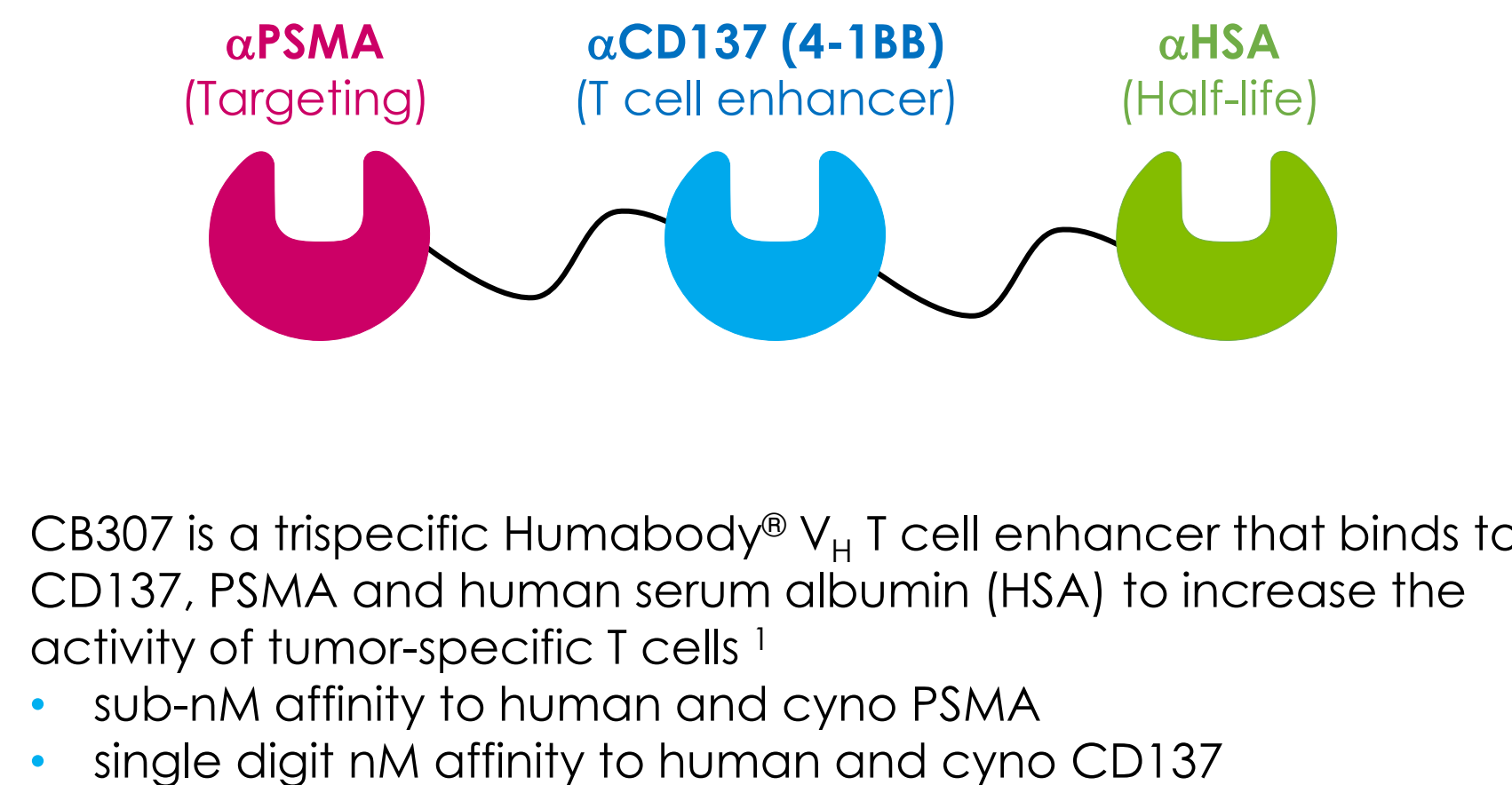


CB307: A novel targeted CD137 agonist for enhancement of immune cell responses to PSMA⁺ tumors

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CB307

Figure 1. CB307 is a half-life extended PSMA x CD137 molecule designed to engage T cells on PSMA⁺ tumors



