We're pushing the limits of genetic medicine

And our goal is no limits

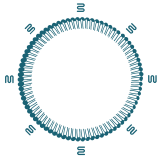
October 2024

generation bio™

Forward Looking Statements

Any statements in this presentation about future expectations, plans and prospects for the company, including statements about our strategic plans or objectives, technology platform, research and clinical development plans, and preclinical data and other statements containing the words “believes,” “anticipates,” “plans,” “expects,” and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: uncertainties inherent in the identification and development of product candidates, including the conduct of research activities, the initiation and completion of preclinical studies and clinical trials and clinical development of the company’s product candidates; uncertainties as to the availability and timing of results from preclinical studies and clinical trials; whether results from preclinical studies will be predictive of the results of later preclinical studies and clinical trials; uncertainties regarding our novel technologies, including our immune-quiet DNA; uncertainties regarding the rapid enzymatic synthesis manufacturing process; challenges in the manufacture of genetic medicine products; whether the company’s cash resources are sufficient to fund the company’s operating expenses and capital expenditure requirements for the period anticipated; as well as the other risks and uncertainties set forth in the “Risk Factors” section of our most recent annual report on Form 10-K and quarterly report on Form 10-Q, which are on file with the Securities and Exchange Commission, and in subsequent filings the company may make with the Securities and Exchange Commission. In addition, the forward-looking statements included in this presentation represent the company’s views as of the date hereof. The company anticipates that subsequent events and developments will cause the company’s views to change. However, while the company may elect to update these forward-looking statements at some point in the future, the company specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing the company’s views as of any date subsequent to the date on which they were made.

Two novel platforms – delivery and cargo – drive differentiated therapeutic opportunities



ctLNP

CELL-TARGETED DELIVERY

REDOSABLE

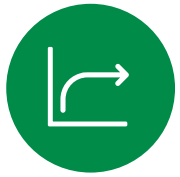
HIGHLY SELECTIVE

MULTI-TISSUE

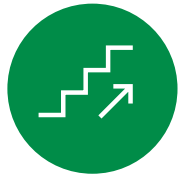
In vivo delivery
to previously unreachable
cell types and tissues

iqDNA

IMMUNE-QUIET CARGO



DURABLE



TITRATABLE

GAIN OF FUNCTION

Express or replace large genes

Portfolio focuses on novel approaches to three program areas

Autoimmune

In vivo T cells

- Redosable *in vivo* CAR-T
- Point of care treatment
- Flexible cargo
- Expand patient access
- Displace *ex vivo* CAR-T

Sickle Cell Disease

In vivo HSCs*

- Redosable *in vivo* editing
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- Validated editing approach
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- Displace *ex vivo* approaches

Hemophilia A

Hepatocytes

- Redosable, years-long effect
- Individualized coverage
- Endogenous Factor VIII
- Expand patient access
- Displace EHLs*, antibodies

Low COGS drive scale, market uptake and share

Cash runway to 2H 2027
to focus on building clinical programs

*Hematopoietic stem cells (HSCs)
*Extended half-life factors (EHLs)

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$

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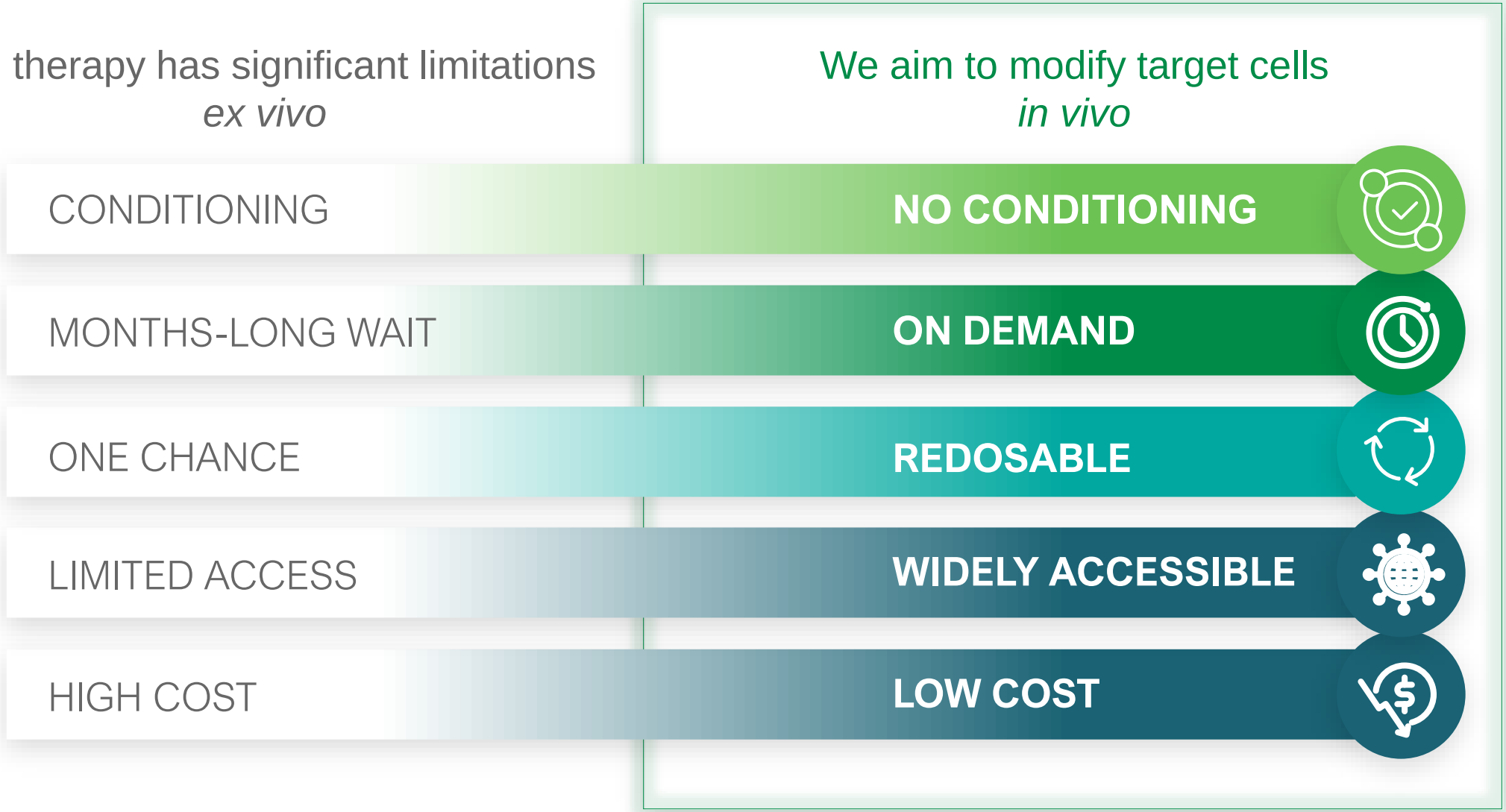
to focus on building clinical programs

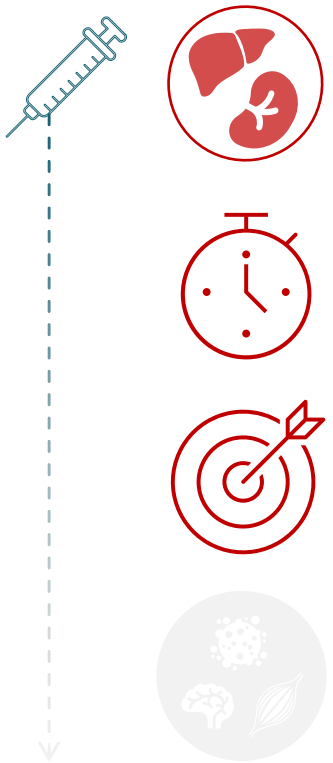
*Hematopoietic stem cells (HSCs)
*Extended half-life factors (EHLs)

Highly selective, potent ctLNP delivery is an ideal *in vivo* therapeutic approach for T cells and HSCs



Traditional LNPs are cleared by the liver and spleen, with little reaching the systemic circulation to access new cell types and tissues

Traditional LNPs



99% CLEARANCE BY LIVER & SPLEEN
very little LNP reaches systemic circulation

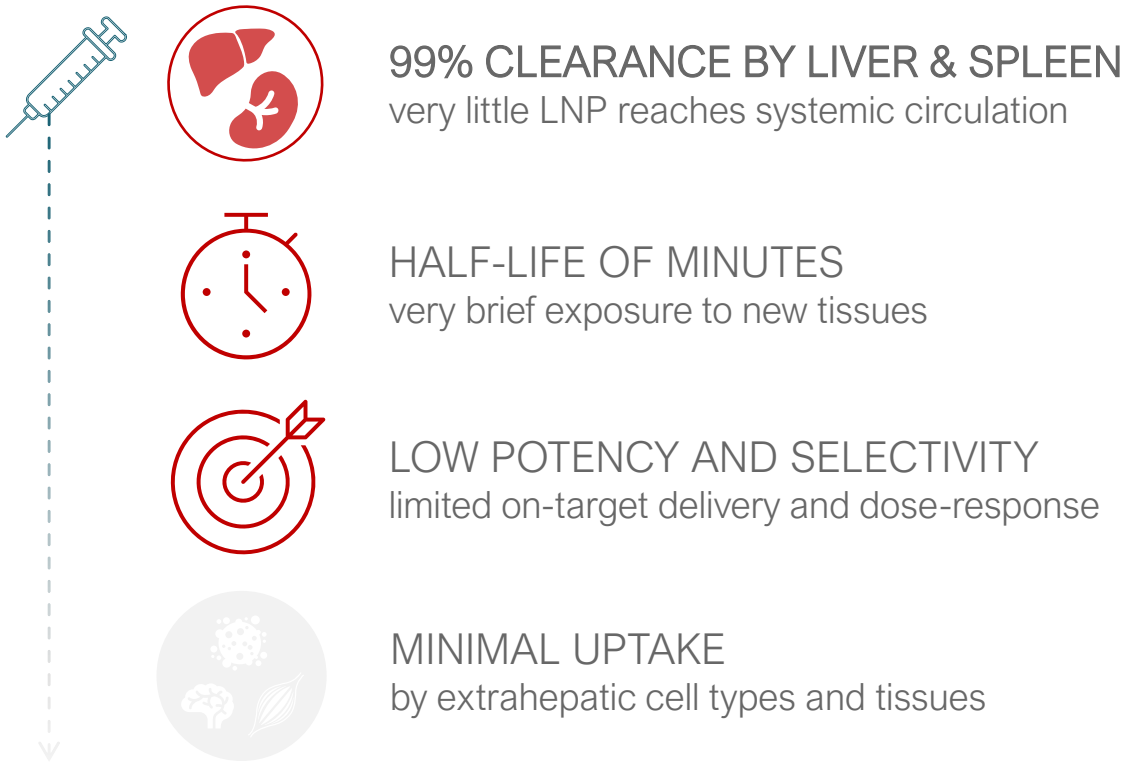
HALF-LIFE OF MINUTES
very brief exposure to new tissues

LOW POTENCY AND SELECTIVITY
limited on-target delivery and dose-response

MINIMAL UPTAKE
by extrahepatic cell types and tissues

By avoiding liver and spleen clearance, ctLNP enables a platform approach to targeting previously unreachable cell types and tissues

