

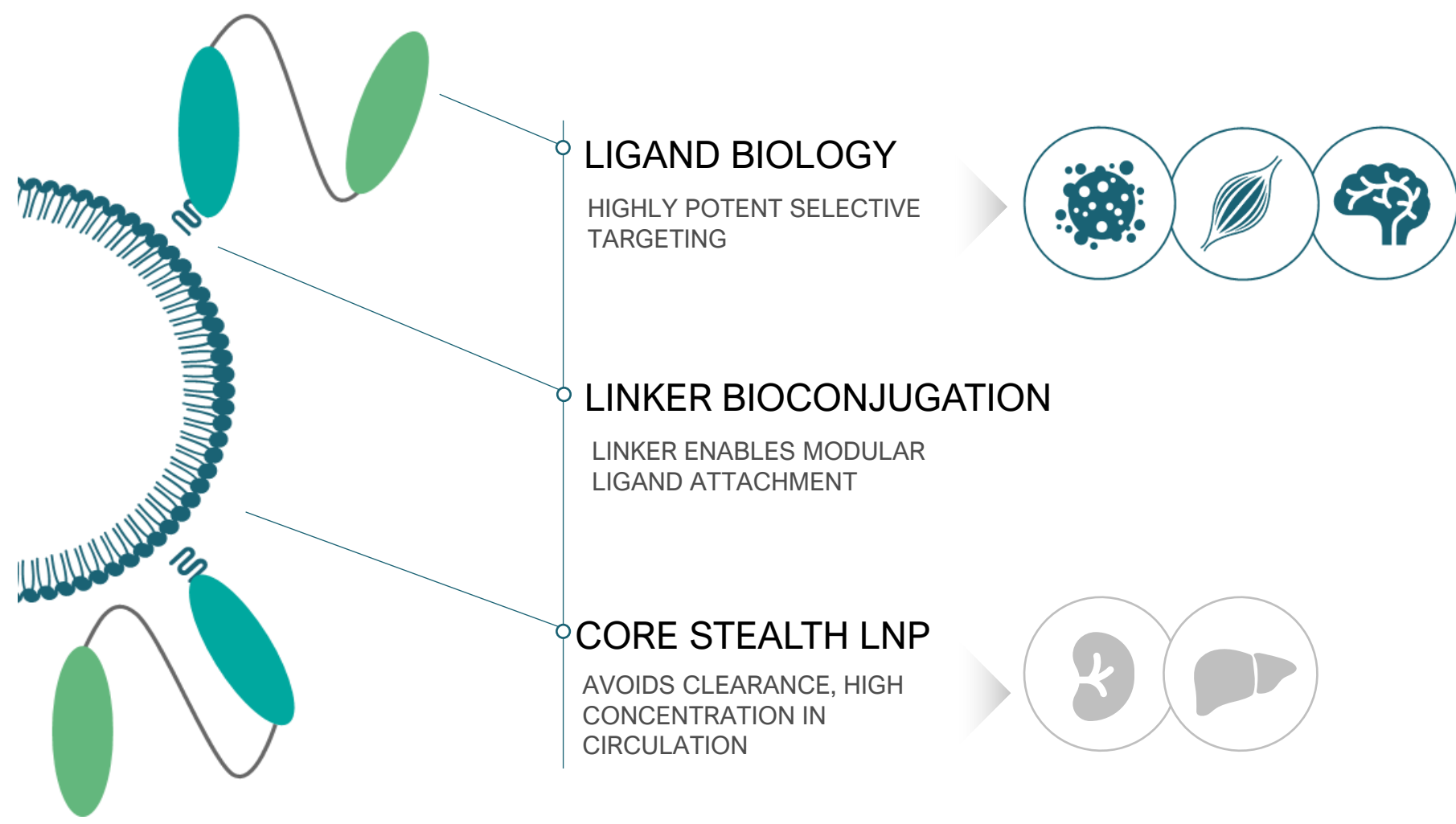


Development of cell-targeted lipid nanoparticle for *in vivo* genetic medicines targeting hepatocytes, T-cells, and hematopoietic stem cells

