OSE Immunotherapeutics

1. Governance

Several governance bodies, with texts and procedures, are in place within OSE Immunotherapeutics to administer the Company, ensure its smooth running and evaluation, including priority missions and major orientations in terms of CSR. The integration of CSR principles into the decision-making and implementation processes is at the heart of OSE's organization.

The Board of Directors

OSE Immunotherapeutics is managed by a Board of Directors whose members come from different backgrounds and have a variety of skills, reflecting its objectives. It is composed of 9 members, 7 of whom are independent, and the average age is 63. With 4 women and 5 men, the Company complies with law n° 2011-103 of January 27, 2011, which stipulates that the Board must include at least 40% of each gender.

The 9 members of the Board of Directors combine international expertise in drug development, marketing, industry and finance, with experience in listed biotechnology companies.

Among its governance missions, the Board of Directors can carry out at any time the controls and verifications it deems appropriate, including in the area of CSR governance.

The Audit Committee

The Audit Committee is responsible for monitoring issues relating to the preparation and control of accounting and financial information. It is responsible for continuously assessing the existence and effectiveness of the Company's financial control and risk management procedures, and is responsible in particular for:
- ensuring the effectiveness of internal control and risk management systems
- To verify the proper functioning of the systems with the assistance of the Finance Department;
- Examine the work program for internal and external audits.

The Compensation and Appointments Committee

This Committee makes recommendations to the Board of Directors on ad hoc matters, in particular:

- Advice and assistance on remuneration, pension and welfare schemes, supplementary pensions, benefits in kind, various pecuniary entitlements of executive directors, grants of free or performance shares, stock options or share purchase options;

- Monitoring the implementation of structures and procedures enabling the application of good governance practices within the Company;

- Ensuring compliance with ethical standards within the Company and in its relations with third parties.

Executive Committee

The Executive Committee of OSE Immunotherapeutics is composed of 6 members, including 4 women. The average age of the members is 44 years.
The 6 members of the Executive Committee combine expertise in all areas of the company, with :

- Nicolas Poirier, Chief Executive Officer and Chief Scientific Officer,
- Dominique Costantini, Director of Development and Strategy;
- Jean-Pascal Conduzorgues, Industrial Director
- Anne-Laure Autret-Cornet, Administrative and Financial Director, HR Director, and CSE referent
- Sophie Fay, Director of External Affairs

CSR Steering Committee

A CSR Steering Committee has been set up within OSE Immunotherapeutics. The purpose of this committee is to provide advice and assistance and to issue a report containing all the points of attention of the company's CSR policy and their monitoring.

2. The rights of the individual

The Rules of Procedure

The Board of Directors, in a resolution dated March 27, 2015, wished to adopt internal regulations in order to specify, complete and implement the rules of organization and operation applicable to it by law (as well as to its committees), the Company's bylaws and regulations, and the rules of ethics applicable to all directors and the principles of corporate governance to which it adheres, in particular with regard to insider trading or market transactions. (MiddleNext Corporate Governance Code for Small and Mid-Sized Companies, December 2009).

In particular, it sets out, in accordance with legislative provisions:

- Measures for the application of health and safety regulations in the company
- The participation of employees in the restoration of working conditions that protect the health and safety of employees
- Rules concerning discipline and the nature and scale of sanctions that can be taken by the employer
- Provisions concerning the respect of disciplinary procedures and the rights of defense of employees
- Provisions concerning the prohibition, prevention and repression of moral and sexual harassment and sexist behaviour.

3. Relationships and working conditions

The Company is developing its HR policy to create a positive work environment that respects the well-being of its employees and promotes their personal development.
A Guide has been drawn up to assist all employees and describe the essential elements of working conditions at the Company's two sites, as well as the elements of risk prevention in terms of health and safety.

Quality of life at work

OSE Immunotherapeutics has put in place various actions to promote a working environment that preserves the balance between professional and private life.
The company offers paid sick leave for parents, as well as paid leave for trainees of more than three months.

In addition, the management of leave is flexible. In particular, the company allows for early leave. And it also ensures that its employees take regular leave to respect their right to rest.

The management also wants to promote a positive and cohesive atmosphere for its employees, through events such as team building and a Christmas lunch.