Traditional LNPs



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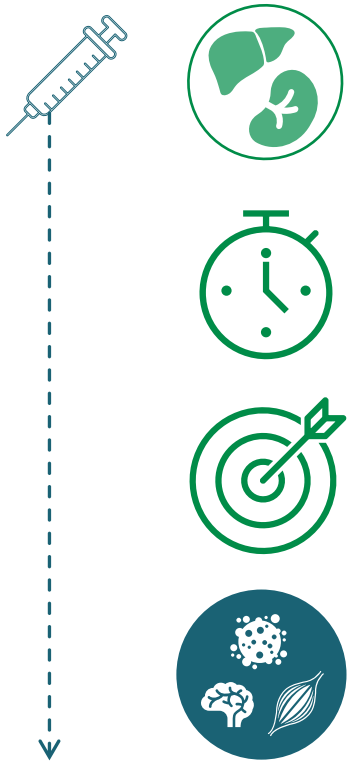
GBIO cell-targeted LNPs



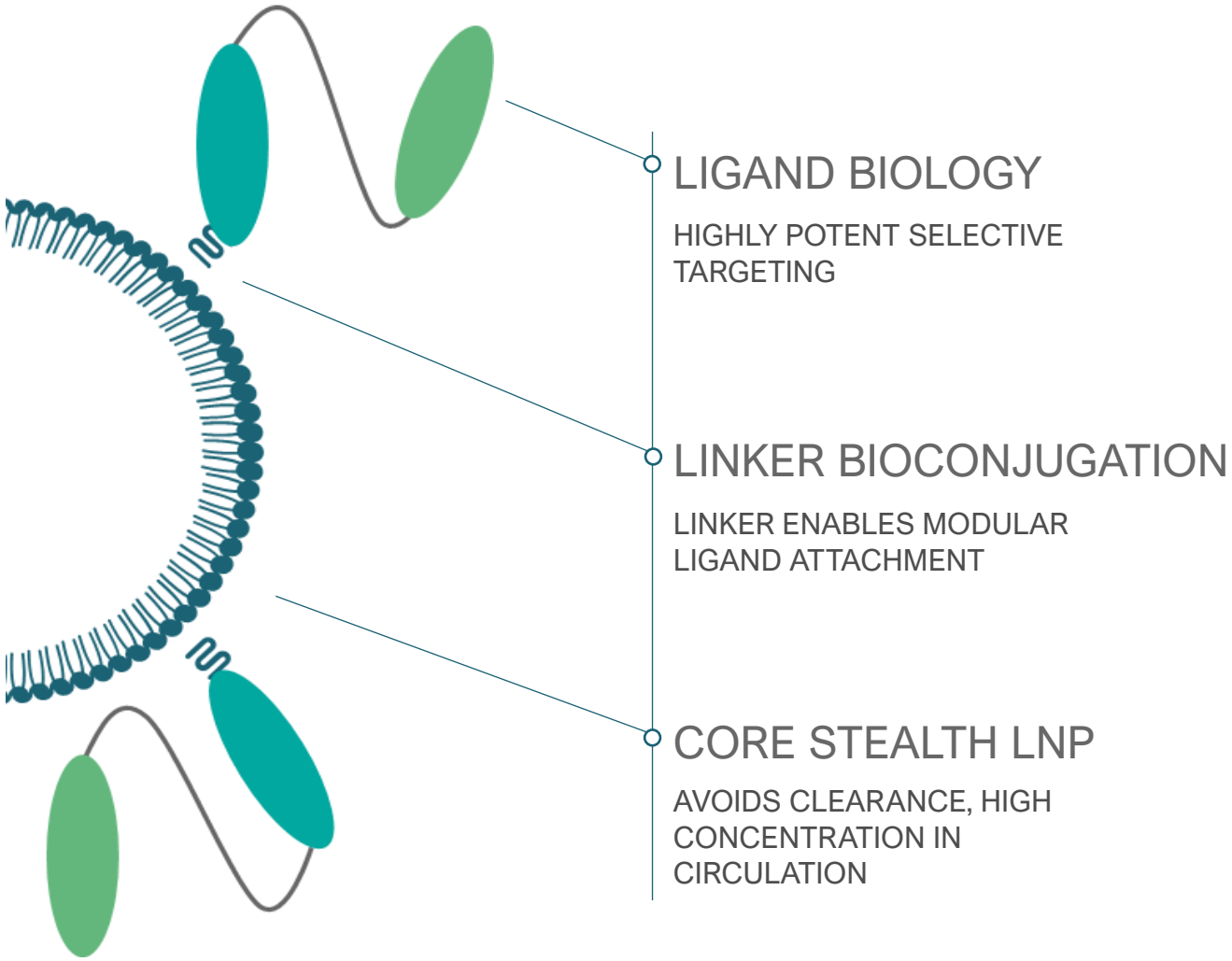
1% CLEARANCE BY LIVER & SPLEEN
almost all ctLNP reaches systemic circulation

HALF-LIFE OF HOURS
long exposure to new tissues

HIGH POTENCY AND SELECTIVITY
efficient on-target delivery, large dose-response

HIGH UPTAKE
by extrahepatic cell types and tissues

ctLNP is a modular proprietary platform based on stealth, linker, and targeting



Key features for multi-tissue delivery

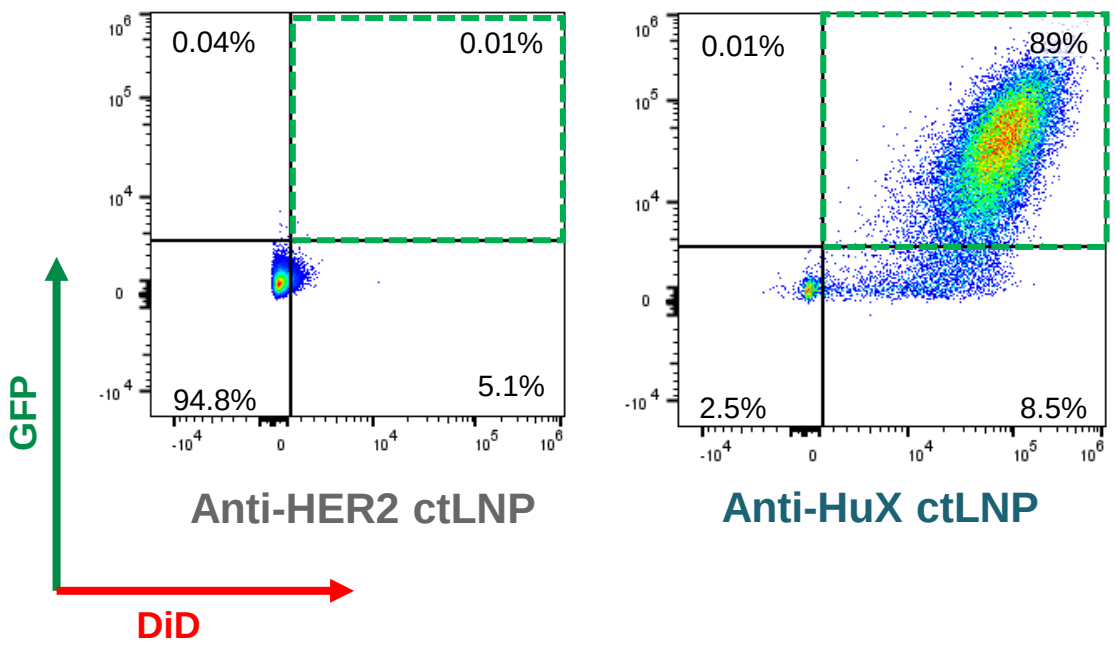
- ✓ Stealth
- ✓ Selective
- ✓ Efficient
- ✓ Specific
- ✓ Potent
- ✓ Works with multiple payloads

generation bio™

T cell ctLNPs demonstrate receptor-specific, dose-dependent uptake *in vitro*

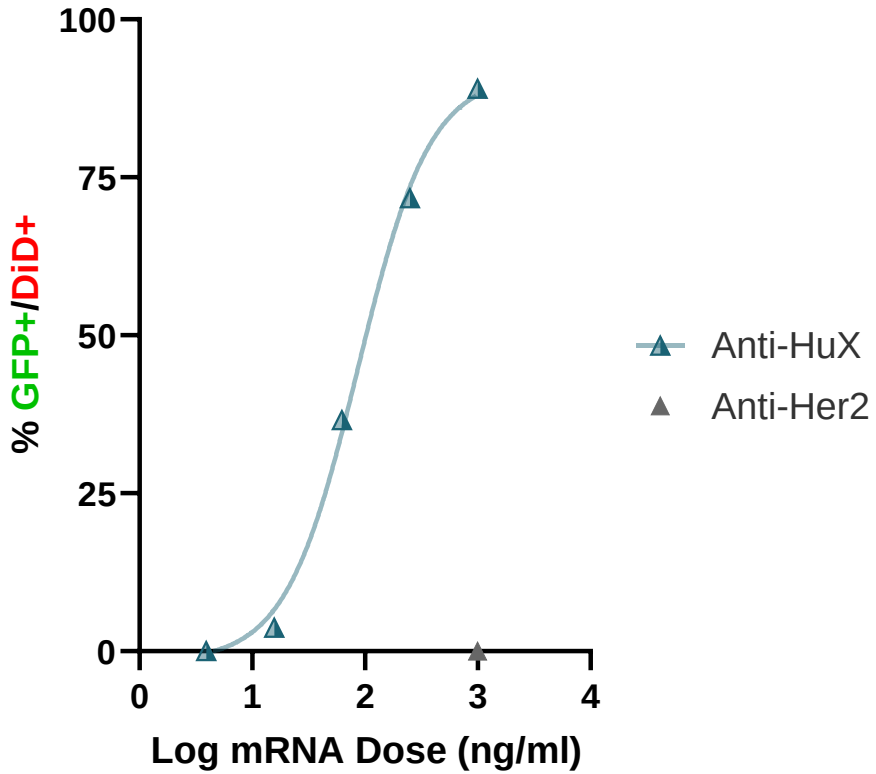
Anti-HER2 ctLNP does not drive uptake or expression in T cells

Anti-HuX ctLNP drives selective uptake and expression in T cells



ctLNP uptake is dose-dependent

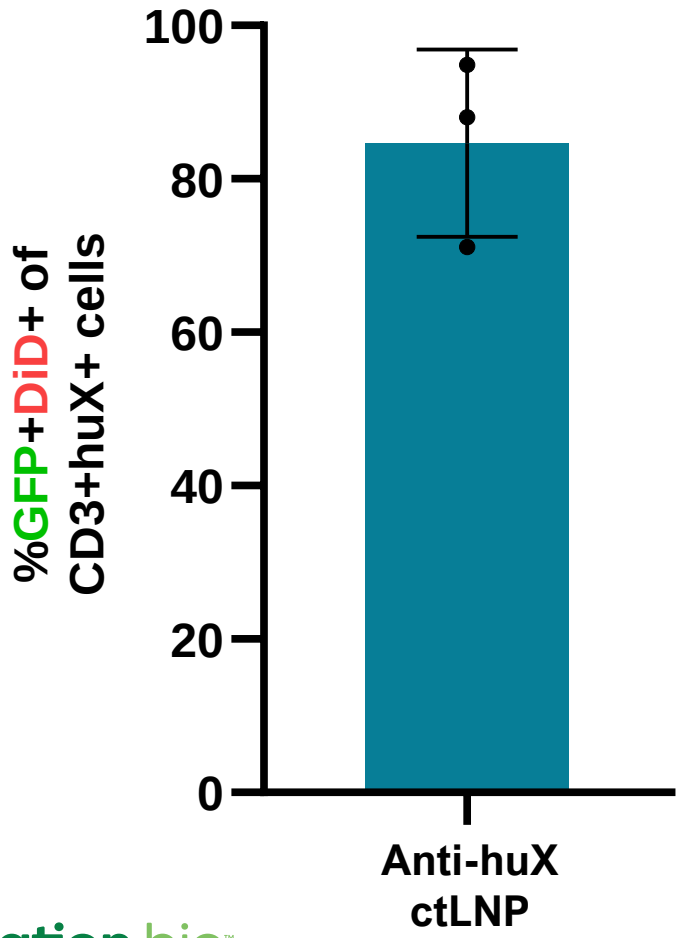
Dose Responsive uptake (DiD) *and* expression (GFP) in primary human T cells