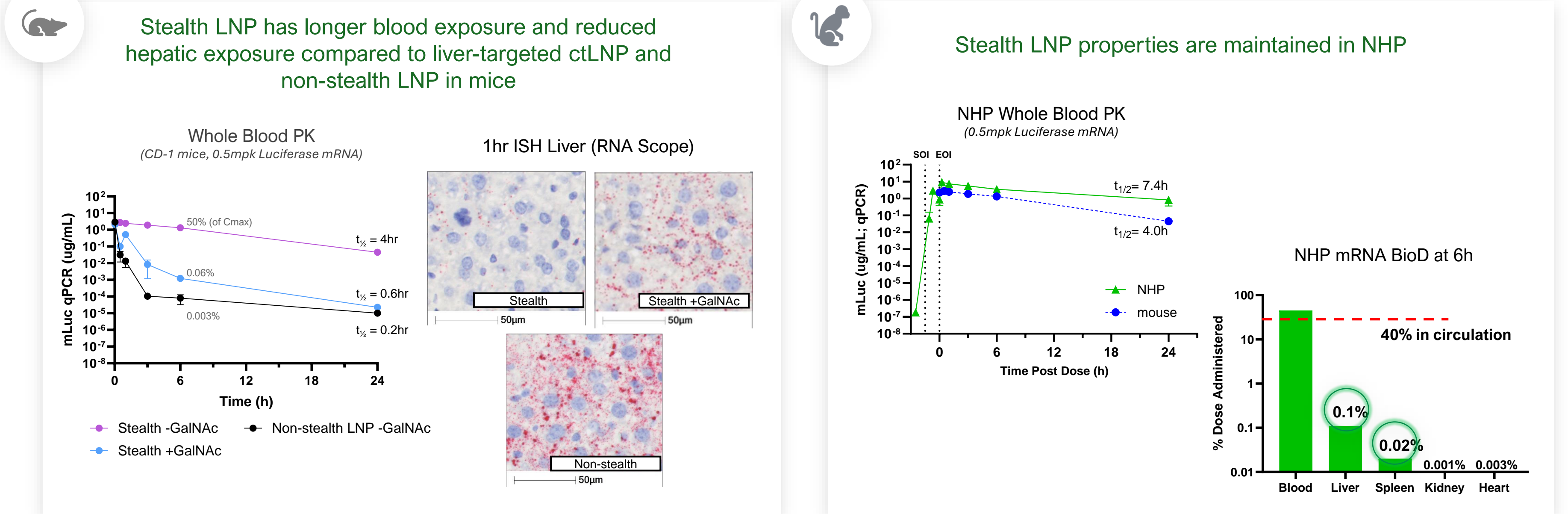
DFN Klatt*, BM Johnston, AF Brouillard, R Gagne, TA Tate, AL Landry, LS Hamm, S Merchant, D Garafola, V Bonnell, CJ Slubowski, T Desilva, AJ Perniciaro, E Cheah, J Keenan, S Serizier, Y Xin, D Rose, L Oonthonpan, V Syrovatkina, S Shah, CJ Martin, RD Monds, NW Silver, DL Bush, MG Stanton, PR Samayoa Generation Bio, Cambridge MA 02142

A Mishra, C McLaughlin, M Garnaas, M Dutra, K Jeffrey, L Guey, J Joyal Moderna Inc, Cambridge MA 02142

