We're pushing the limits of genetic medicine

And our goal is no limits

November 2023

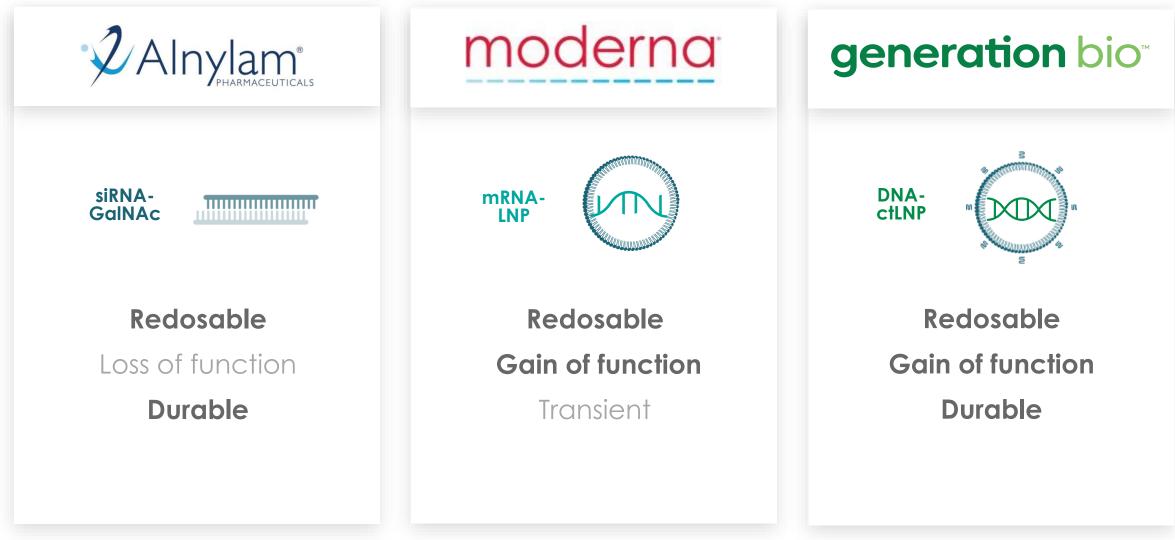
Forward Looking Statements

Any statements in this presentation about future expectations, plans and prospects for the company, including statements about our strategic plans or objectives, our technology platform, including our rapid enzymatic synthesis (RES) technology, our research and clinical development plans, and our 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 RES manufacturing process; expectations for regulatory approvals to conduct trials or to market products; 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 guarterly 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.

