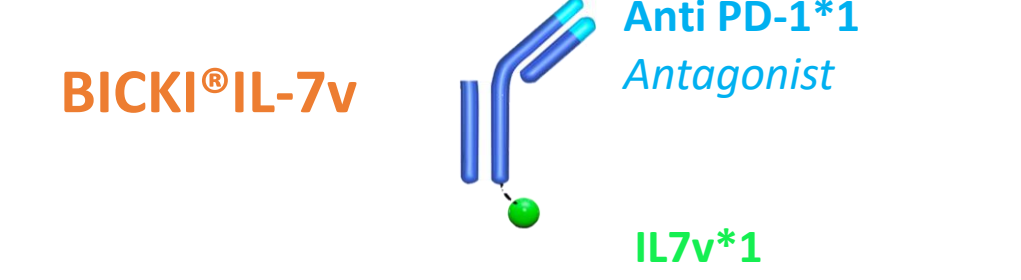


Anti-PD-1/IL-7v bispecific antibody promotes TCF1+ stem like T cells expansion and long-lasting in vivo efficacy

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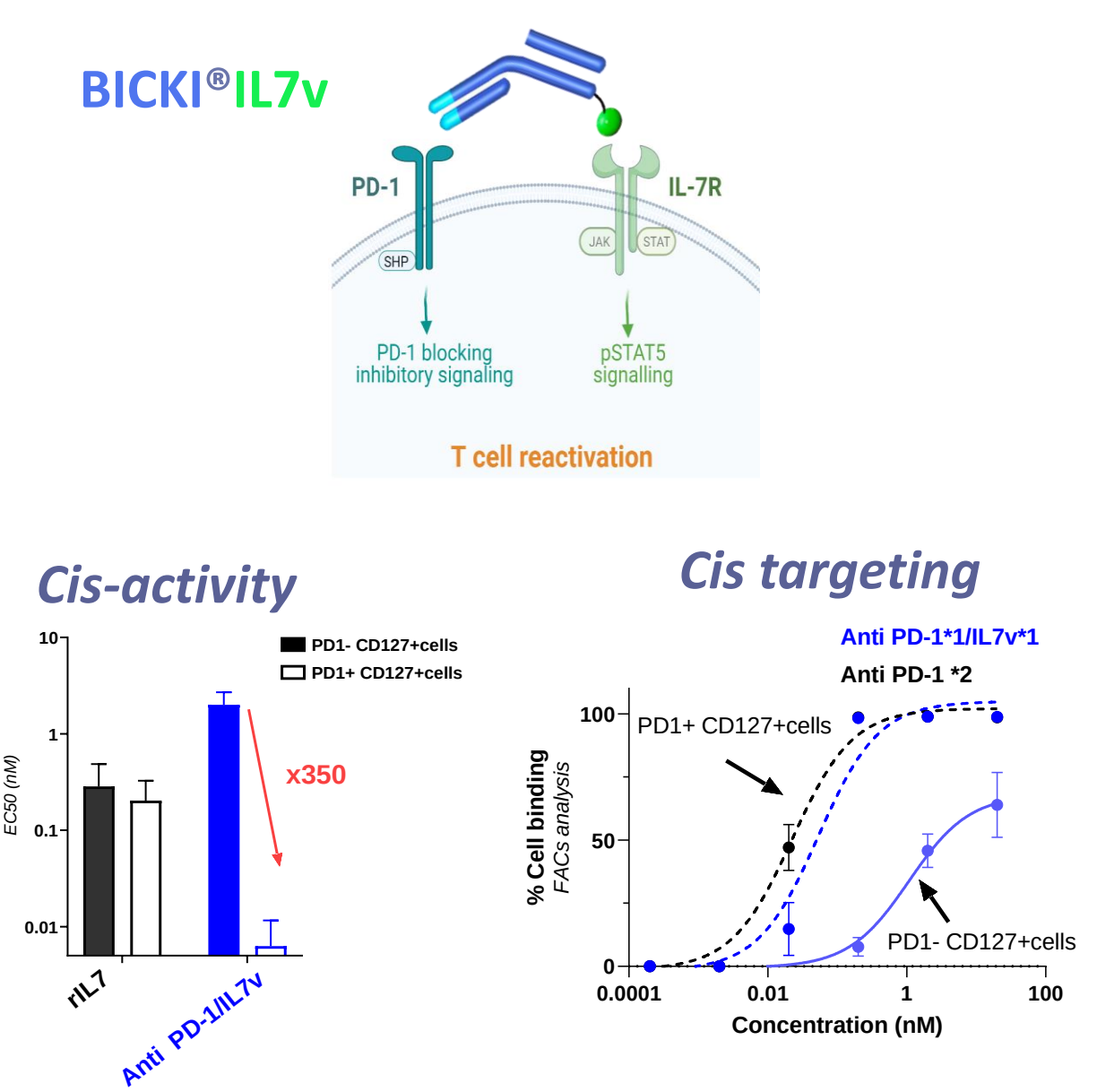
Introduction

