



Mobilize: A Modular and Versatile Targeted LNP Delivery Platform for Extra-hepatic RNA Therapeutics

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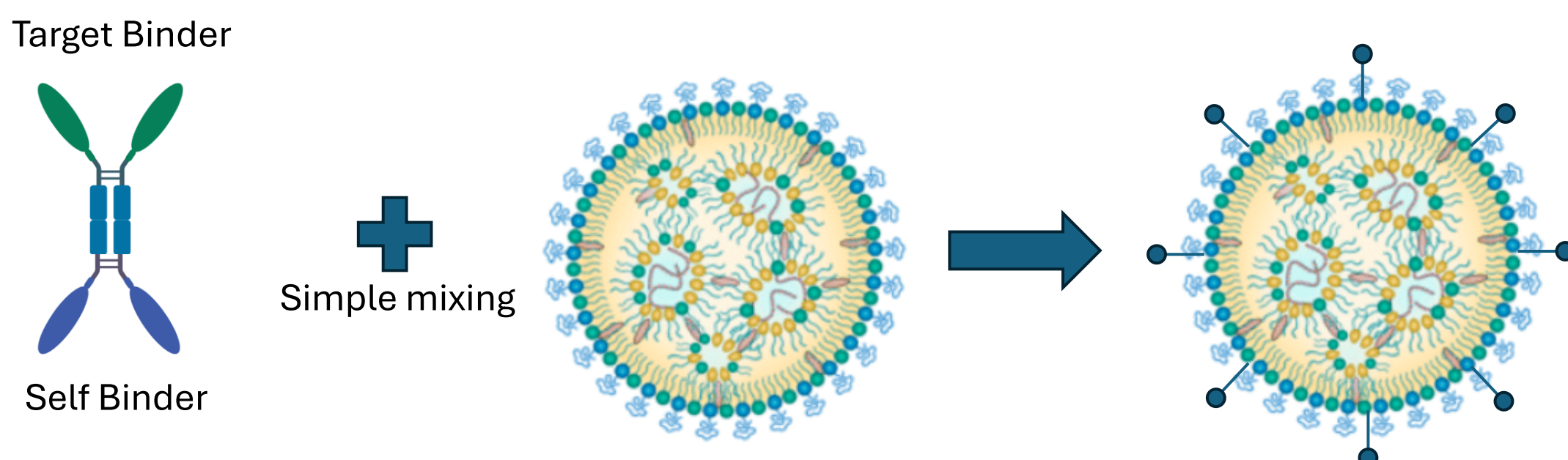


Mote Therapeutics, Lexington, MA

Introduction

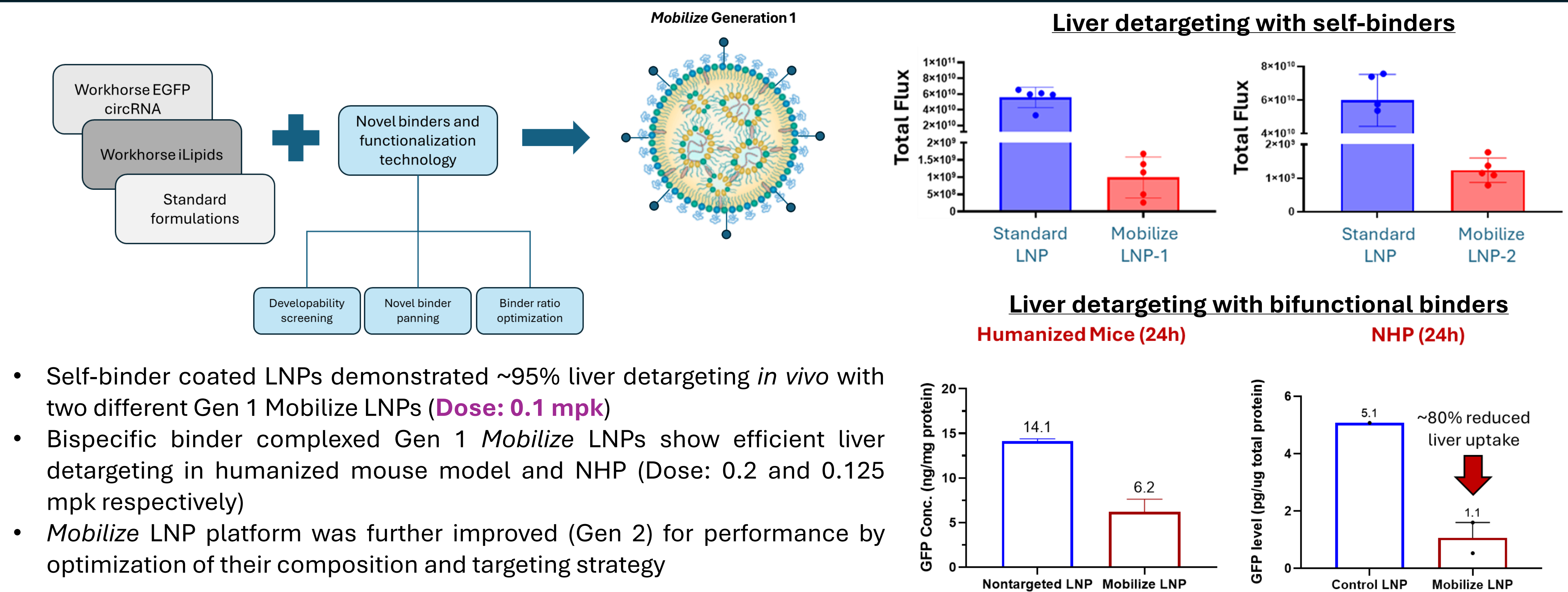
Lipid nanoparticles, or LNPs have demonstrated tremendous potential as a nonviral drug delivery system with successful clinical translation for both hepatic tissue and vaccine delivery. However, their utility for extrahepatic tissue delivery *in vivo* has been limited. Growing interest in *in vivo* chimeric antigen receptor (CAR) and genome editing technologies have led to a push for development of tissue-specific delivery methods with minimal off-target effects. Selective Organ Targeting (SORT) or CellSeeker™ technologies are prime examples that have demonstrated success in tissue-specific delivery *in vivo*. However, these approaches have specificity, scalability and translational challenges. We have developed *Mobilize* as a modular, versatile and scalable targeted LNP platform that solves the manufacturing challenges while retaining high efficacy.