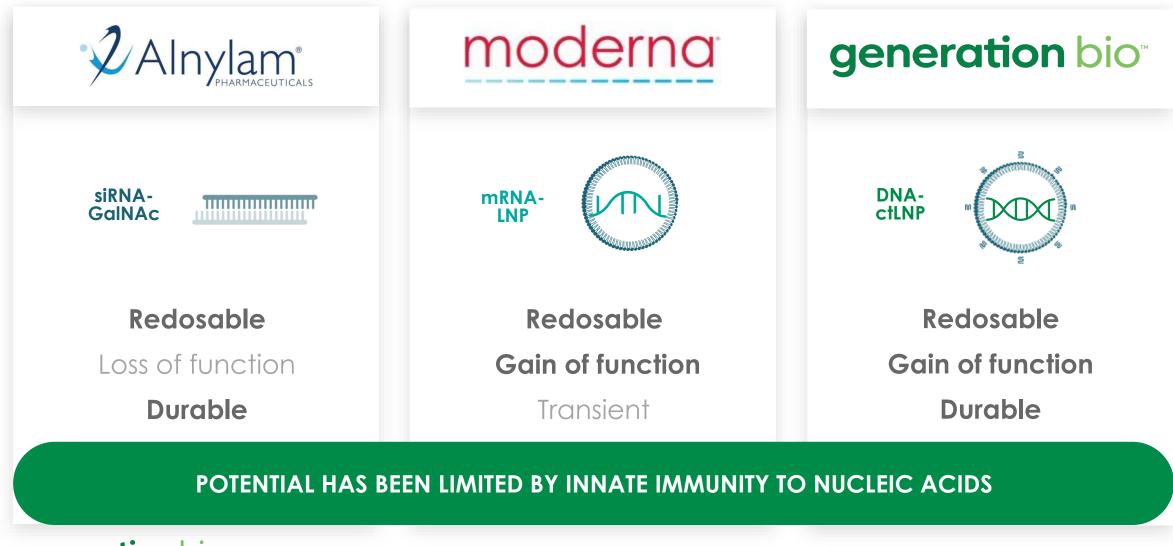
Company Overview

Geoff McDonough

GBIO is bringing DNA to non-viral genetic medicines

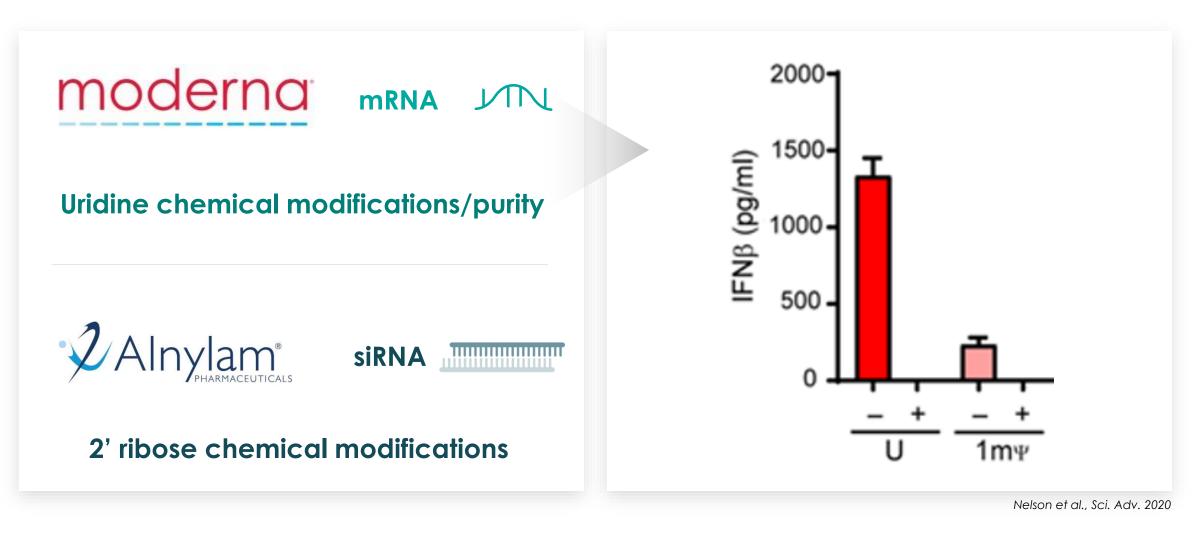