To counteract *de novo* and acquired resistance mechanisms, we have designed a second generation of PD-1 antibody: BICKI®IL-7 by fusing IL-7 mutein cytokine (IL-7v) to the anti-PD-1 antibody Fc portion (BICKI : Bispecific Checkpoint Inhibitor). With the BICKI®IL-7v, we aim to selectively cis deliver IL-7 cytokine to PD-1+ T cells and restore their effector anti tumor functions and favor a long-term survival signal.

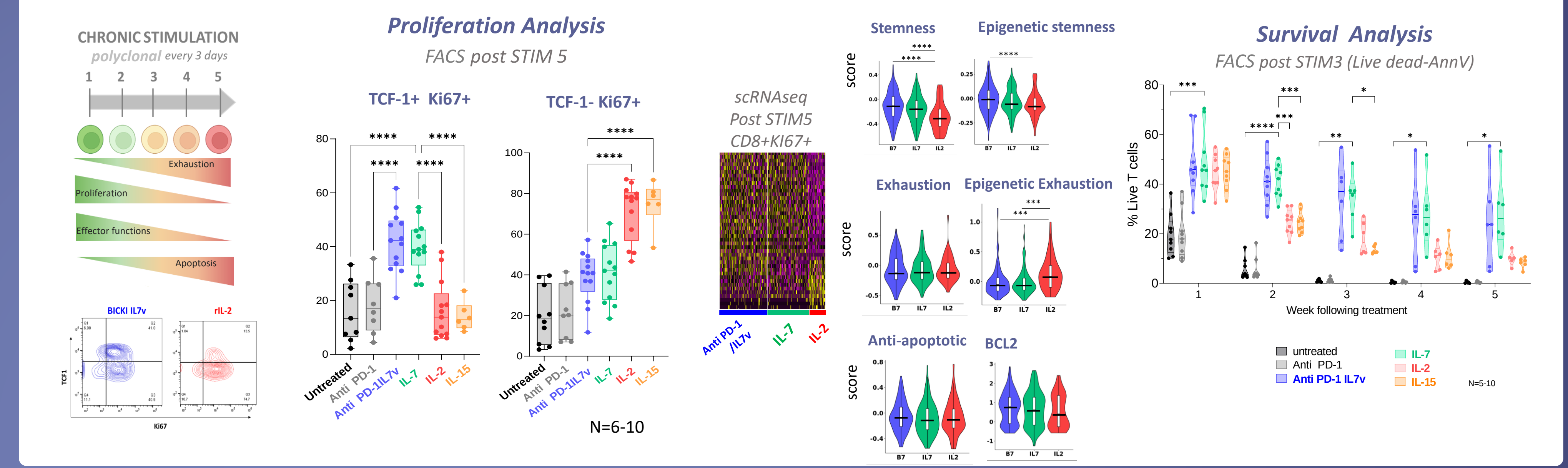


We have demonstrated (Poster #826) that IL-7R and IL-7R pathway gene expression is significantly correlated with better long-term OS and/or PFS across several cancers. Higher IL-7R and IL-7R pathway expression by tumor-specific T-cell clonotype is significantly correlated with ICI response, higher stemness & proliferative signature, lower exhaustion and apoptosis markers, providing a strong rationale of co-targeting IL-7 to PD-1 to sustain durable tumor-specific T-cell response. BICKI®IL-7v design construction was optimized for higher (1) *cis*-delivery to PD-1+ tumor specific T cells (2) Improved PK profile and, (3) enhanced in vivo activity.