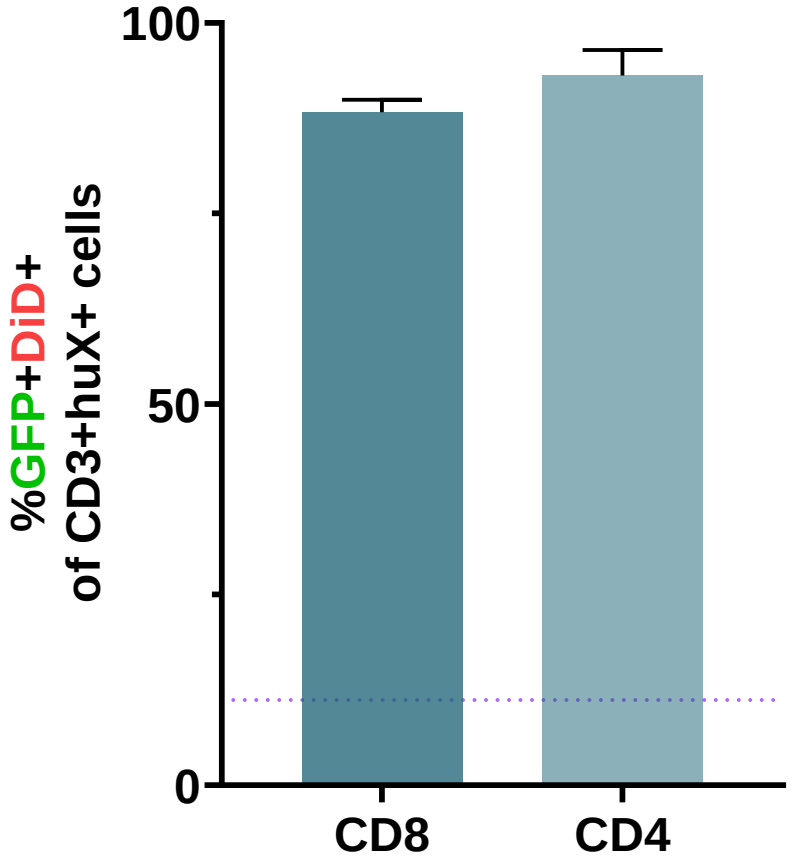
ctLNP drives highly efficient delivery to target-positive T cell population

GFP expression in circulating T cells

(hPBMC mice; 0.5mpk; 24hrs post dose)

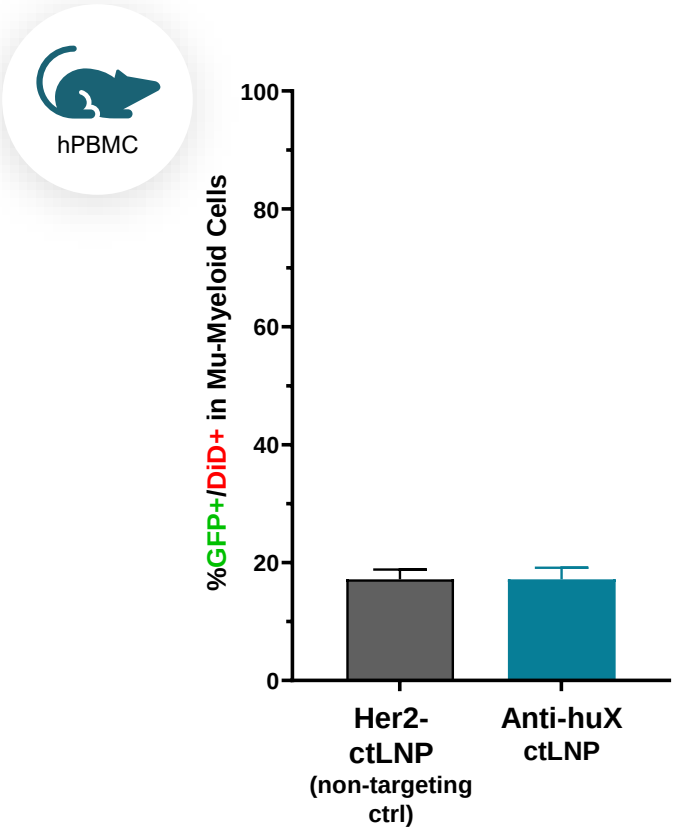


Highly efficient delivery to target expressing T cells

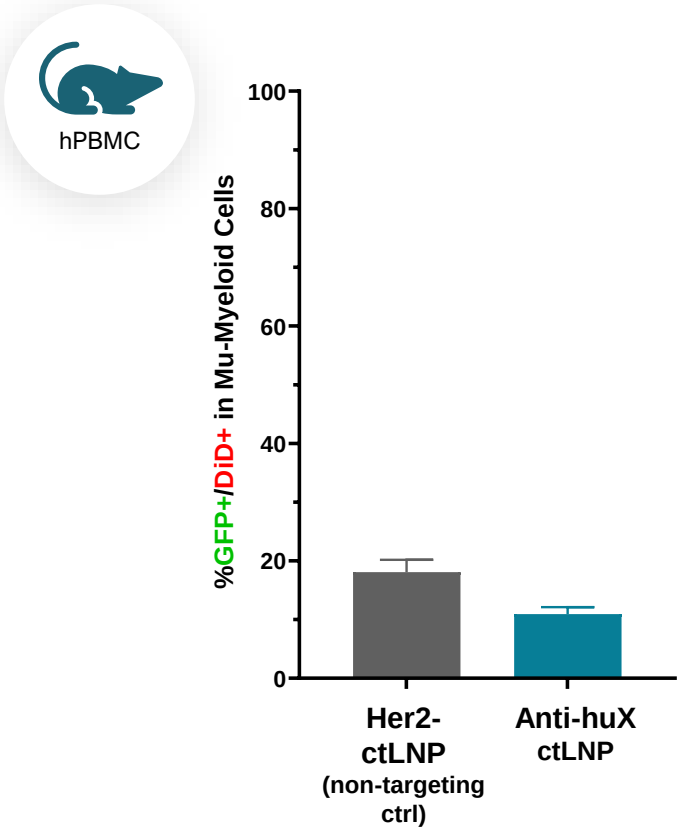


Off-target uptake and expression remains at baseline for T cell ctLNP

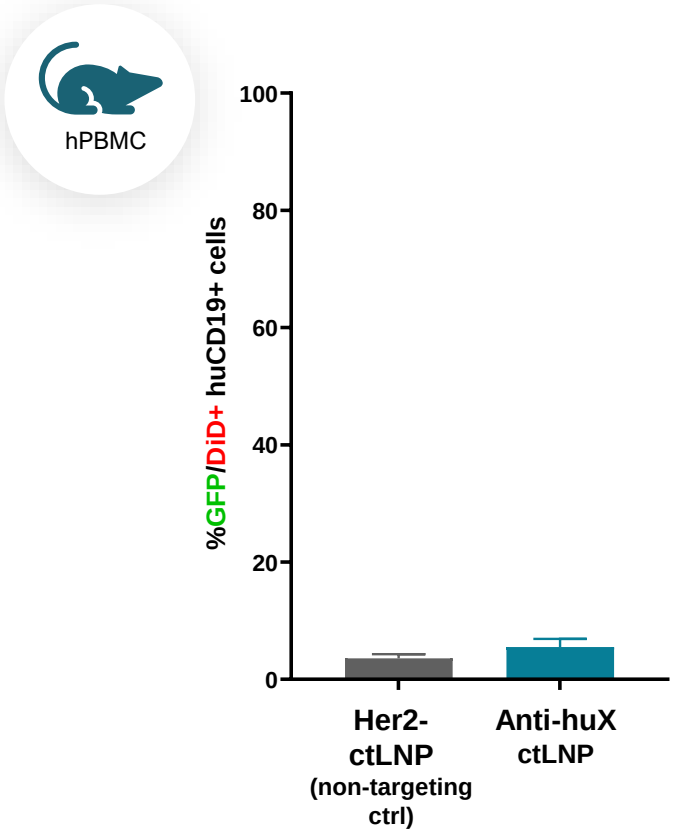
GFP Expression in Circulating Myeloid Cells