Finally, particular care is given to the layout of offices and common areas, to make them pleasant to work in.

All this is reflected in a low absenteeism rate (1.39% in 2022).

Teleworking

The context of the Covid-19 health crisis encouraged the development of teleworking within the Company, which implemented the necessary measures to guarantee the health and safety of its employees. Subsequently, the practice of telecommuting has been widely extended to employees whose positions allow it.
The company has chosen to adopt a telework charter, which has been approved by the members of the Works Council. It provides for increased use of teleworking for employees with disabilities, those suffering from disabling diseases, pregnant employees and family carers.

OSE Immunotherapeutics wishes to preserve team synergy, managerial proximity and a feeling of belonging, which is necessary for any collective organization. Thus, the recommendation is for two days of teleworking per week, but this volume can be adjusted by the employee and his/her manager, while ensuring that internal relations continue to be good.

Teleworking, which is widely favored by teams, offers a better balance between personal and professional life, gives employees greater autonomy in the organization of their day, reduces the constraints associated with travel, and improves the carbon footprint of everyone.

A principle that has become essential with the development of teleworking, the right to disconnect is guaranteed for all employees, and the company communicates on good practice recommendations, such as:

- Limiting the sending of emails after 6pm
- Encouraging "disconnection" times during the day to focus on a task at hand
- Deactivate notifications
- Favouring a lunch break time
- Activate automatic responses in Outlook in case of absence, with a contact to whom to redirect requests.

Social dialogue

A Social and Economic Committee (CSE) has been in place since December 2019, with 4 elected members. Its role is to ensure the collective expression of employees allowing their interests to be taken into account in decisions relating to the management and economic and financial development of the Company, the organization of work, and professional training.

It is the employees' spokesperson vis-à-vis management and ensures that the French Labor Code is properly applied.

The CSE has negotiated a company agreement on the length and organization of working hours at OSE Immunotherapeutics in response to the Company's decision, in agreement with the CSE, to organize employees' working hours. The system for organizing and calculating working time, as set out in the Agreement, is designed to meet the requirements of legislation, the organizational needs of the company in terms of the proper functioning and development of its business, and the desire of employees to reconcile their professional and personal lives as well as possible.

Social indicators

OSE Immunotherapeutics recruits mainly on permanent contracts, allowing for long-term salary relationships (95% permanent contracts by January 2023). Each year, the company also takes on several work-study students and trainees at various levels (from discovery courses for schoolchildren to Master's degree apprentices), as well as CIFRE employees (thesis).

The proportion of women is largely represented in the teams: 66% of women in the teams, 60% of women on the Executive Committee, and 85% of managers are women.

In addition, the age pyramid is balanced, with the Company recruiting both talented young graduates and very experienced employees (for example, employees over 50 years of age represent 19% of the permanent workforce as of December 31, 2022).

Health and safety of teams

The health and safety of our employees is one of the company's primary concerns.
As part of its production process and its research and development activities, the company uses biological and chemical products that technicians, engineers and researchers may come into contact with. A Health and Safety representative has been appointed at the Nantes site, and these employees are made aware of and trained in the risks present in the laboratories and in good manufacturing practices, behavior and gestures in this environment.
More generally, the Company takes all necessary steps, in compliance with regulations, to identify occupational hazards, limit their occurrence or impact, and provide a solution to any such hazards.

Two members of the laboratory have been trained as first aiders and the Paris team includes many physicians.

First aid training has been provided to all teams at the Nantes site and will soon be extended to the Paris site.

Employees can contact management at any time to make an appointment to discuss sensitive issues related to safety and working conditions. They can also contact their manager, the HR department, members of the Works Council and the occupational health department.

Team development and management dynamics

The management of OSE Immunotherapeutics is proud of the passion and commitment of its teams.

It promotes a managerial dynamic based on individual and collective development, empowerment and trust. Thus, it aims to encourage innovation and interaction within and between teams.

The company supports the development of its employees, and values them, particularly through internal promotion. Indeed, the majority of positions of responsibility have been filled internally.

The company also provides training for young people, in particular through the integration of doctoral students via CIFRE (Convention Industrielle de Formation par la Recherche) theses, and also through training courses dedicated to specialties, or more generalized courses such as English or management.