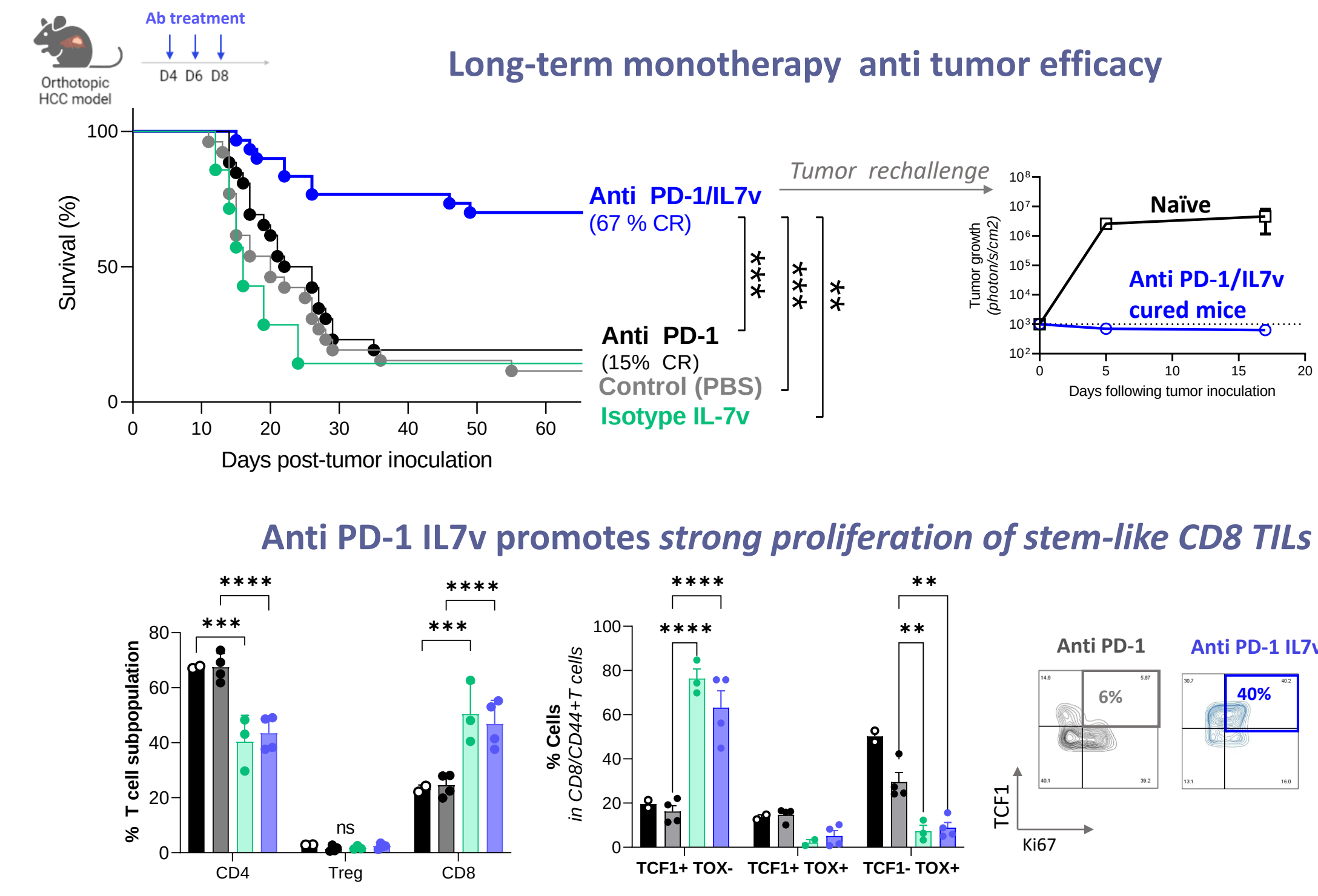
1/ Selective cis-activity on PD-1+ CD127+ T cells