GFP Expression in Splenic Myeloid Cells

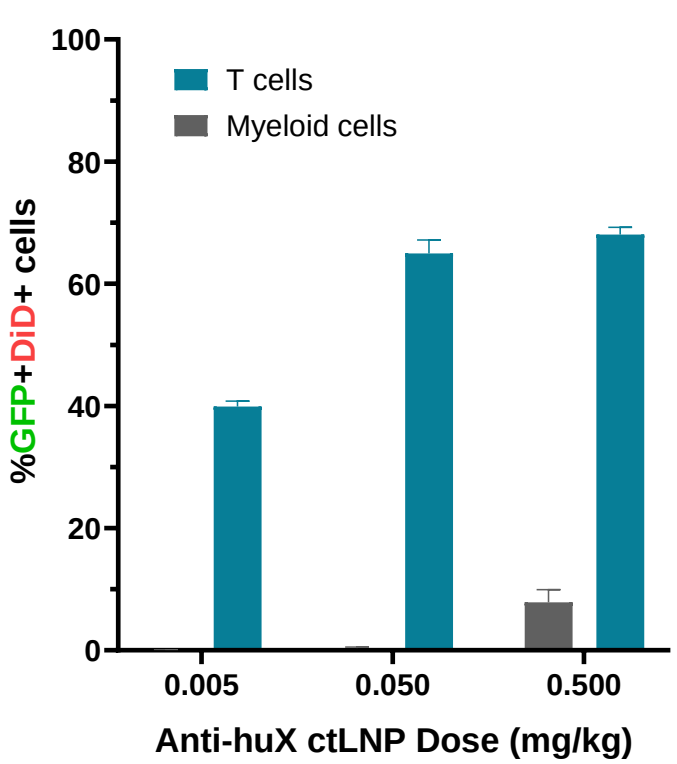


GFP Expression in Splenic B Cells

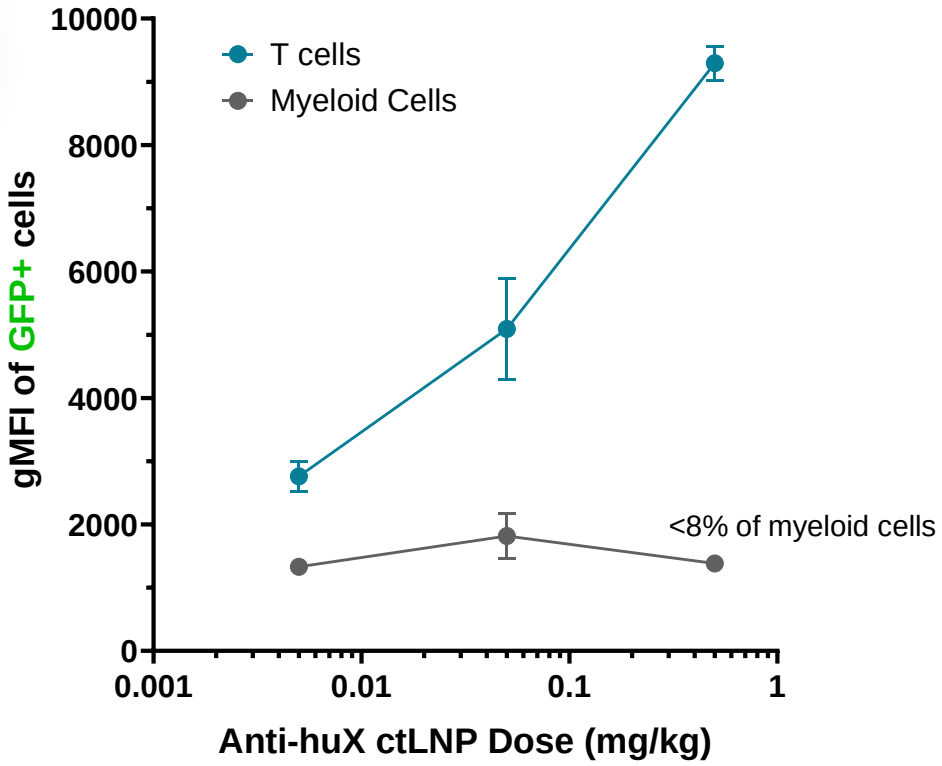


T cell ctLNP demonstrates potent and selective *in vivo* delivery, with dose response from 0.005 mg/kg to 0.5 mg/kg

Efficient dose-dependent T cell transduction

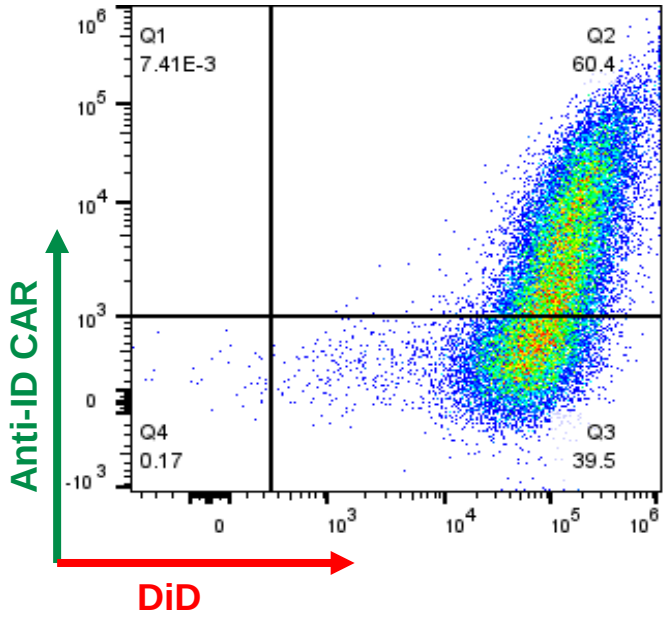


Expression in T cells increases with dose, without increase in off-target cell uptake

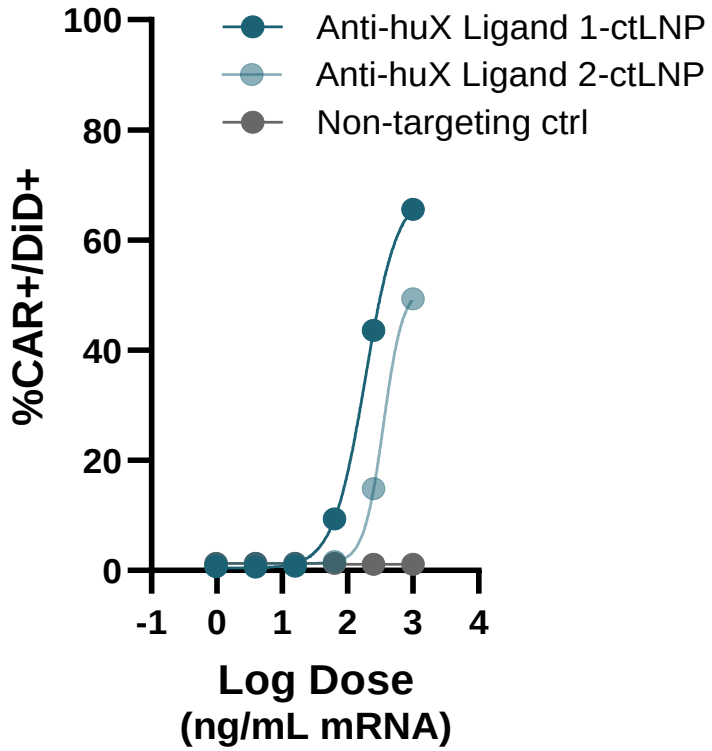


T cell ctLNP drives high level of functional CAR expression in T cells *in vitro*

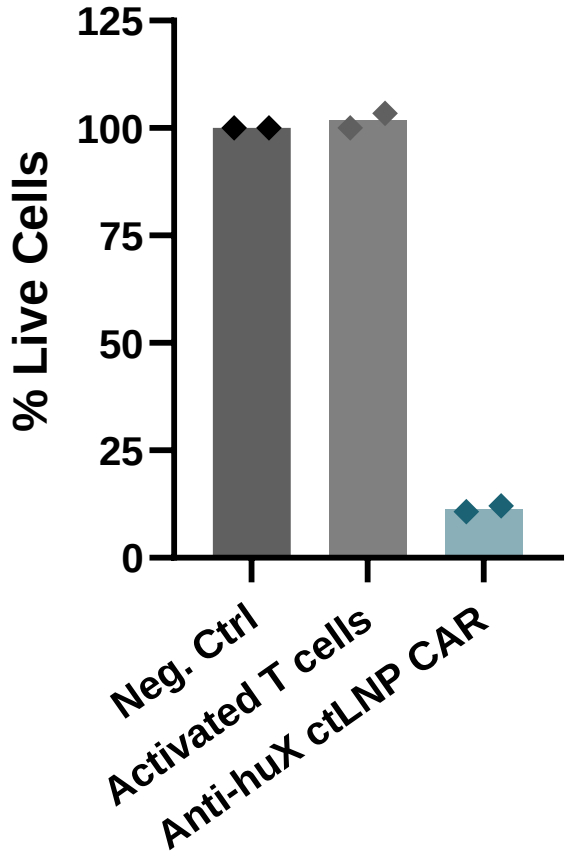
Robust CAR expression



Dose-dependent



Functional in cell killing assay

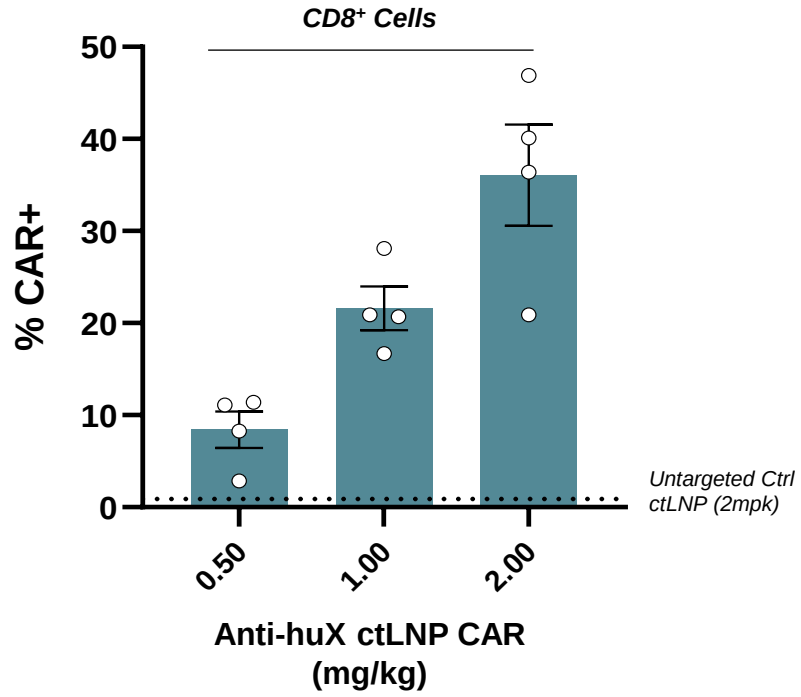


T cell ctLNPs show robust uptake, expression of CAR encoding mRNA *in vivo*

Efficient, dose-responsive CAR expression

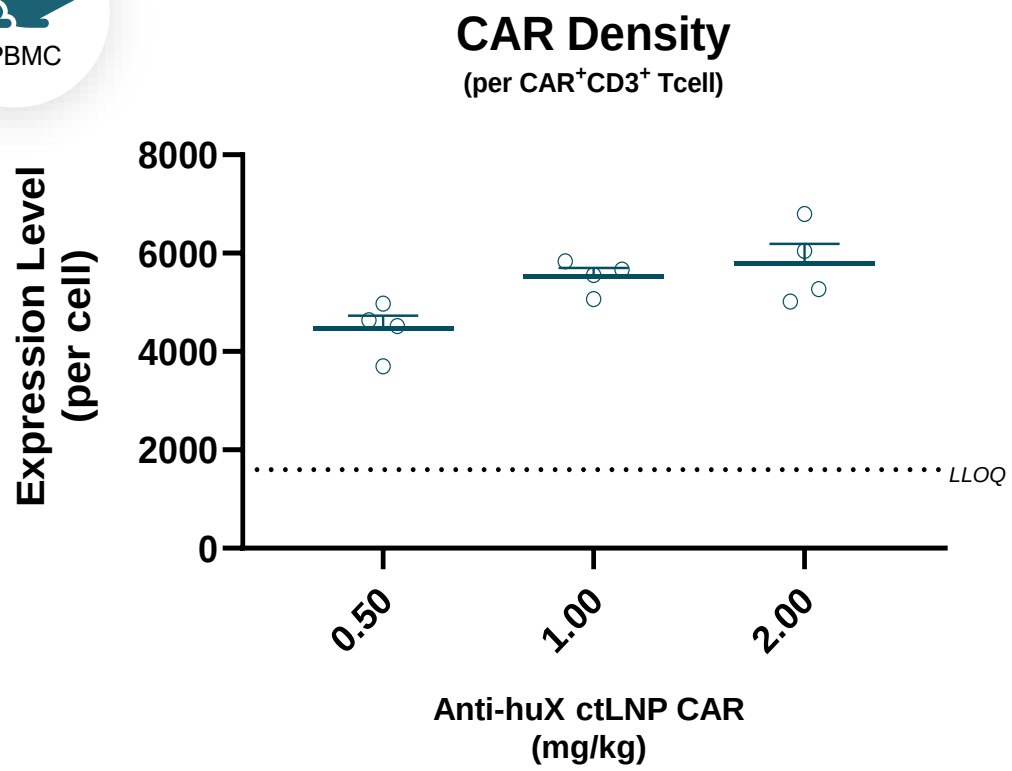
(hPBMC mice; splenocytes; 48hrs post dose)