An annual interview is held at the end of the year between the employee and his/her manager. The purpose of this meeting is to review the achievements of the past year and to look ahead to the coming year. It also provides an opportunity to discuss the employee's feelings, quality of life at work, career path and motivations.

A professional interview is also held every two years, during which the employee and the manager can take stock of the employee's career path, consider possible changes in skills and the training methods to be implemented.

Employee shareholding

Since its creation, the company has been keen to involve its employees in the successes they create through the allocation of free shares. This is also a way of attracting and retaining the right profiles and skills to help the company achieve its objectives.

At the end of 2022, nearly 3% of the capital will be represented by employee shareholders.

4. The environment

The company is evenly distributed between Nantes and Paris, with the research teams historically based in Nantes and the development teams in Paris. The administrative teams are spread over the two sites.

Consumption of resources (electricity; water)

Research and development activities do not include industrial production or distribution. Consequently, resource consumption is relatively limited.
However, the Company ensures that it respects the prerogatives initiated by the government and asks its employees to behave responsibly with regard to ecological constraints.
Thus, for example, the level of heating is limited and employees are asked to turn it down to a minimum during times of absence (weekends, teleworking days, vacations), to turn off computer equipment in the evening rather than leaving it on standby, to empty their mailboxes regularly, etc. In Nantes, there are also detectors to turn on and off the lights.

Waste management

The Company uses few raw materials and its activity does not result in any significant discharge into the environment or greenhouse gases. On the office side, the Company has greatly reduced its paper printing over the last 3 years and half of the printers have been eliminated, while the number of employees has continued to increase. The company has also drastically reduced the purchase of plastic water bottles, set up water fountains and provided all employees with glass bottles.
In addition, all waste resulting from experiments carried out by employees is treated in accordance with the regulations in force. The Company favors the use of reusable materials (glass erlen, cloth blouse) rather than disposable ones in order to limit its waste. In addition, it makes every effort to optimize the packaging of products delivered and to work with companies committed to environmental issues. Finally, all recyclable waste is recycled and the Company works with an Association for the specific recycling of cardboard in a short channel in Nantes.

Other actions in favor of the environment

As of 2018, environmental issues have led the company to purchase bicycles, which are made available to employees for short-distance travel during working hours. The implementation of telecommuting reduces the environmental impact of daily home-office trips.

Similarly, the internal travel policy promotes the use of trains whenever possible, as opposed to airplanes or cars.

Finally, the Company does not own a fleet of cars.

5. Fair practices (business ethics)

Ethics

OSE Immunotherapeutics is committed to the respect by each employee of ethical values in the conduct of professional activities, in relations between employees and with external contacts, and in individual behavior. Ethical values are intrinsic to the Company and to each individual and are reflected in all formal and official documents that support and guide the activities.

Relationships with Suppliers

The Company has developed an internal supplier management procedure, which applies to all OSE employees or subcontractors involved in supplier management (selection, qualification and monitoring), for all services where Good Practices must be respected, whether for services, sales of goods or equipment.

The responsibilities and process described aim to ensure that:
- OSE subcontracts in the best possible conditions and at fair market conditions
- Supplier selection, qualification and monitoring is efficient, objective and transparent. The decision to select a supplier must take into account all aspects of the relationship, i.e.: product quality, level of service, level of experience, price, references, responsiveness and customer service, flexibility, potential for long-term relationships.

In addition, the supplier questionnaire includes a CSR section in which OSE asks if they have a CSR policy/strategy and that they document their response.
This last element is part of the analysis and the rating of the file.
The company works mainly with companies based in France and Europe. It works with the United States mainly for services (and limits the carbon impact linked to transport), and exceptionally, only if the product does not exist in these priority markets, may be required to seek products beyond.

Relationship with customers, civil society and product liability

The company does not commercialize products on the market. However, we do license our products to pharmaceutical companies to develop them for the market.
We are committed to scrupulously following all regulations related to the development of drug candidates.

Cybersecurity

The Company has established an IT Charter that defines the best practices to be followed. A review of IT risks is made by the IT Manager to the CEO at least once a year. In addition, as the IT Manager reports directly to the Finance Department, which is the Company's CSR Advisor, the link to Comex is facilitated.
With regard to training, all of the company's employees were made aware of the cybersecurity risk by the DGSI in 2021 and regular information is sent by the IT department on the subject.