GBIO is bringing DNA to non-viral genetic medicines

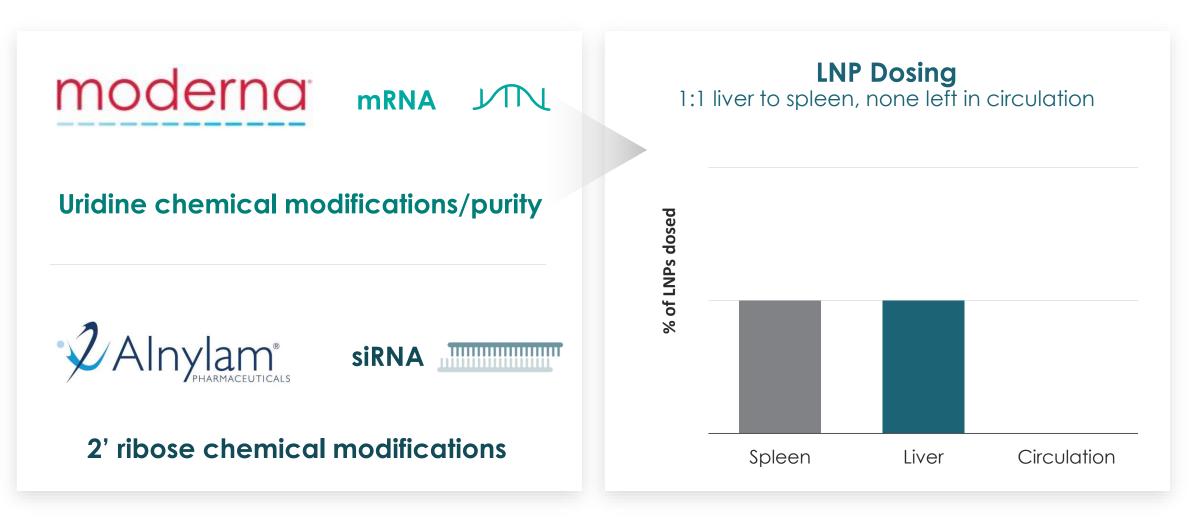


generation bio^{*}

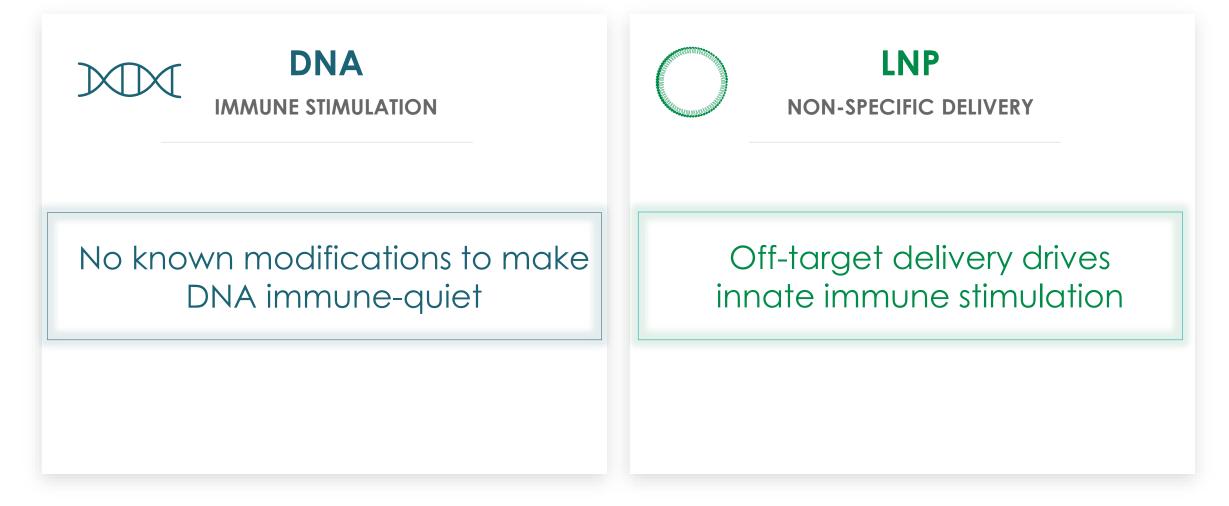
Immune-quiet cargo was the gating innovation for RNA...