hPBMC



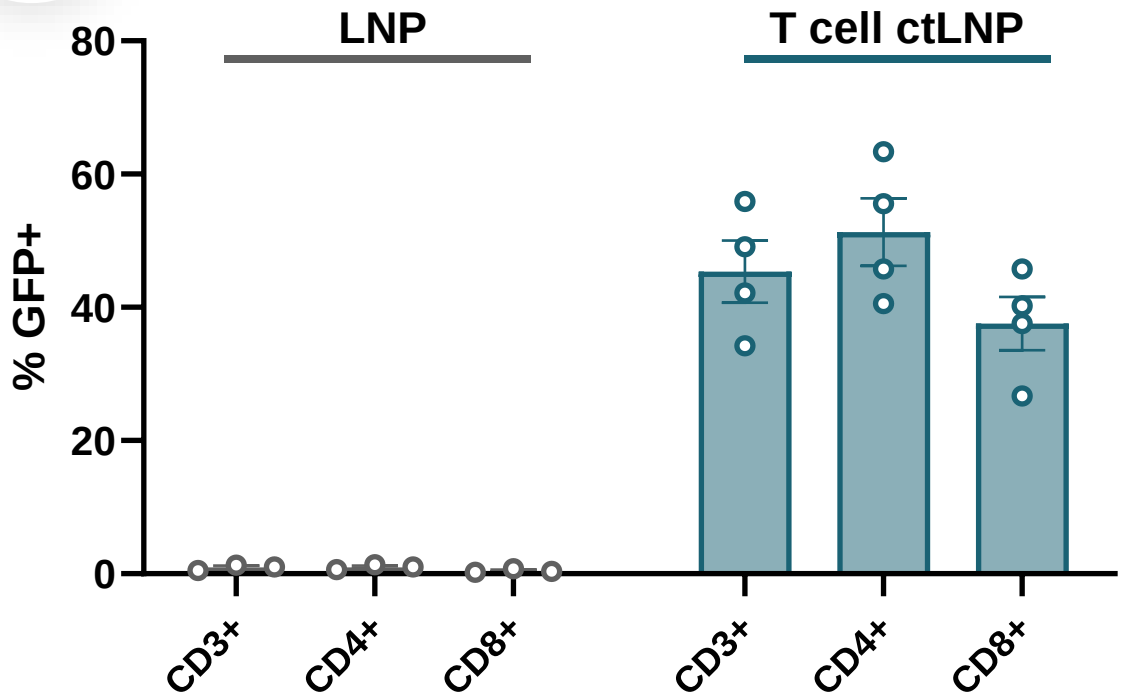
Robust surface presentation on CAR-T cells

hPBMC

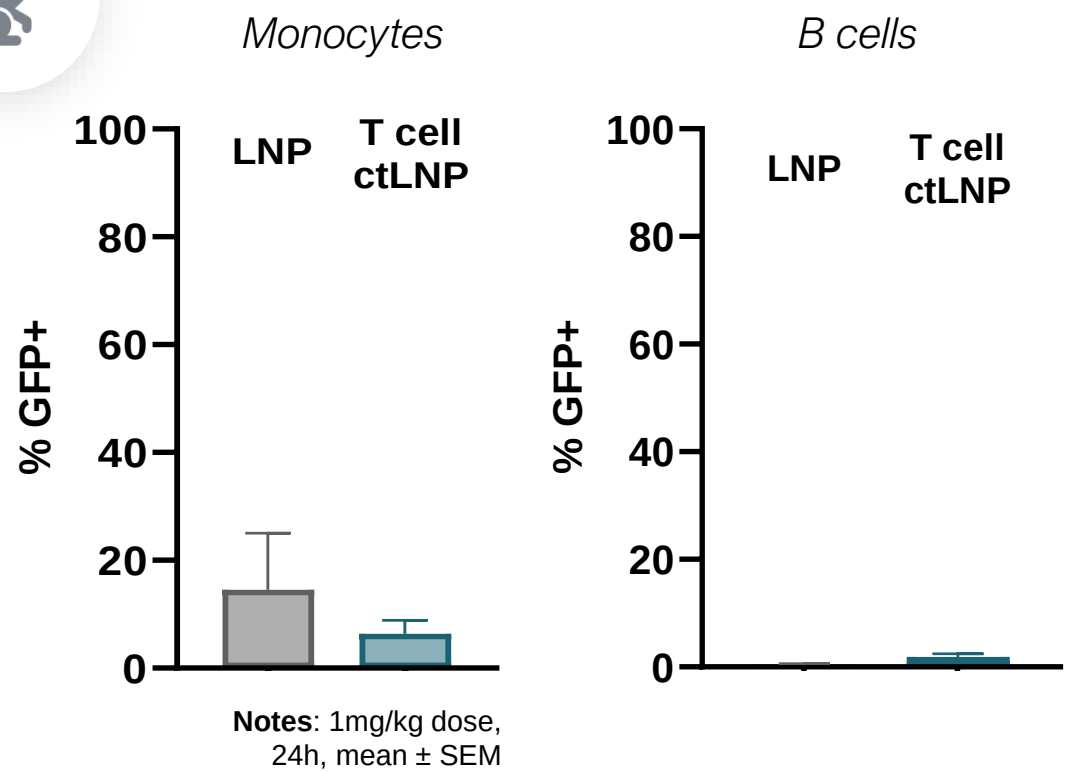


Highly selective, *in vivo* delivery of mRNA to T cells confirmed in NHPs

Majority of T cells transduced, with balanced biodistribution



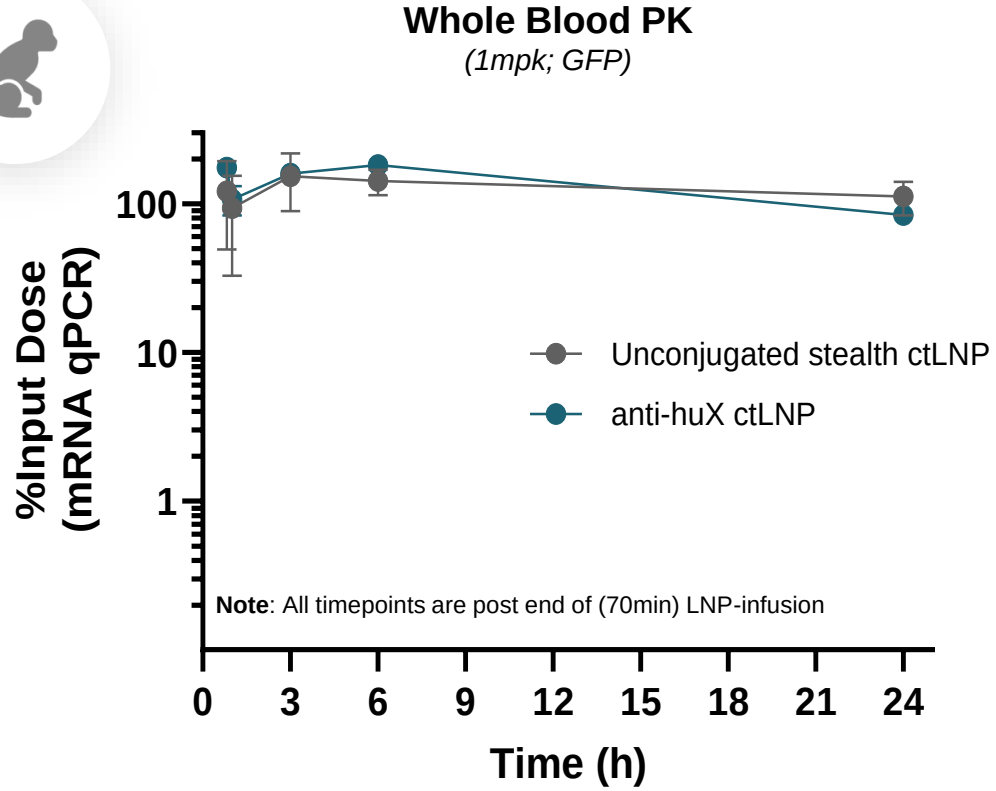
Monocyte & B cell uptake remains below baseline



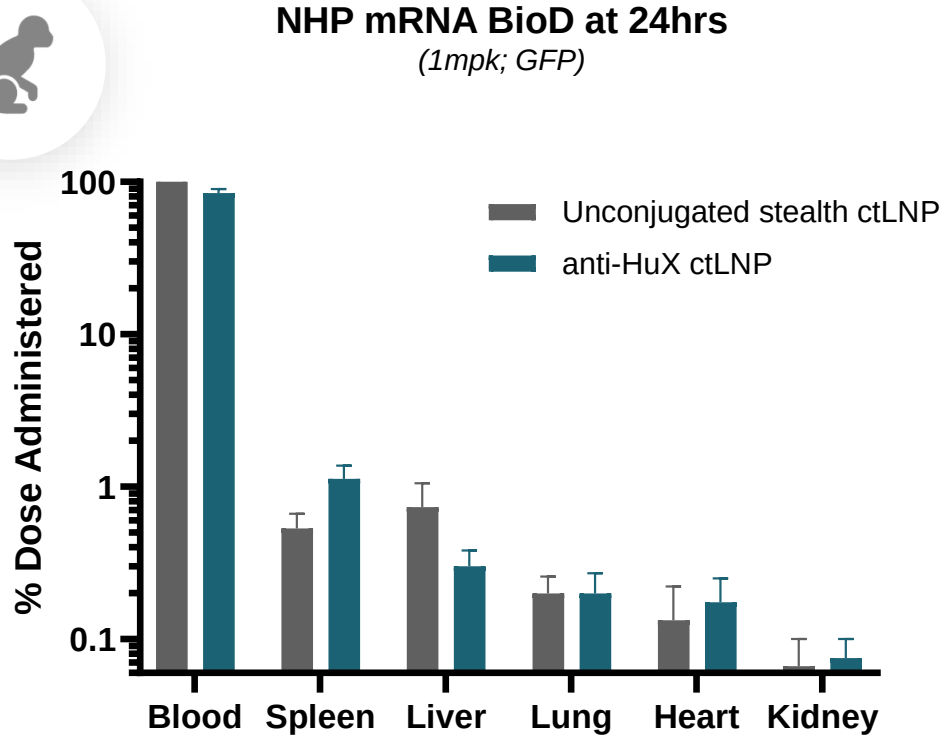
Notes: 1mg/kg dose, 24h, mean ± SEM

ctLNP base composition has long half-life in circulation and very low liver and spleen clearance in NHP