CB307 molecular mechanism of action

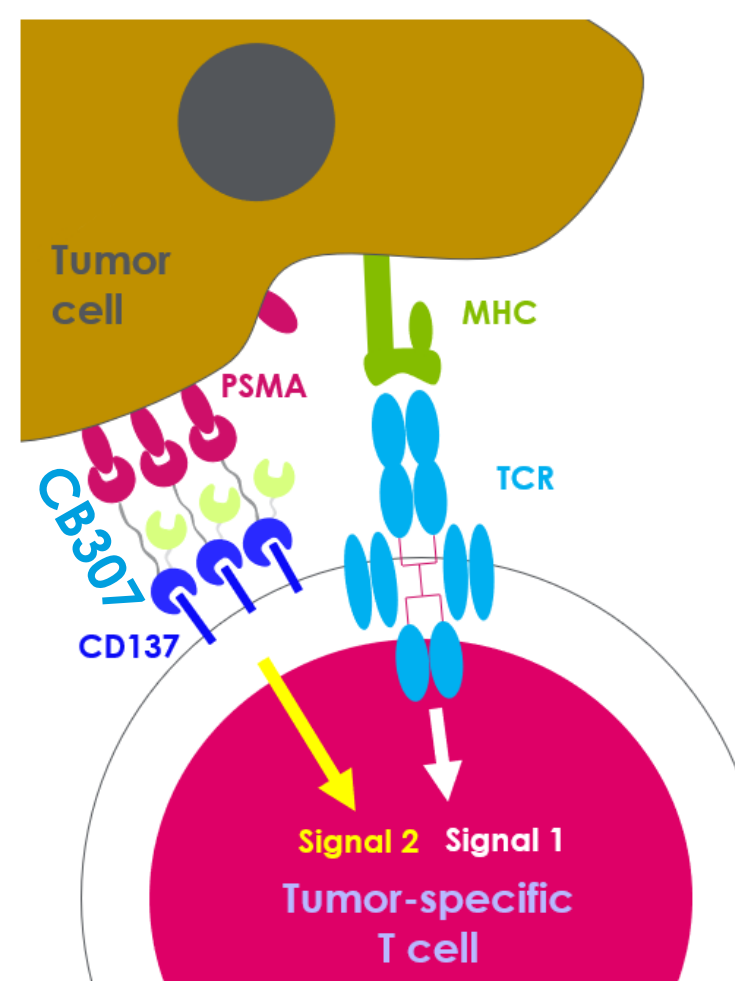
Prostate-specific membrane antigen (PSMA, FOLH1)

- PSMA is a clinically validated target for imaging and therapeutics in metastatic castration resistant prostate cancer (mCRPC)^{2,3}
- PSMA is also expressed in a variety of solid tumors⁴

CD137 (4-1BB, TNFRSF9)

- Co-stimulatory receptor expressed on activated, antigen experienced T cells and NK cells
- Early clinical studies of CD137 agonist antibodies were hampered due to either lack of efficacy or severe liver toxicity⁵
- Co-targeted CD137 agonist T cell enhancers have shown an improved cytokine release syndrome (CRS) profile in recent clinical studies^{6,7}

Figure 2. CB307 mechanism of tumor associated antigen (TAA) dependent T cell enhancement



CB307 in combination with CPI drives enhanced T cell activation and tumor killing

Figure 3. CB307-driven T cell activation is enhanced in combination with αPD(L)1 in 2D cocultures