Mobilize platform

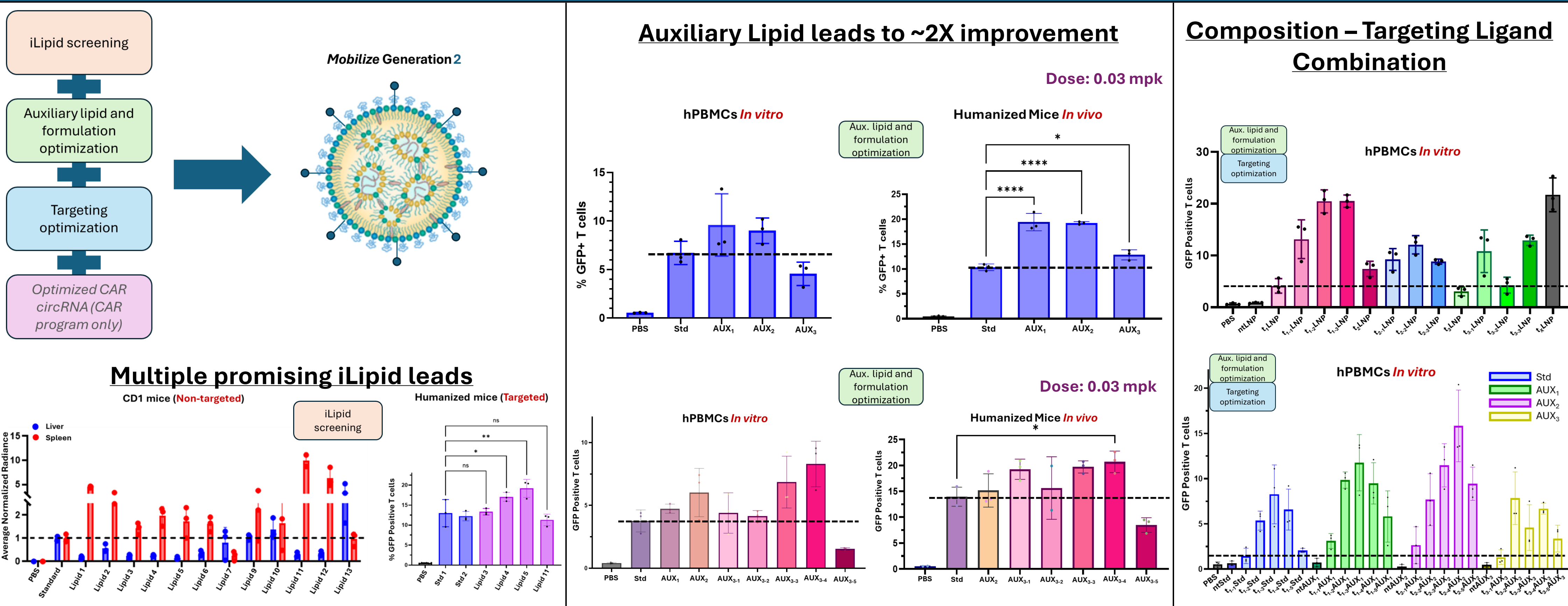


Mobilize produces high quality LNPs without typical limitations of downstream chemical functionalization, multistep production processes and variability in product quality. We have developed this platform with circular RNA (circRNA) encoding Green Fluorescent Protein (GFP) as payload, and three different targeting ligands for T cell specific delivery. The formulations are characterized by size, polydispersity index (PDI), encapsulation efficiency (EE) and stability using DLS