... allowing RNA to use non-selective LNP delivery



DNA innate immunity had no known solution

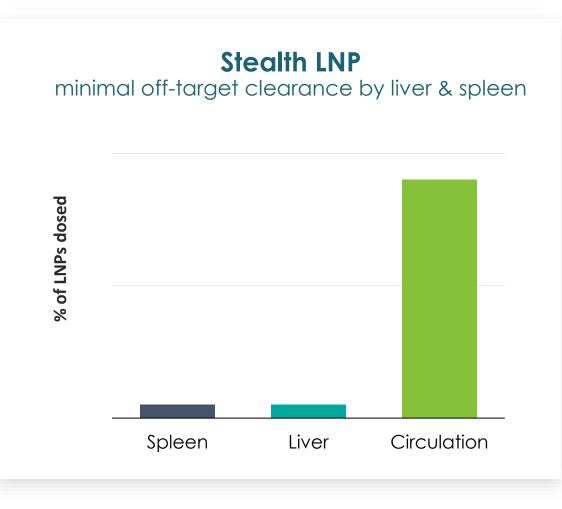


We began by focusing on selective delivery



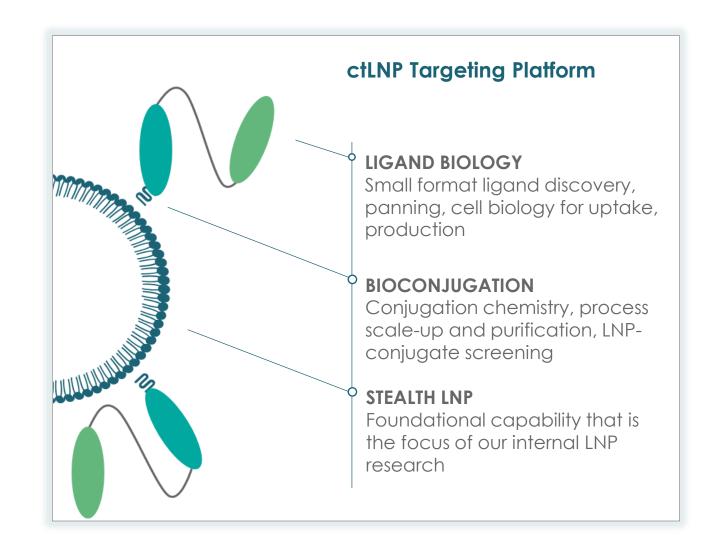
Off-target delivery drives innate immune stimulation