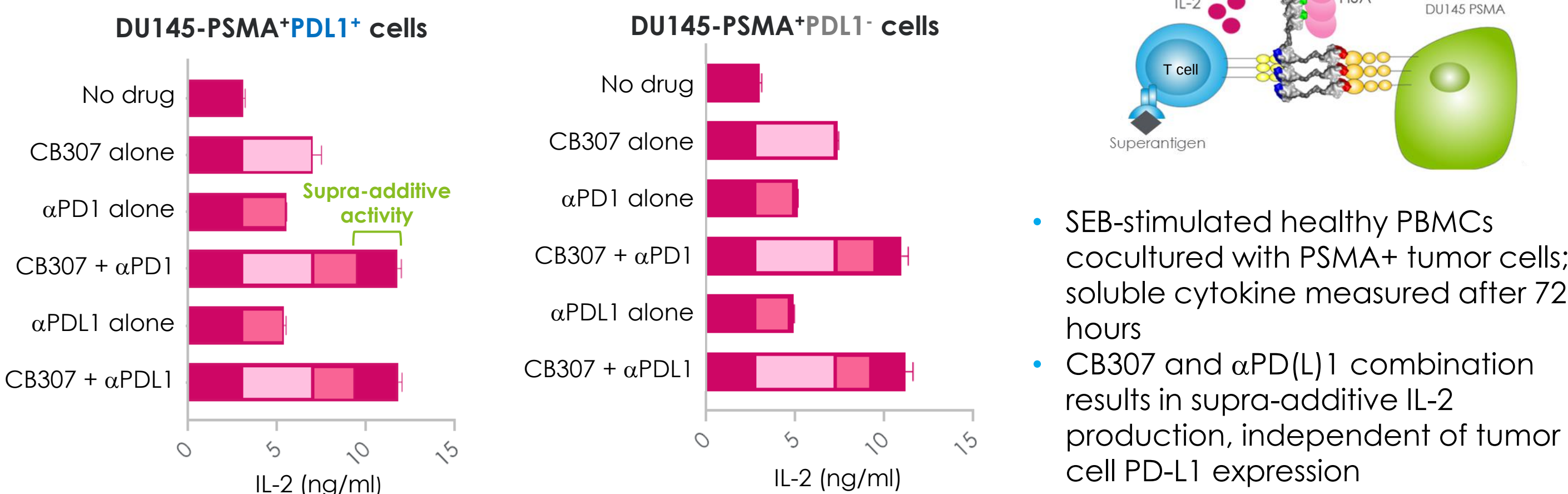
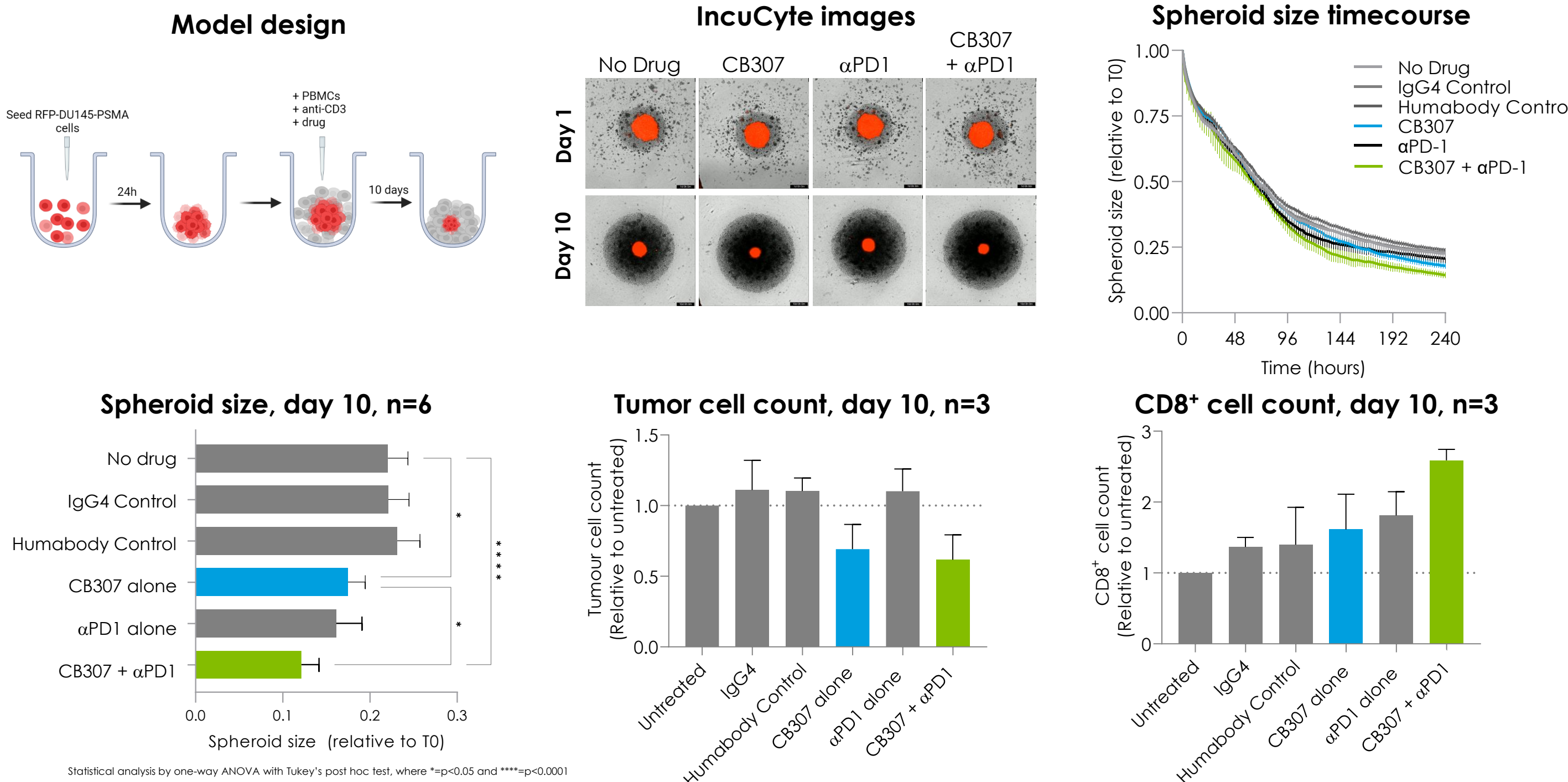