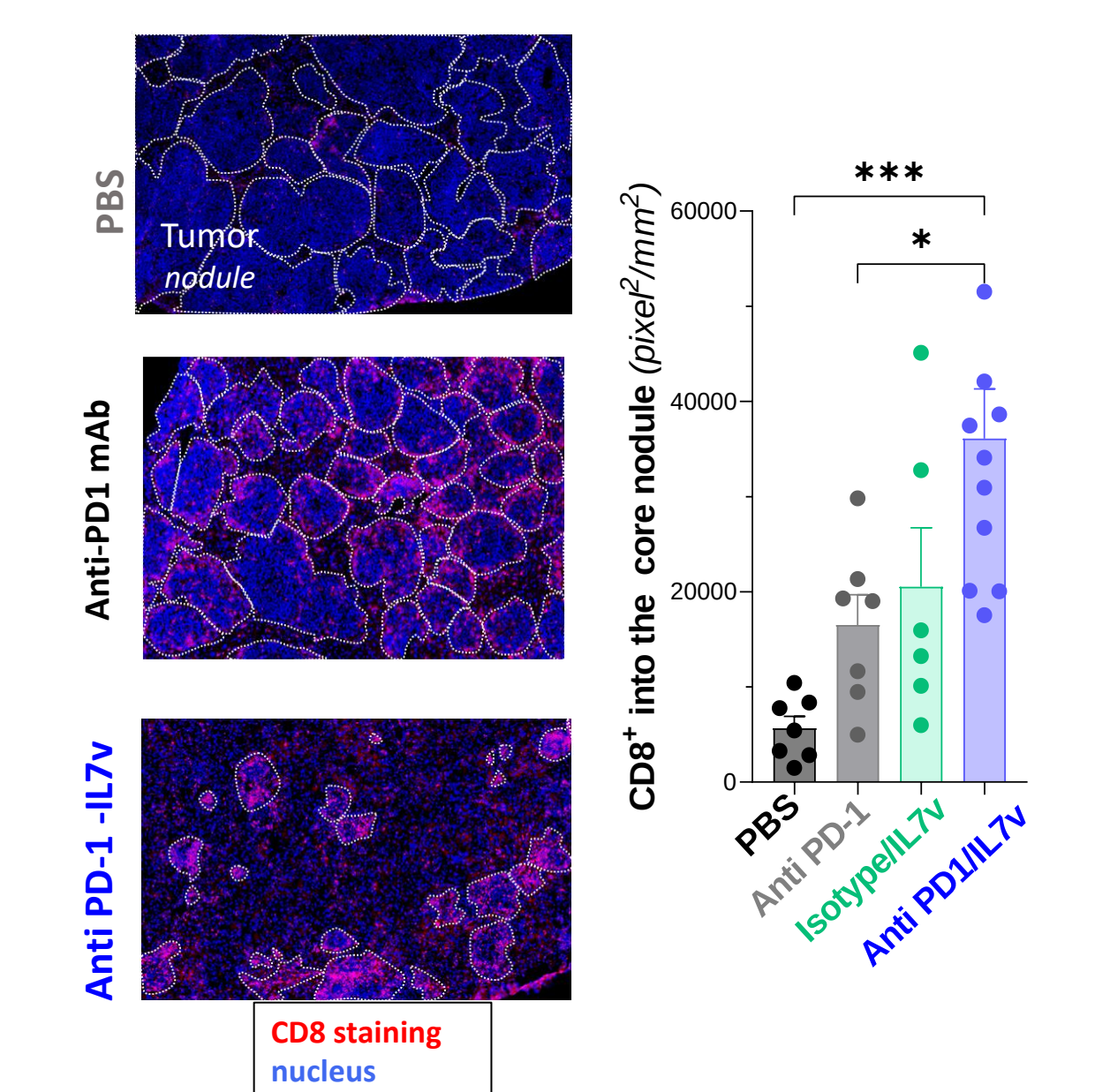
2/ Anti PD-1/IL7v and IL-7 promotes long term proliferation and survival of stem-like TCF1+ CD8 T cells following chronic stimulation