Long circulation time in NHP

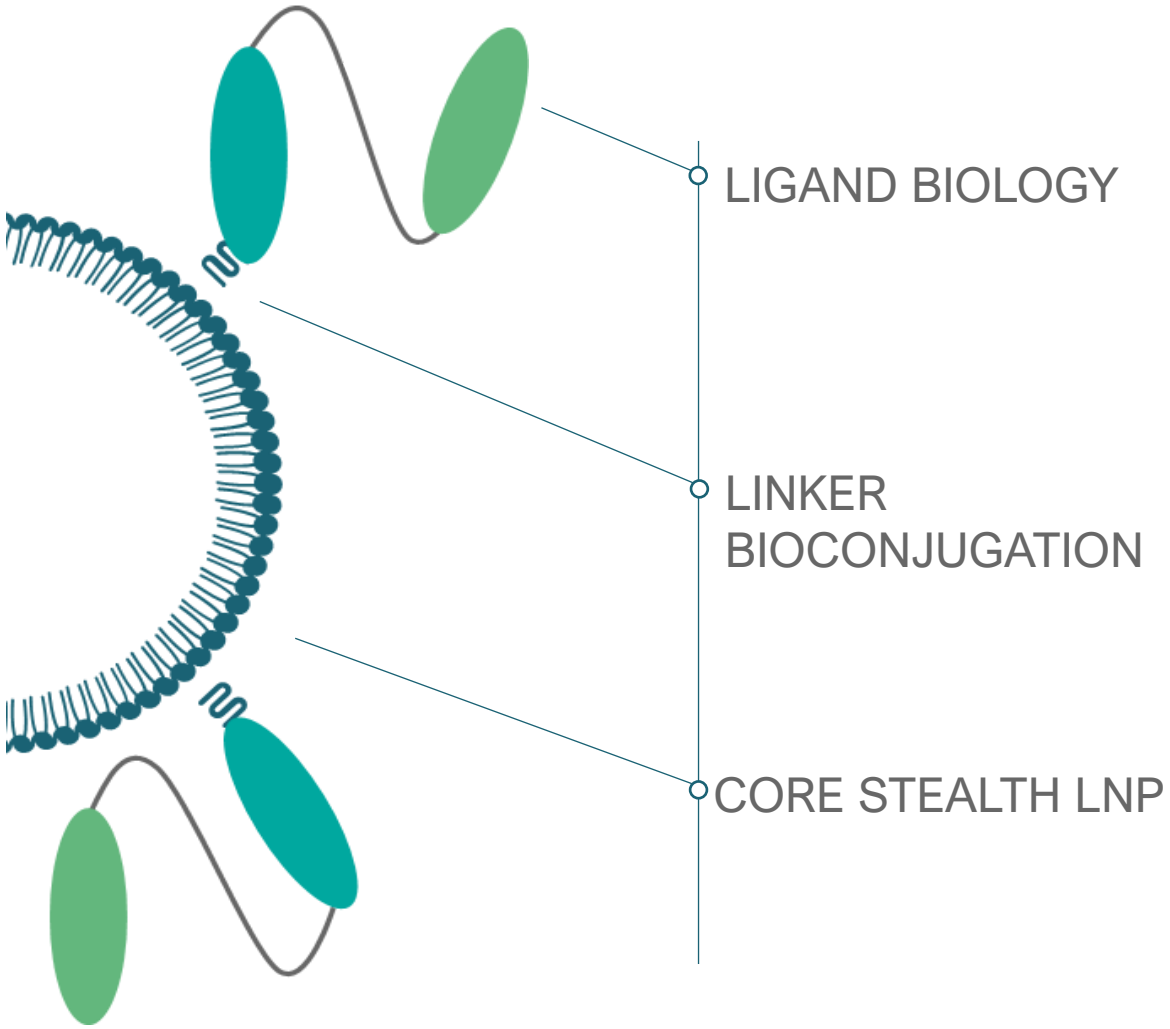


Majority of drug remains in circulation, avoiding rapid clearance by liver or spleen

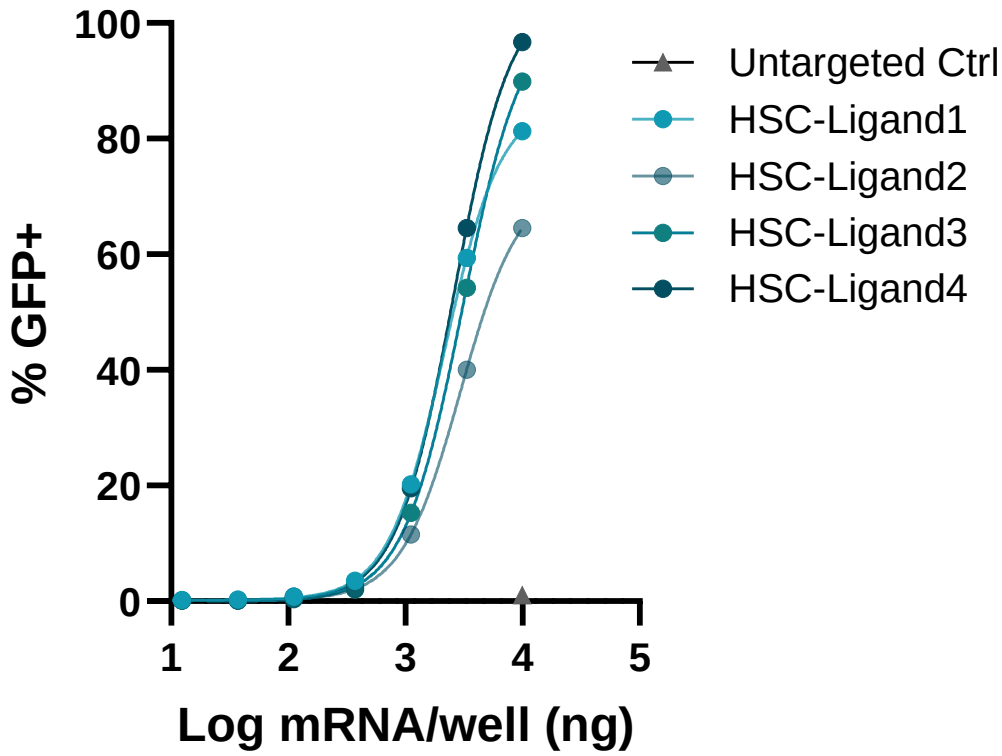


Consistent with mouse data with latest stealth ctLNP; majority of drug remains in circulation

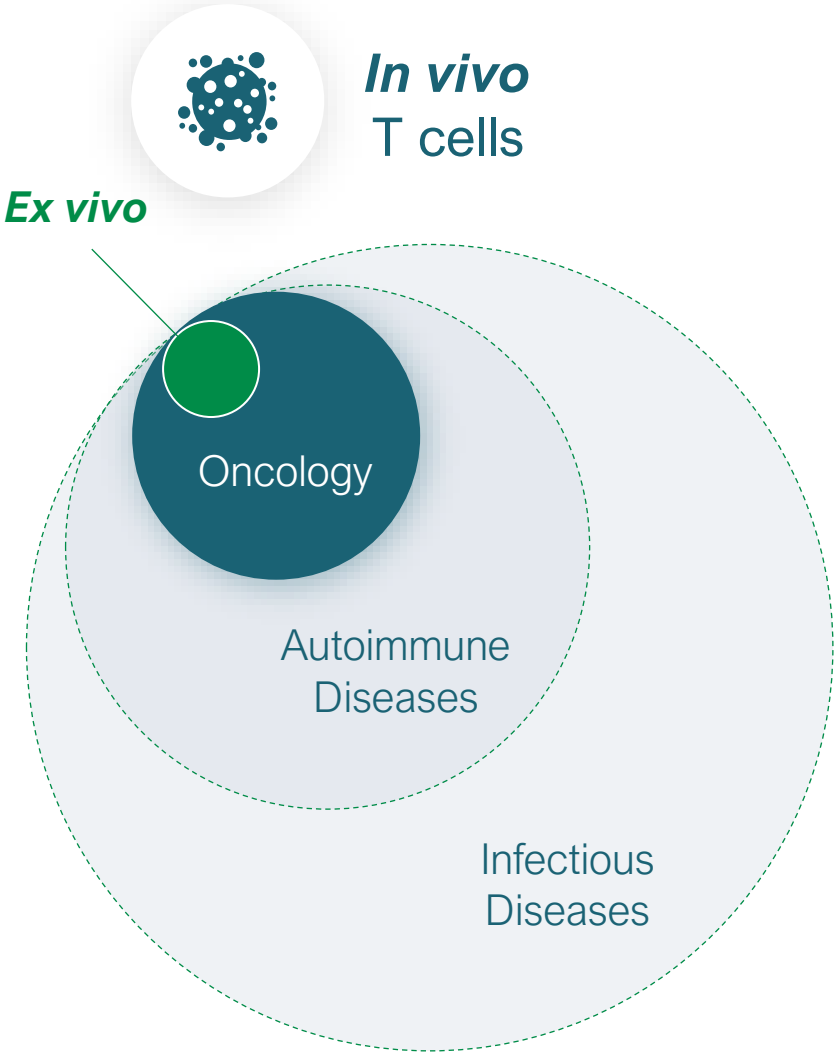
We are deploying our ctLNP system to selectively target HSCs and other extrahepatic cell types

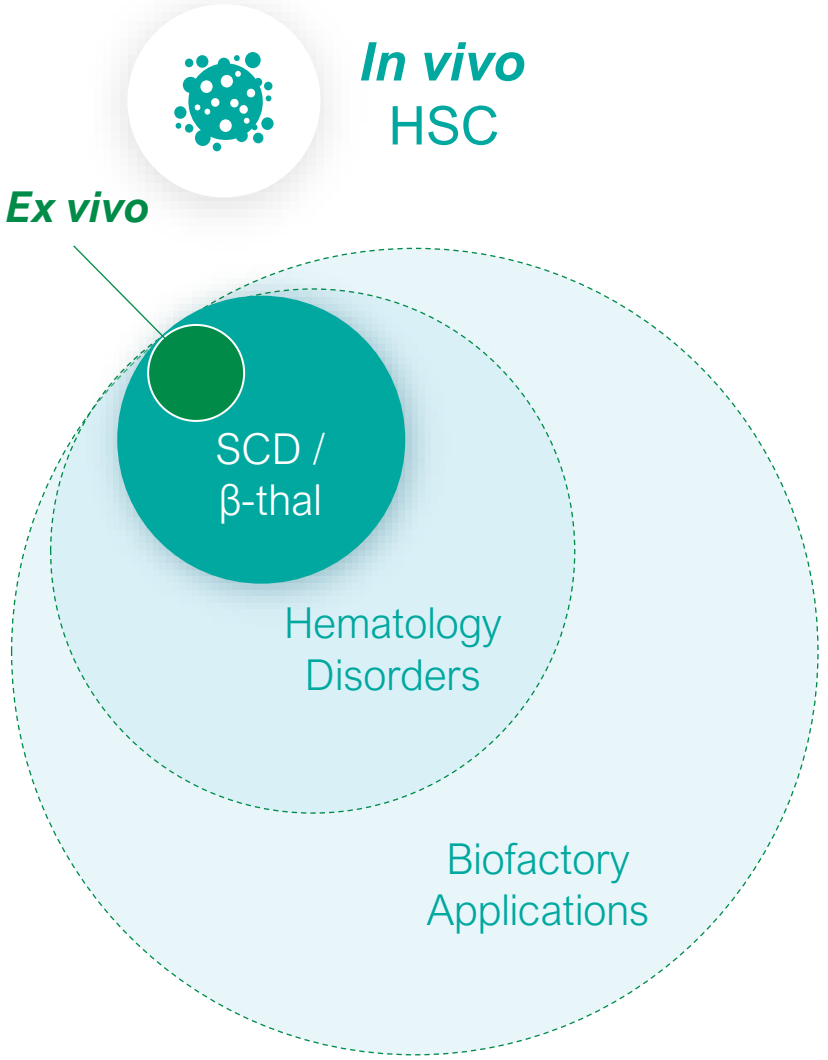


ctLNP delivery to primary HSCs



Redosable *in vivo* therapeutic profile expands the opportunity for T cells and HSCs, and drives growth into new areas