Finally, concerning the infrastructure, the Company works with secure internet lines, the computer accounts are protected by passwords that change regularly. We also have encrypted hard drives, anti-virus and anti-spam software.

And the company is actively working on the implementation of computer intrusion tests.

Protection of personal data

OSE Immunotherapeutics is committed to the protection of personal data and the respect of privacy. All employees are involved in respecting the rules relating to the protection of personal data, which are formalized in a procedure.

A Data Protection Officer has been appointed to implement the necessary measures and ensure compliance and monitoring of the rules in this area.

4. Appendix E - Cross-reference tables

INFORMATION FROM THE PROVISIONS OF APPENDICES 1 AND 2 OF THE COMMISSION DELEGATED REGULATION (EU) 2019/980 OF MARCH 14, 2019 SUPPLEMENTING REGULATION (EU) 2017/1129 OF THE EUROPEAN PARLIAMENT AND THE COUNCIL

The cross-reference table below can be used to identify in the Universal Registration Document the information required under Appendices 1 and 2 of the Delegated Regulation (EU) 2019/980 of March 14, 2019.

Commission Delegated Regulation (EU) 2019/980 of March 14, 2019, Supplementing Regulation (EU) 2017/1129 (Appendices 1 and 2)		**niversal Registration Document**
Number	**Section**	**Reference**
1	**Responsible persons, third-party information, experts' reports and approval from the competent authority**	**1**
1.1	Persons responsible for information	1.1
1.2	Statement of the persons responsible	1.2
1.3	Person acting as an expert	1.3
1.4	Statement regarding third-party information	1.4
1.5	Statement regarding approval of the Universal Registration Document by the competent authority	1.5
2	**Auditors**	**2**
2.1	Name and addresses of the Company's Statutory Auditors	2.1
2.2	Change of Statutory Auditors	2.2
3	**Risk factors**	**3**
4	**Information about the Company**	**4**
4.1	Company purpose and commercial name	4.1
4.2	The Company's place of registration, its registration number and legal entity identifier	4.2
4.3	Date and term of incorporation of the Company	4.3
4.4	Domicile, legal form, legislation, country of incorporation, address, telephone number and website	4.4
5	**Business overview**	**5**
5.1	Principal activities	5.1
5.2	Principal markets	5.2
5.3	Important events in the development of the Company's business	5.3
5.4	Strategy and objectives	5.4
5.5	The extent to which the Company is dependent on patents or licenses, industrial, commercial or financial contracts or new manufacturing processes	5.5

5.6	Competitive position	5.6
5.7	Investments	5.7
6	**Organizational structure**	**6**
6.1.	Description of the Group and the position of the Company	6.1.
6.2	List of the Company's significant subsidiaries	6.2
7	**Review of the financial position and results**	**7**
7.1	Financial position	7.1
7.2	Operating profit	7.2
8	**Capital resources**	**8**
8.1.	Company's capital (both short and long term)	8.1.
8.2	Source and amount of cash flows	8.2
8.3	Financing requirements and structure	8.3
8.4	Restrictions on the use of capital resources	8.4
8.5	Sources of funds needed to fulfill the commitments referred to in item 5.7.2	8.5
9	**Regulatory environment**	**9**
10	**Information on trends**	**10**
10.1	Recent trends or significant change in financial performance (or negative statement)	10.1
10.2	Trends, uncertainties, demands, commitments or events that are reasonably likely to have a material effect on the Issuer's prospects	10.2
11	**Profit/(loss) forecasts or estimates**	**11**
12	**Administrative, management and supervisory bodies, and senior management**	**12**
12.1	Information on members of the administrative, management or supervisory bodies;	12.1
12.2	Conflicts of interest	12.2
13	**Compensation and benefits**	**13**
13.1	Amount of compensation and benefits in kind	13.1
13.2	Total provisions for pensions and retirement	13.2
14	**Operating procedures of the administrative and management bodies**	**14**
14.1	Expiration date of the current term of office	14.1
14.2	Service contracts	14.2
14.3	Audit Committee and Compensation Committee	14.3
14.4	Statement on the corporate governance regime	14.4
14.5	Potential material impacts on the corporate governance	14.5
15	**Employees**	**15**