and the Ribogreen assay. We further assess the impact of targeting ligand surface functionalization and fluorescence signal as a function of targeting ligand density *in vitro* in Jurkat cells, primary human T cells, and human PBMCs. *In vivo* efficacy of the *Mobilize* platform is confirmed in both a humanized mouse model and non-human primates (NHP), demonstrating the promise of the platform towards clinical translation.

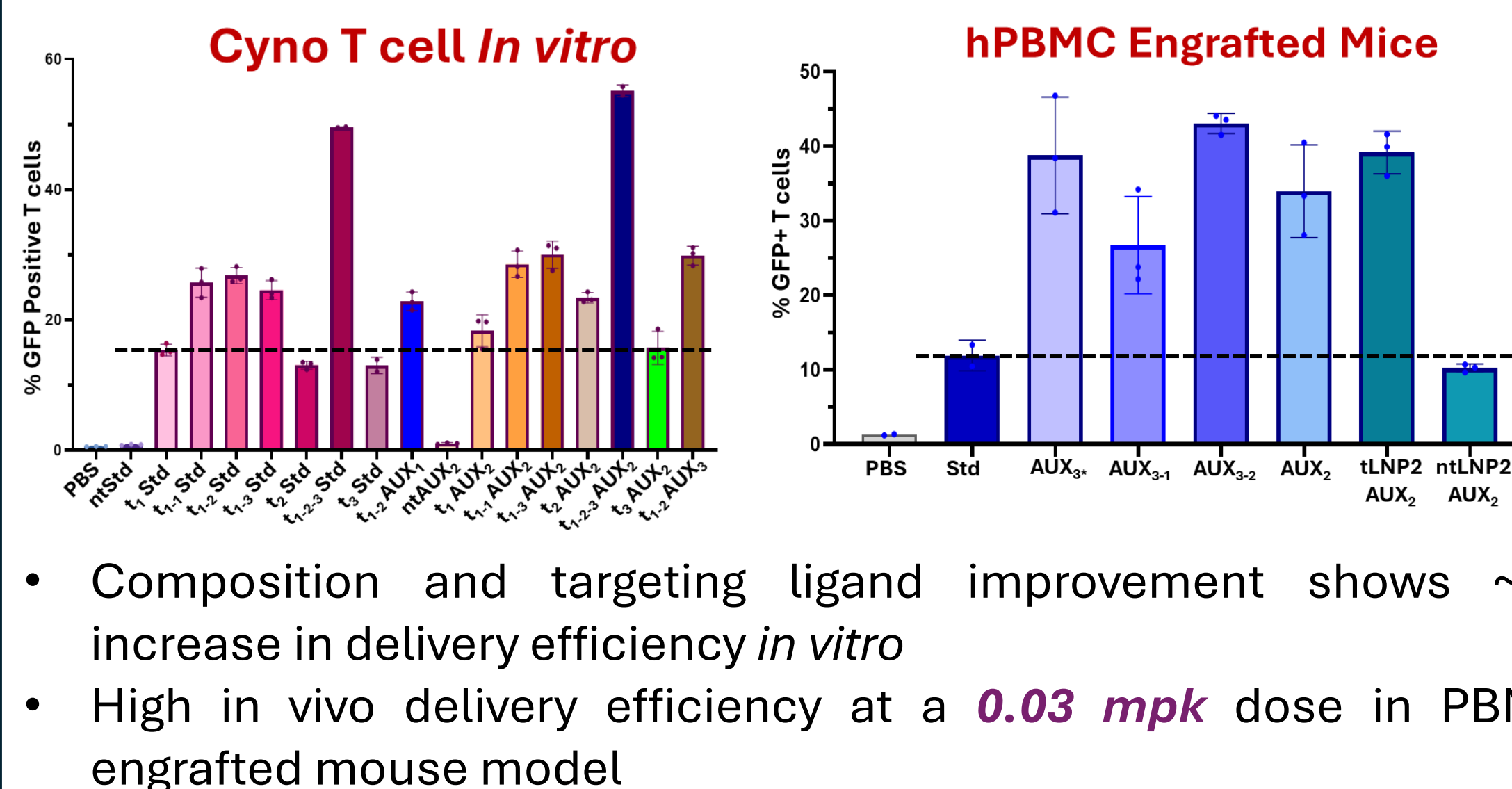
Mobilize Generation 1 targeted LNPs show efficient liver detargeting