Key 2024 milestones for *in vivo* T cell and HSC programs

In vivo T cells

- ✓ Stealth profile avoids liver and spleen
- ✓ Efficient, potent, selective delivery
- ✓ Highly tunable ligand system
- ✓ High levels of CAR expression
- ✓ CARs are functional
- ❑ Evaluate murine disease models to support program development

In vivo HSCs

- ✓ Apply T cell learning to HSC targeting
- ✓ Identify HSC-specific ligands
- ✓ Confirm selective HSC uptake in vitro
- ❑ *In vivo* HSC delivery in humanized mice
- ❑ *In vivo* HSC editing in humanized mice

*Hematopoietic stem cells

Portfolio focuses on novel approaches to three program areas

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Low COGS drive scale, market uptake and share

$

Cash runway to 2H 2027
to focus on building clinical programs

*Hematopoietic stem cells (HSCs)
*Extended half-life factors (EHLs)

Winning in the evolving $13B Hemophilia A market will require differentiation across three key dimensions

	Extended Half-Life	Bispecifics	gb
COVERAGE	5-15%	15%	5 – 50%
DURATION	1 week	1-3 weeks	3-5 years
ACCESS	Limited	Limited	Global

Expanding 'Hemophilia Free' Space for Patients

GBIO is bringing the unique features of DNA to non-viral genetic medicine

Alnylam® PHARMACEUTICALS

siRNA-GalNAc

Redosable

Loss of function

Durable

moderna

mRNA-LNP

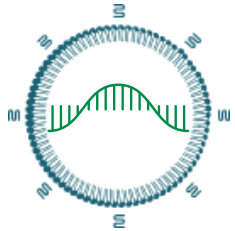
Redosable

Gain of function

Transient

generation bio™

iqDNA-ctLNP



Redosable

Gain of function

Durable

Immune-quiet cargo was the gating innovation for RNA therapeutics

Alnylam® PHARMACEUTICALS

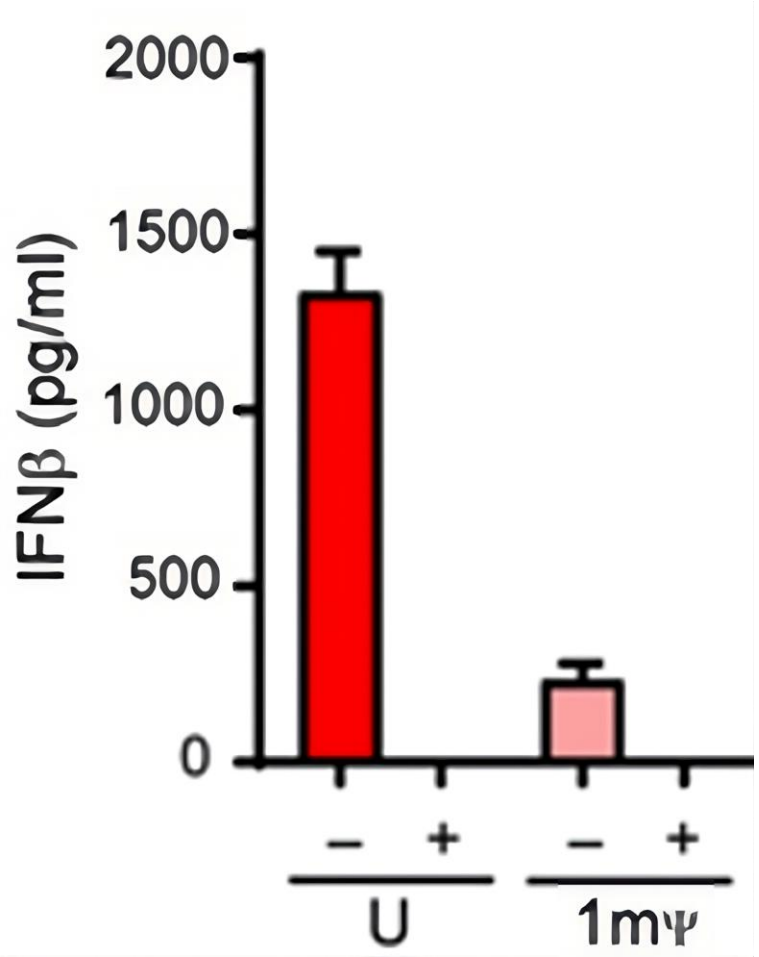
siRNA

2’ ribose chemical modifications

moderna

mRNA

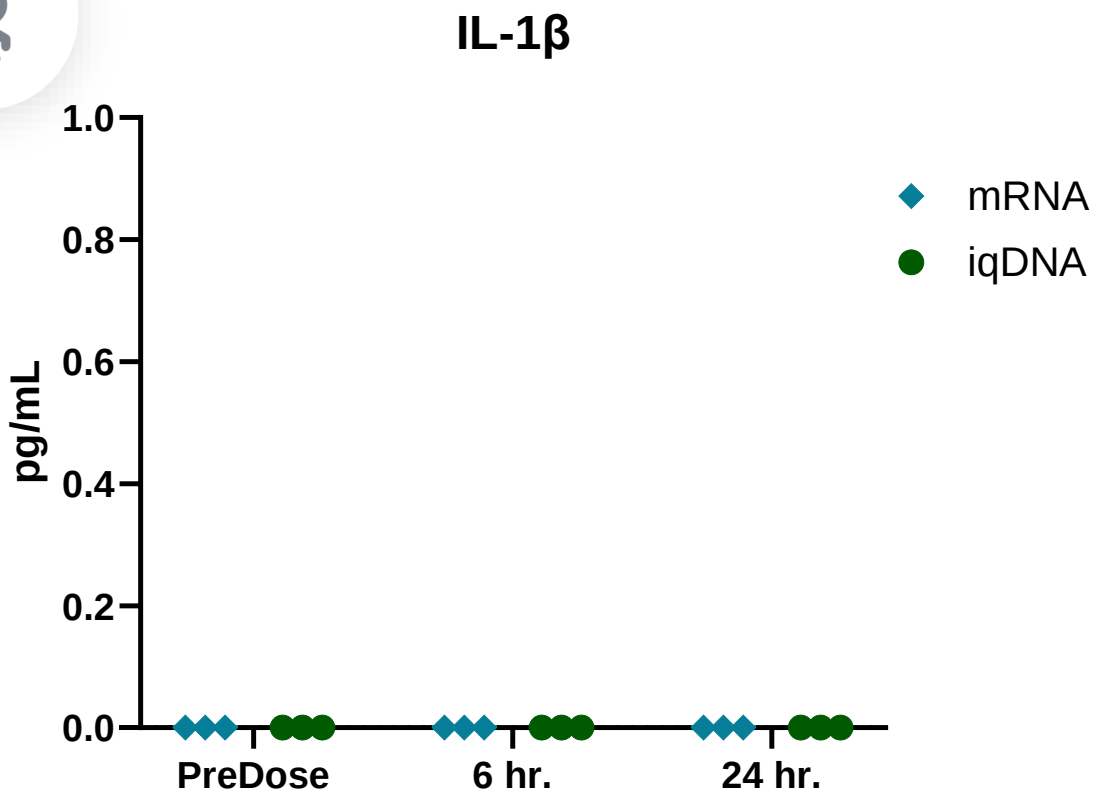