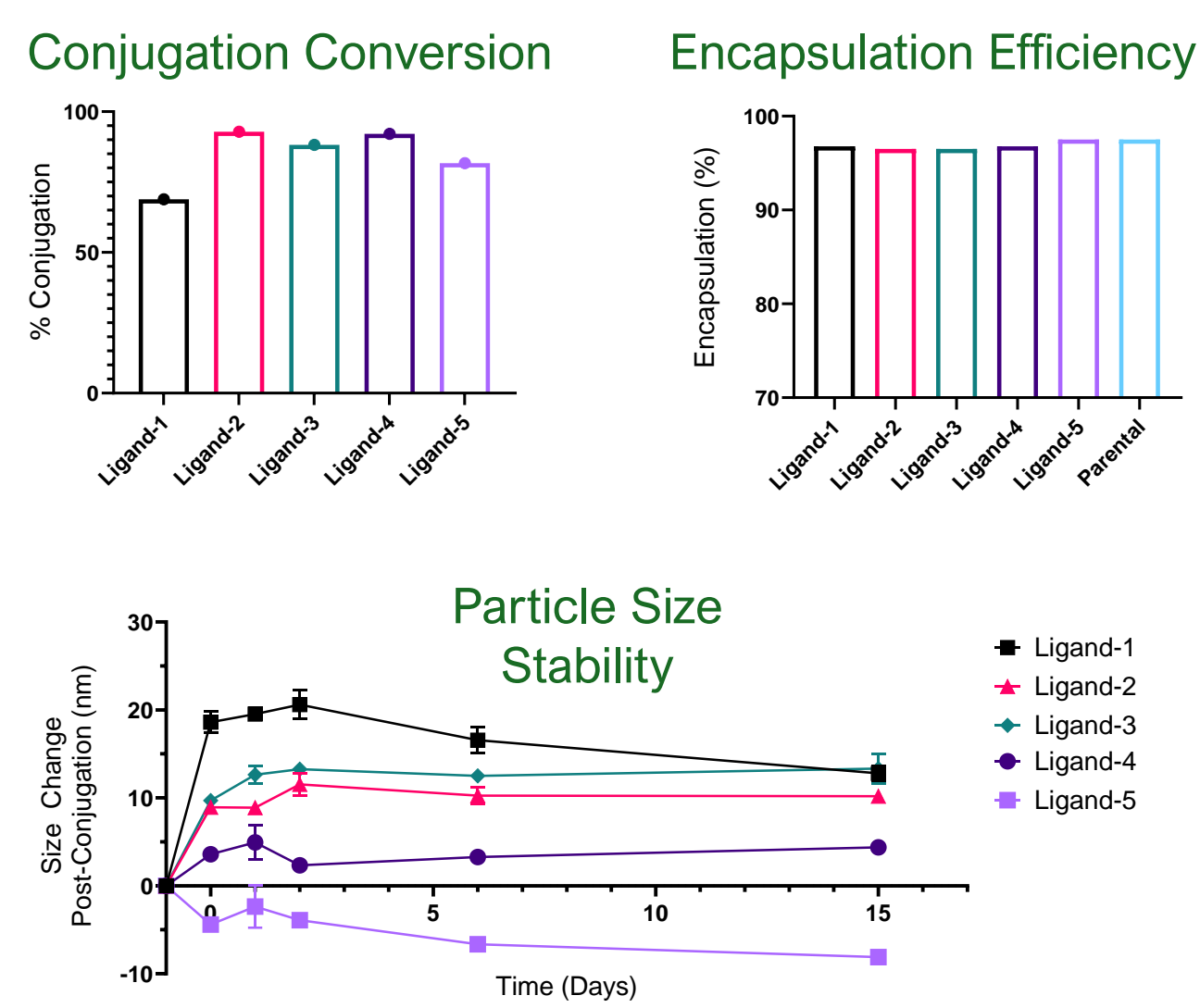
ctLNP is a modular platform that provides *in vivo* delivery to previously unreachable cell types and tissues



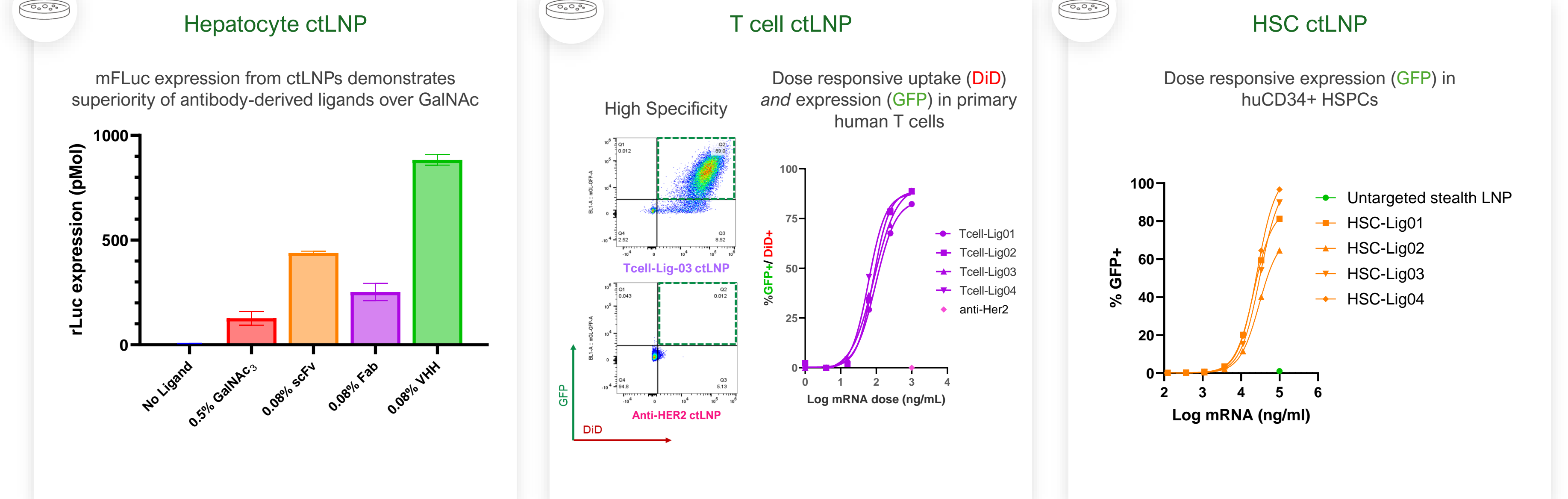
Untargeted stealth LNP demonstrates prolonged circulation and avoids rapid clearance by liver and spleen while maintaining endosomal escape