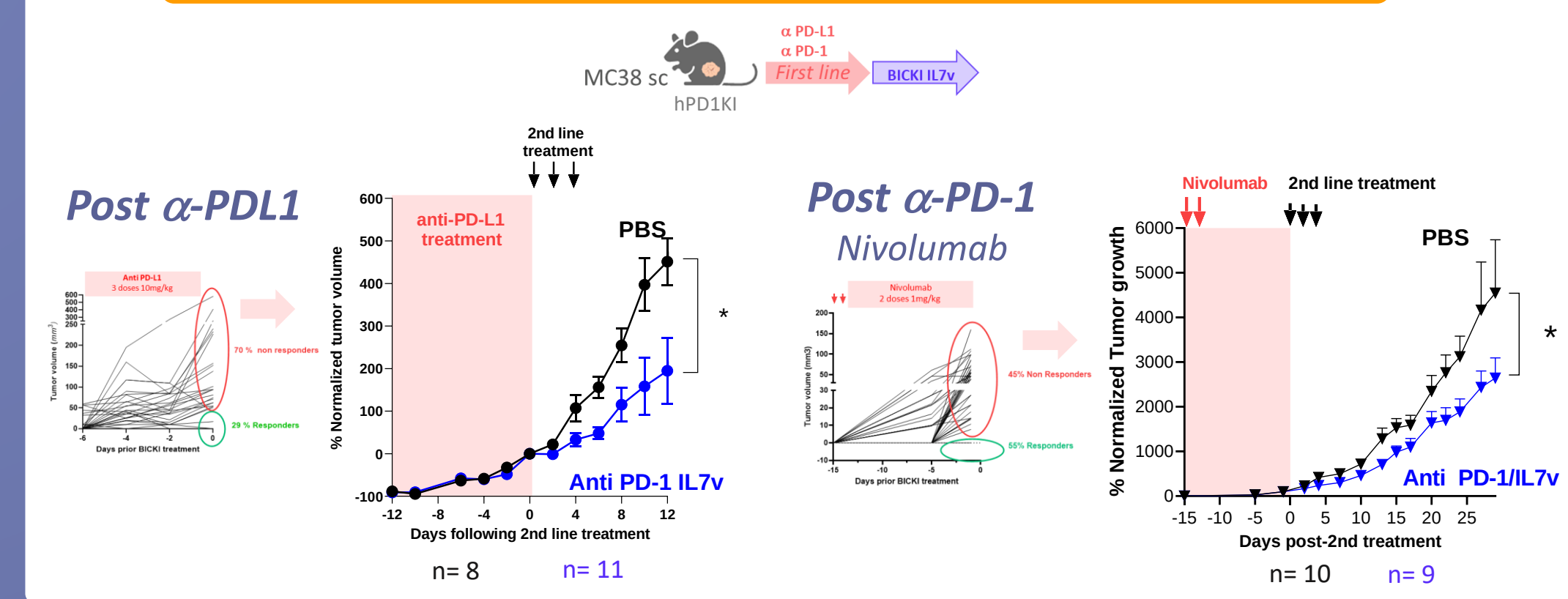
3/ Anti PD-1 IL7v in vivo efficacy by promoting infiltration and proliferation of TCF1+ stem like CD8 T cells



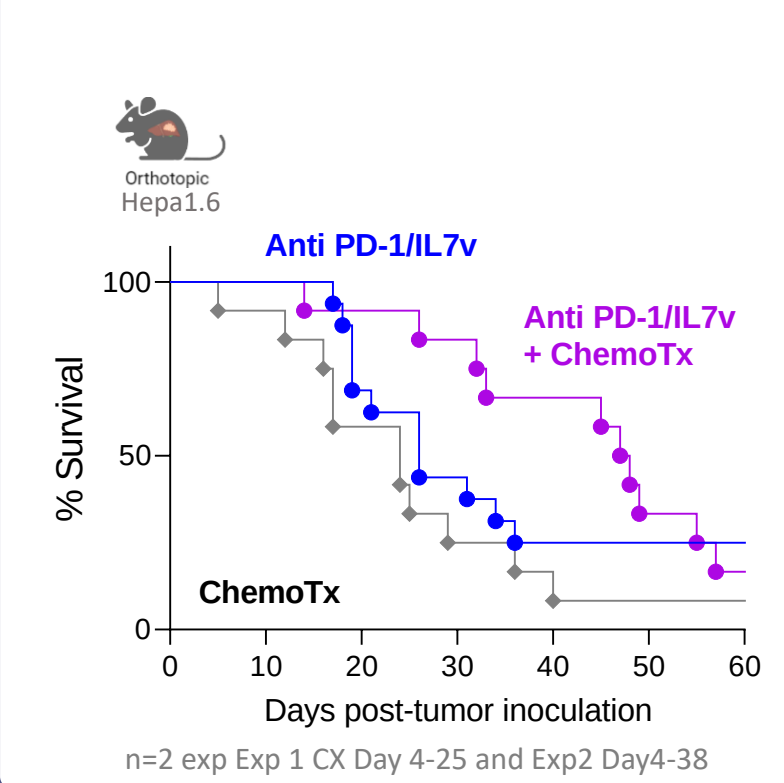
Anti PD-1 IL7v overcomes T cell exclusion Enhanced CD8 T cell infiltration into tumor nest



4/ Anti PD-1/IL7v efficacy post α-PD(L)1 relapse model



5/ Combinatorial efficacy with Chemotherapy



Conclusion

BICKI®IL7v

To sustain a durable PD-1+ stem like CD8 T cell response

- Conserved high PD-1 binding and PD-1/PD-L1 antagonist activity
- Allows a selective delivery of IL-7 on PD-1+ cells and synergistic activation of TCR signaling
- BICKI®IL7 preferentially boosts the proliferation of PD-1+ CD127+ TCF1+ stemness T cells in mouse and human.
- Significant *in vivo* anti tumor efficacy in PD-1 sensitive, resistant syngeneic orthotopic model and humanized models
- In vivo* efficacy post αPD-1 or α-PDL1 refractory tumor and superior therapeutic efficacy in combo with Chemo