15.1	Number of employees	15.1
15.2	Shareholdings and stock options	15.2
15.3	Employee shareholding	15.3
16	**Main shareholders**	**16**
16.1	Name of any person who has a percentage interest in the share capital or voting rights which is notifiable	16.1
16.2	Main shareholders and voting rights	16.2
16.3	Information on control	16.3
16.4	Description of any arrangements which may result in a change in control	16.4
17	**Related-party transactions**	**17**
18	**Financial information concerning the Issuer's assets, liabilities, financial position and results**	**18**
18.1	Historical financial information	18.1
18.2	Interim and other financial information	18.2
18.3	Auditing of historical annual financial information	18.3
18.4	Pro forma financial information	18.4
18.5	Dividend policy	18.5
18.6	Legal and arbitration proceedings	18.6
18.7	Significant change in the Issuer's financial position	18.7
19	**Additional information**	**19**
19.1	Stated capital	19.1
19.2	Company's constitution and Bylaws	19.2
20	**Material contracts**	**20**
21	**Documents available**	**21**

CROSS-REFERENCE TABLE FOR THE MANAGEMENT REPORT

The cross-reference table below can be used to identify the information in this Universal Registration Document which included the management report to be published in accordance with the provisions of Article L. 225-100 of the French Commercial Code.

Management report	**Paragraph in this document**
Presentation of the Company’s position during the past fiscal year (Article L. 232-1 II)	Appendix A, 1.2
Major events between the reporting date and the publication of the management report (Article L. 232-1 II)	Appendix A, 1.3
Foreseeable changes to the Company's position (Article L. 232-1 II)	Appendix A, 1.3
List of existing subsidiaries (Article L. 232-1 II)	6.2

Research and development activities (Article L. 232-1 II)	5.1.3
Objective and comprehensive analysis of business development	Appendix A
Financial and any relevant non-financial key performance indicators	7.2
Description of main risks and uncertainties	3
Information on the use of financial instruments (Article L. 225-100-1 1° to 3° and 6°)	18.1.6 (3., note 13)
Main features of the internal control and risk management procedures concerning the preparation and processing of accounting and financial information (Article L. 225-100-1 5 °)	Appendix A, 8
Adjustments in the event that securities giving access to capital are issued (Article L. 228-99)	N/A
Executive corporate officers' requirements to hold shares until the termination of their positions by the Board of Directors when deciding on the allocation of free shares (Article L. 225-197-1 II para. 4)	Appendix C, 4.3
Non-tax-deductible expenses and reintegrated expenses following a tax adjustment (Articles 223 quater and 22 quinquies of the French General Tax Code).	N/A
Identity of the direct or indirect holders of more than one-twentieth, one-tenth, three-twentieths, one-fifth, one-quarter, one-third, one-half, two-thirds, eighteen-twentieths, nineteen-twentieths of the share capital or voting rights (Article L. 233-13)	16.1.1
Share buy-back transactions (Article L. 225-211 para. 2)	N/A
Securities transactions carried out by management (Article 223-26 of the General Regulations of the French Financial Markets Authority)	Appendix A, appended to the report
Employee shareholding (Article L. 225-102)	15.2
Breakdown of currently valid delegations	19.1.4
Payment terms for customers and suppliers (Article L. 441-6-1 para. 1)	Appendix A, 2.5

CROSS-REFERENCE TABLE FOR THE ANNUAL FINANCIAL REPORT

The cross-reference table below can be used to identify any information in this Universal Registration Document which makes up the annual financial report to be published in accordance with Articles L. 451-1-2 of the French Monetary and Financial Code and 222-3 of the General Regulations of the French Financial Markets Authority.

Number	**Section**	**Paragraph in this document**
1	Separate financial statements	18.1.5
2	Consolidated financial statements	18.1.6
3	Management report (see above)	Appendix A
4	Statement by natural persons who take responsibility for the annual financial report	1.1

5	Statutory Auditors' report on the separate financial statements	18.1.1.2
6	Statutory Auditors' report on the consolidated financial statements	18.1.1.1