Bioconjugation platform leverages site specific conjugation of targeting ligands to generate stable ctLNPs

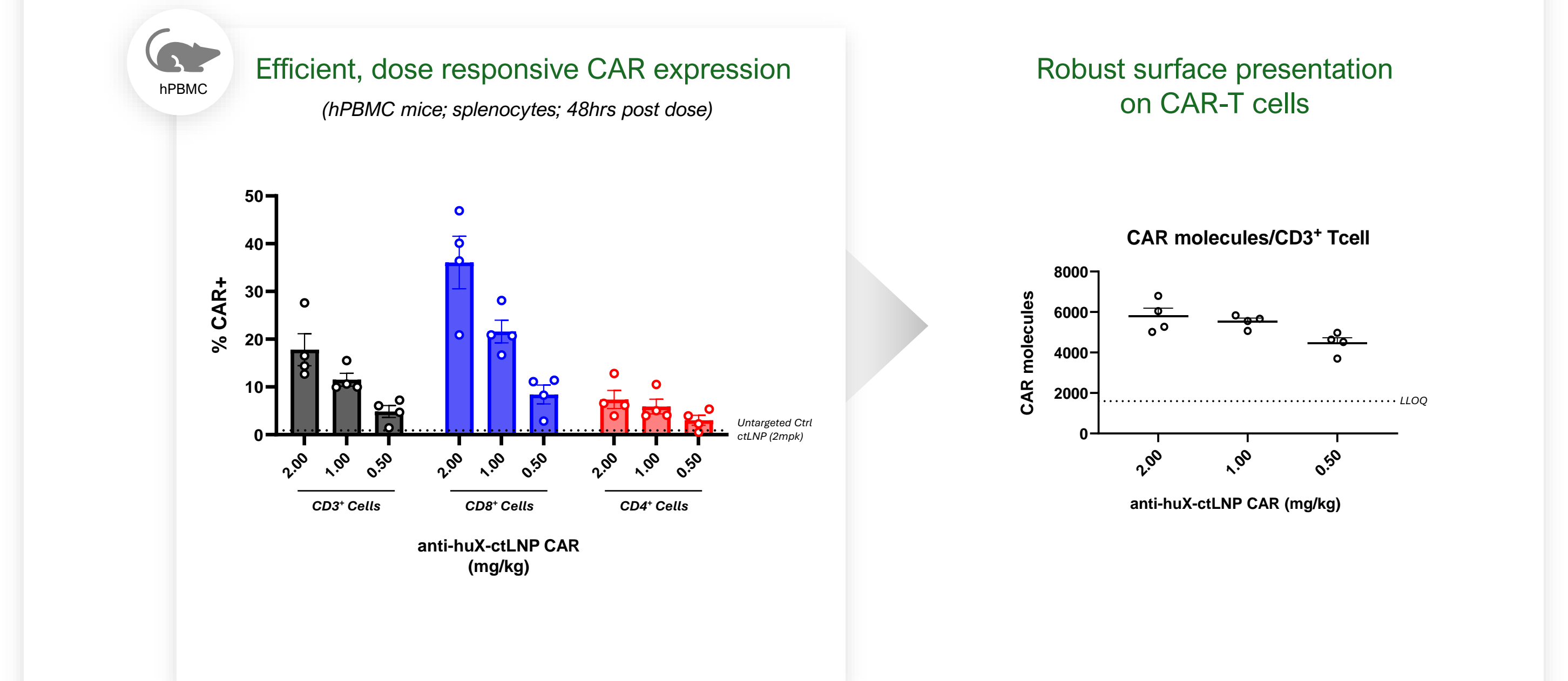
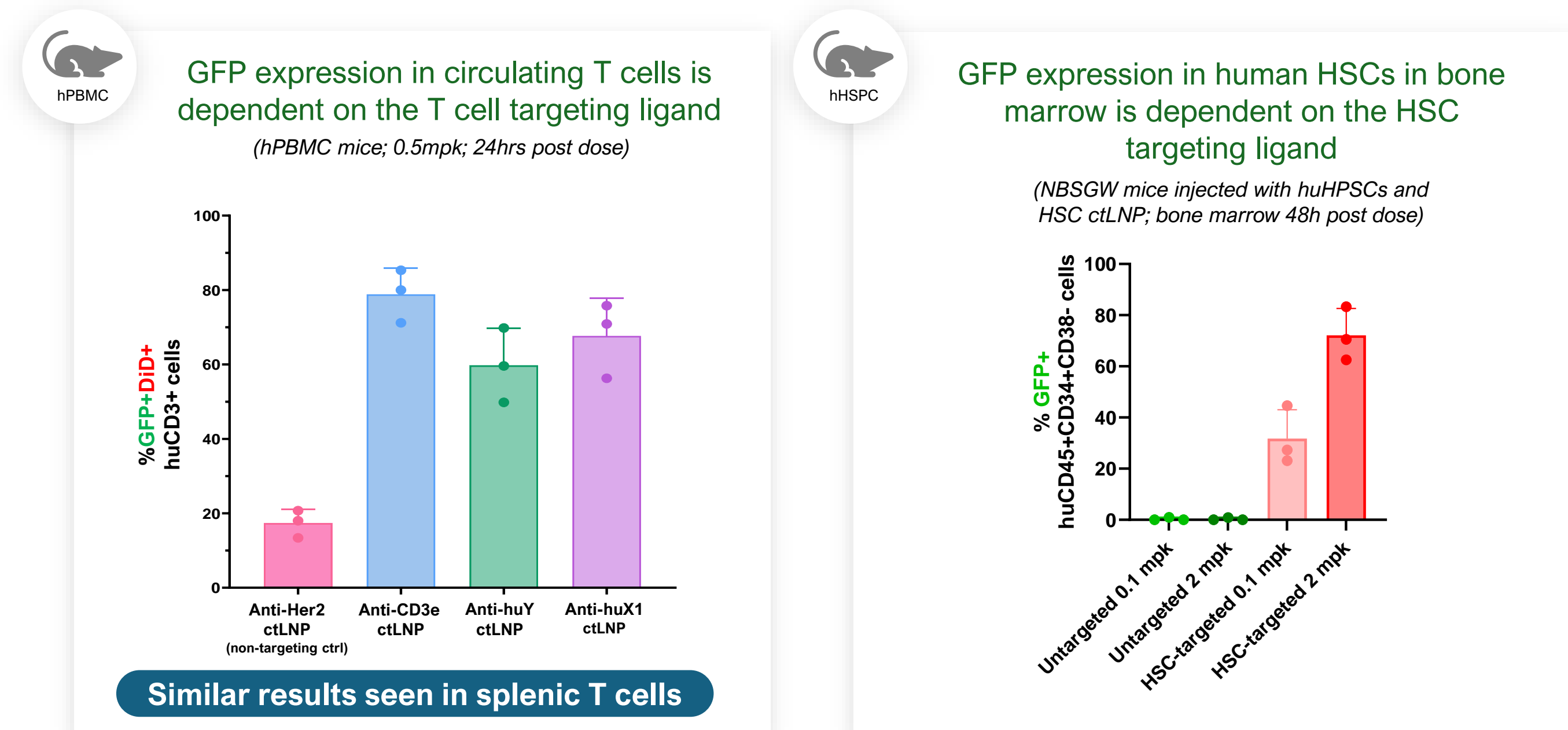


Bioconjugation of a targeting ligand to the stealth LNP enables cell-specific uptake and expression of mRNA cargo *in vitro*



T cell & HSC specific ctLNPs demonstrate uptake and expression of mRNA cargo in humanized mice

T cell ctLNPs show robust uptake and expression of CAR encoding mRNA in humanized mice



ctLNP-CAR T cells are functional *in vivo*, leading to deep target cell depletion in humanized mice

T cell ctLNP demonstrates robust T cell targeting in peripheral blood of NHP with minimal delivery to off-target cells