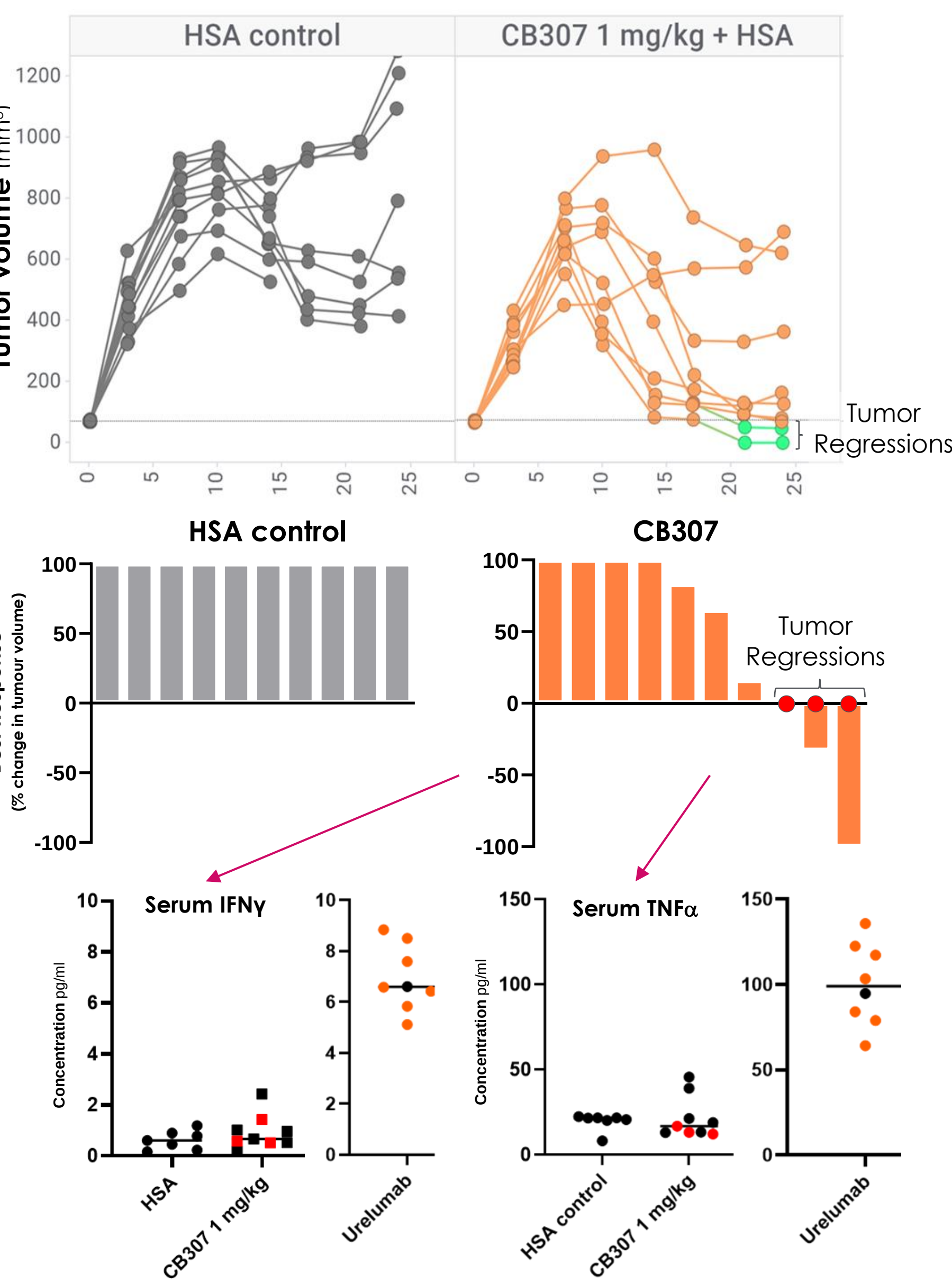
Figure 4. CB307-driven tumor killing is enhanced in combination with αPD1 in 3D spheroids



- RFP-DU145-PSMA spheroids cocultured with αCD3-stimulated healthy PBMCs; spheroid size measured by RFP signal; end point cell counts measured by flow cytometry
- CB307-induced spheroid killing is enhanced in combination with αPD1
- Spheroid size and tumor cell number both reduce with combination treatment, while CD8⁺ cell count increases

CB307 in vivo pharmacology - tumor kill without peripheral activation

Figure 5. CB307 can regress RM1 hPSMA-inducible tumors in a hCD137 transgenic syngeneic mouse model system (Crown Bioscience)



- Dox-inducible hPSMA-expressing RM1 mouse prostate tumor cells on hCD137 transgenic mice
- Tumor regression from CB307 treatment (red symbols) associated with low peripheral cytokine detection, highlighting safety versus other CD137 targeting therapies