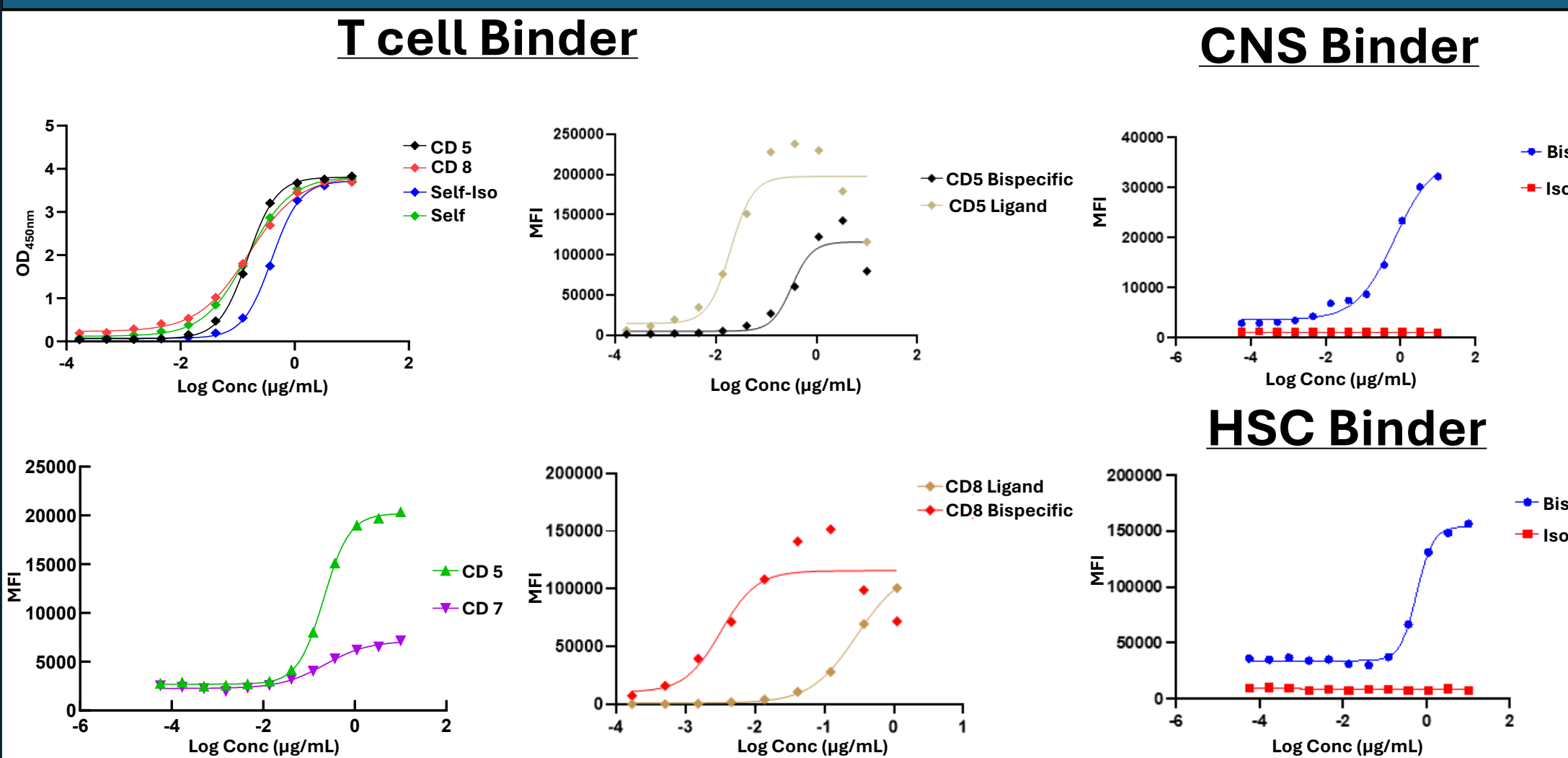
Mobilize Generation 2: Composition and targeting ligand optimization



Mobilize Gen 2 improves delivery



Modular Targeting Platform



Conclusions

- We have developed a targeted LNP platform technology for delivery of RNA
- Our Gen 1 LNPs show specific delivery to T cells in mice and NHP with no overt toxicity at high doses
- Our Gen 2 LNPs were optimized for composition and targeting ligand density to achieve ~5X improvement over Gen 1 LNPs
- Next Steps:** Successful safety and efficacy validation of *in vivo* CART in NHP disease model at low dose