Uridine chemical modifications/purity



Immune-quiet DNA (iqDNA) is the gating innovation for DNA therapeutics

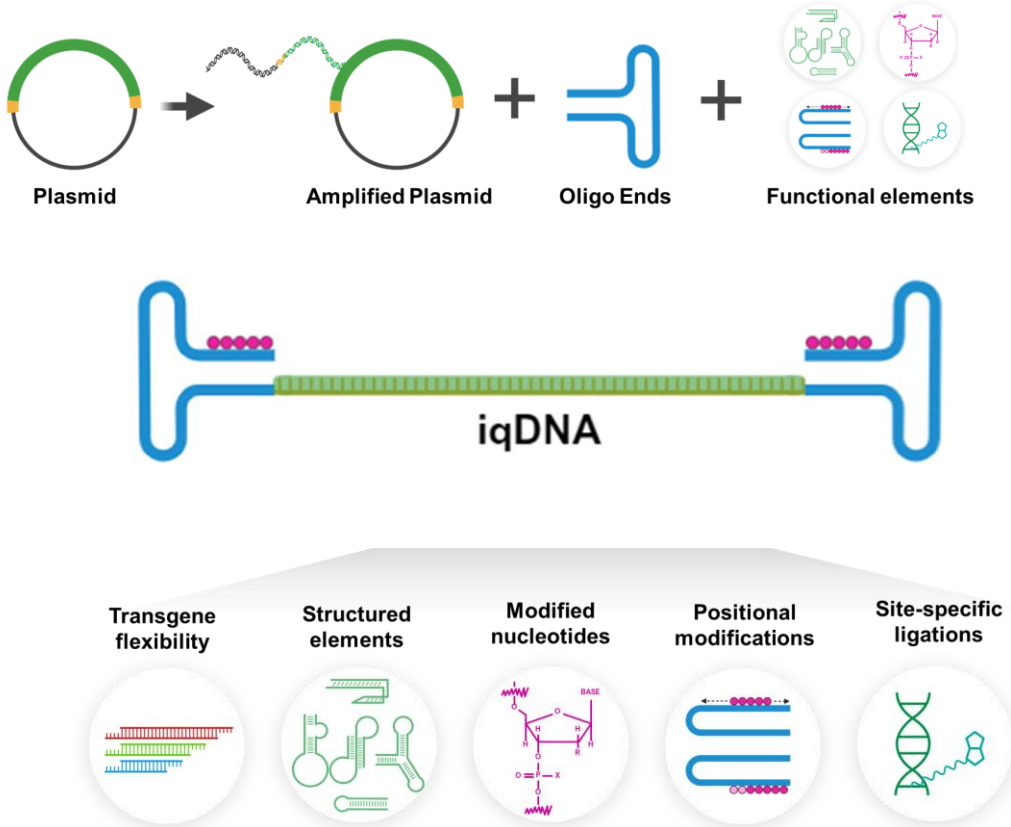
generation bio™

Immune-quiet DNA

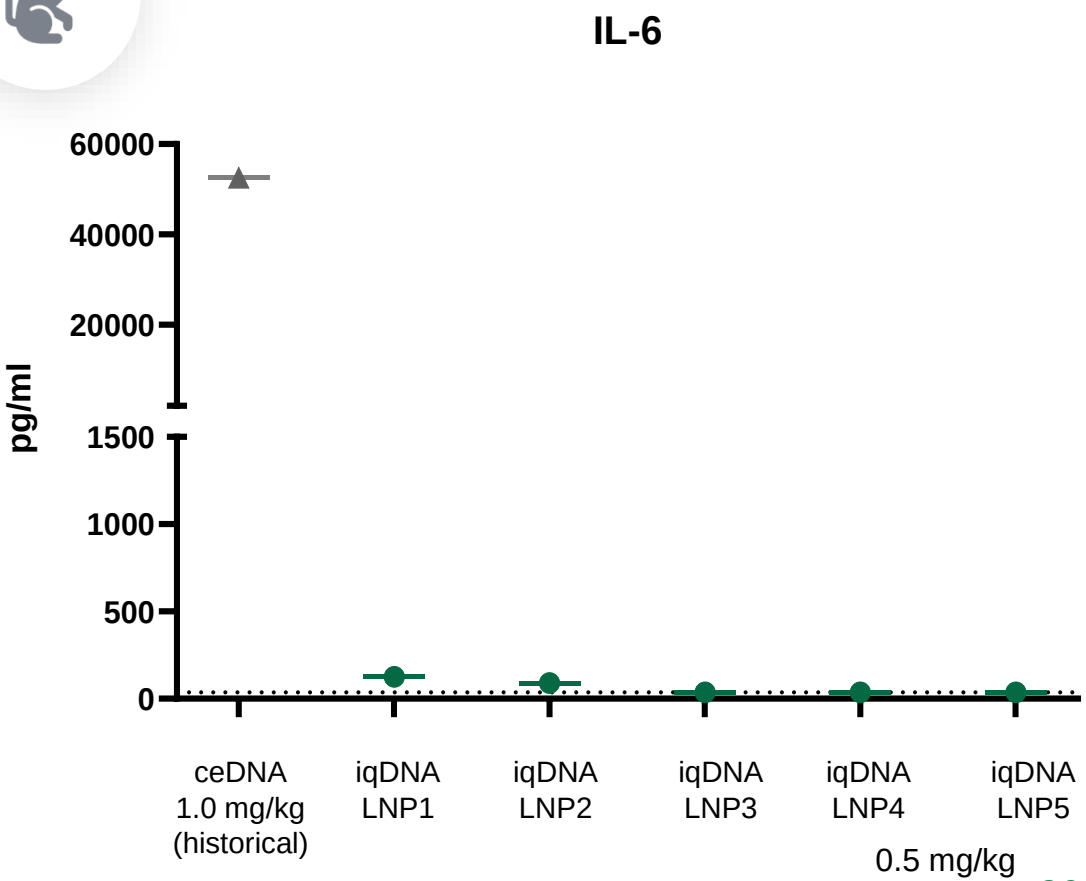


We invented iqDNA using rapid enzymatic synthesis (RES), a proprietary cell-free production method that continues to drive optimization

Proprietary rapid enzymatic synthesis enabled the discovery of iqDNA

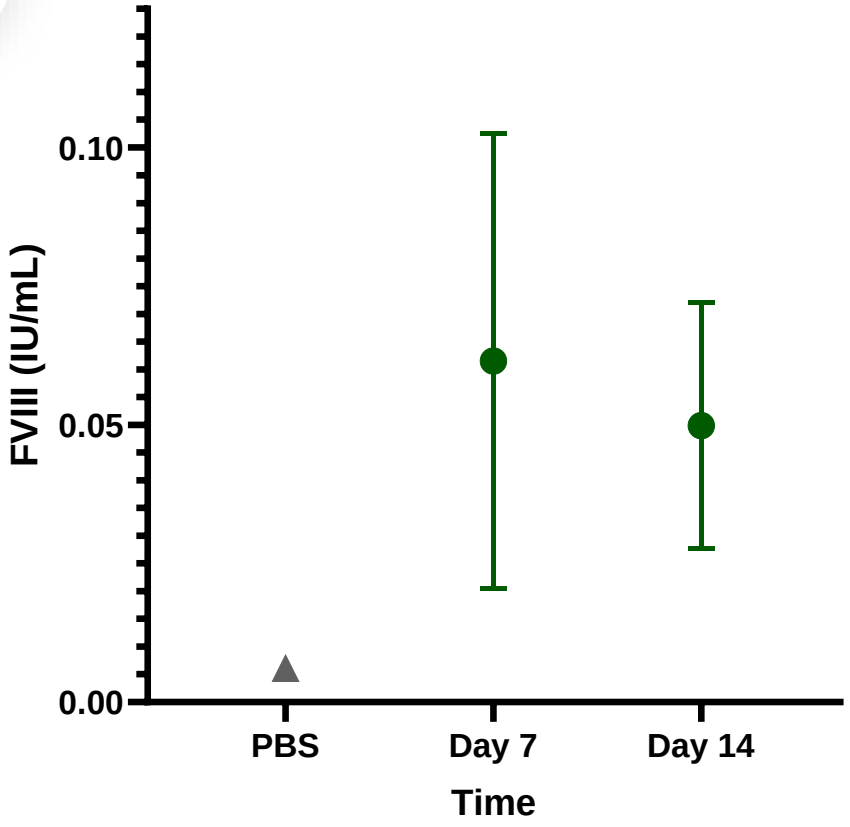


iqDNA profile translates to NHPs across LNPs

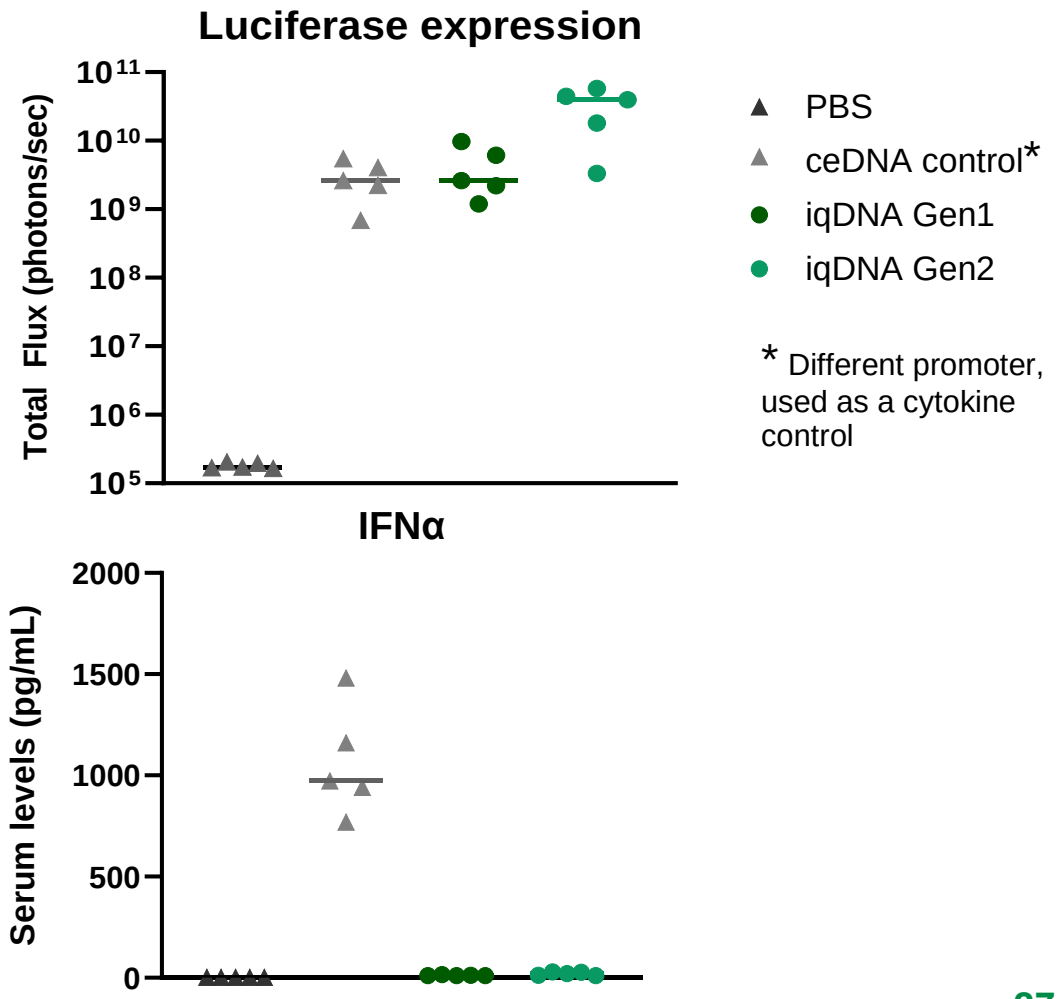


We are testing a second generation iqDNA with increased potency

Gen 1 iqDNA demonstrates durable expression



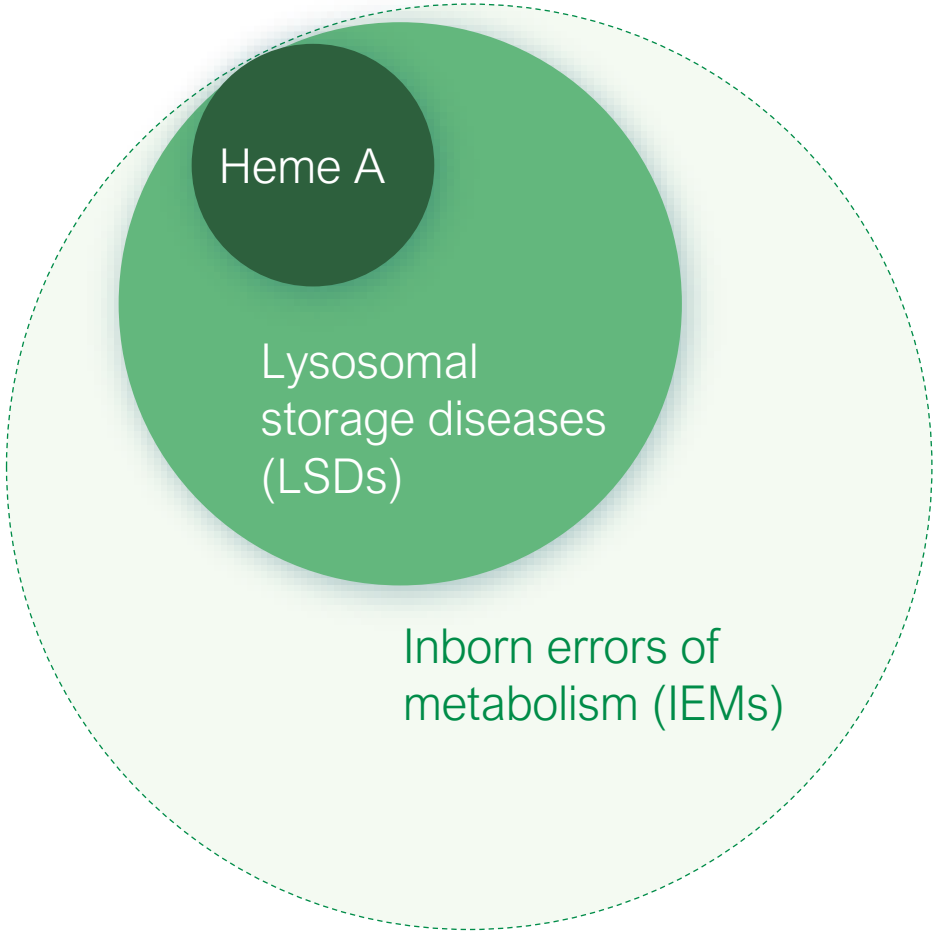
Gen 2 iqDNA demonstrates increased potency and remains immune quiet



Hemophilia A profile opens a large set of follow-on indications

COVERAGE	**High**
DURATION	**3-5 years**
ACCESS	**Global**

Expanding 'Disease Free' Space for Patients



Key 2024 milestones to establish target iqDNA expression levels for liver diseases

Hepatocytes

- ✓ iqDNA is not detected by innate immune sensors
- ✓ Avoids innate immune detection across species
- ✓ Robust and durable expression
- ✓ RES-enabled structural changes increase iqDNA potency for reporter molecules in mice
- ❑ Demonstrate improved iqDNA potency for Factor VIII in mice

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- Flexible cargo
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to focus on building clinical programs

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*Extended half-life factors (EHLs)


We're pushing the limits of genetic medicine
And our goal is no limits
Thank You
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