The first breakthrough was our stealth LNP to avoid clearance

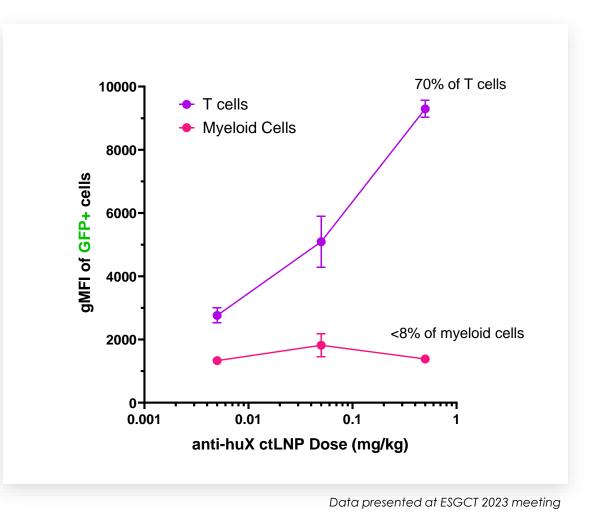


generation bio^m

Bioconjugation and targeting led to the ctLNP delivery platform



Milestone achieved for selective in vivo delivery to T cells



ctLNP platform opens broad therapeutic opportunities

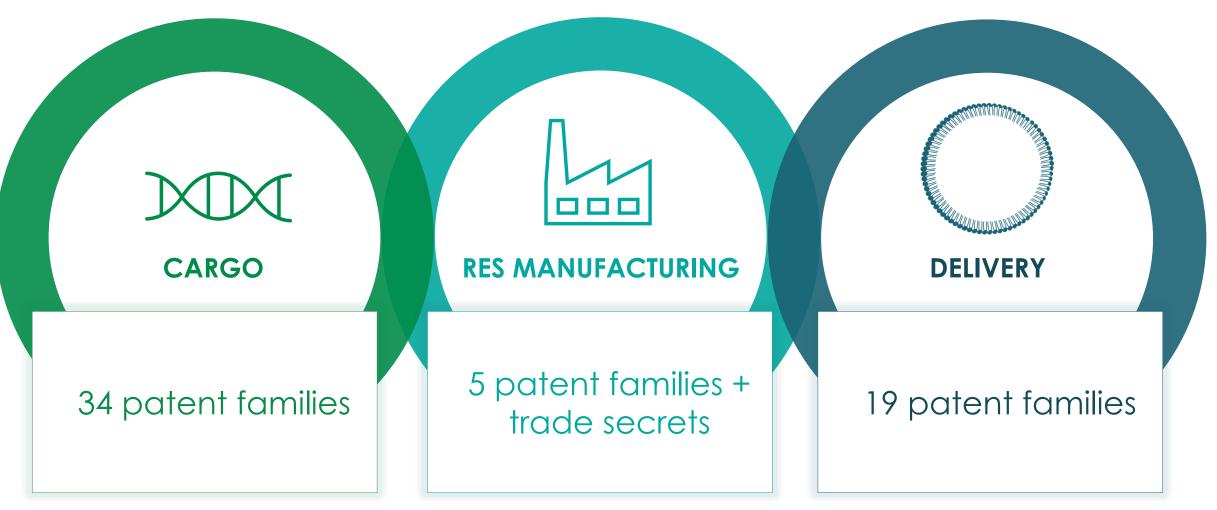


Opens new indications by accessing unreachable cell types & tissues



generation bio^{**}

We have made deep investments in our platform 425 pending applications, 58 patent families



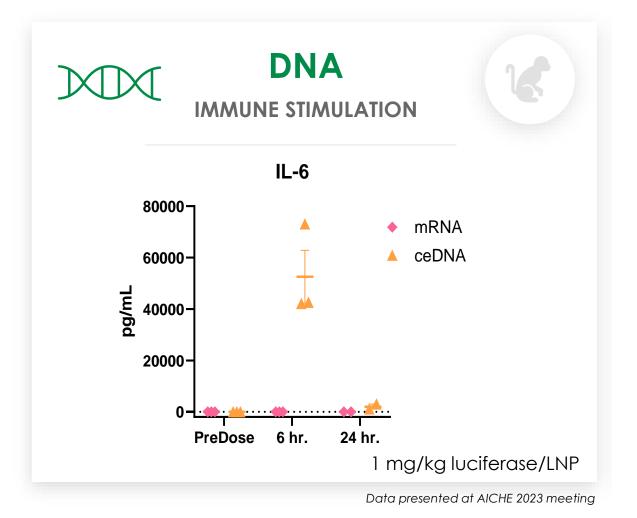
generation bio

As of September 24, 2023

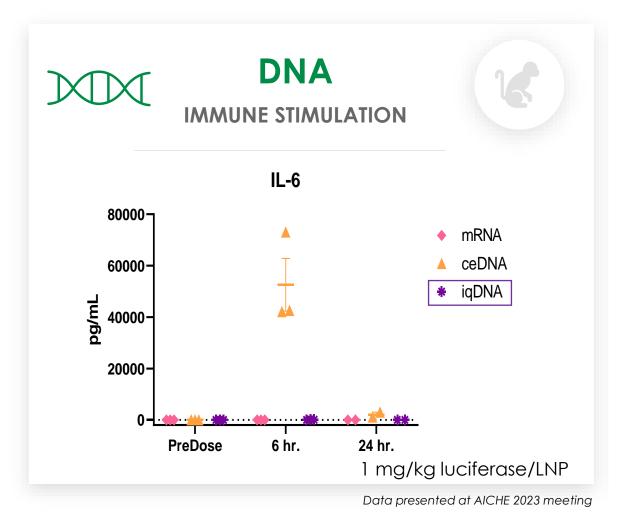
DNA innate immunity had no known solution

DNA **IMMUNE STIMULATION** No known modifications to make DNA immune quiet

RNA modification was inspiration for immune-quiet DNA



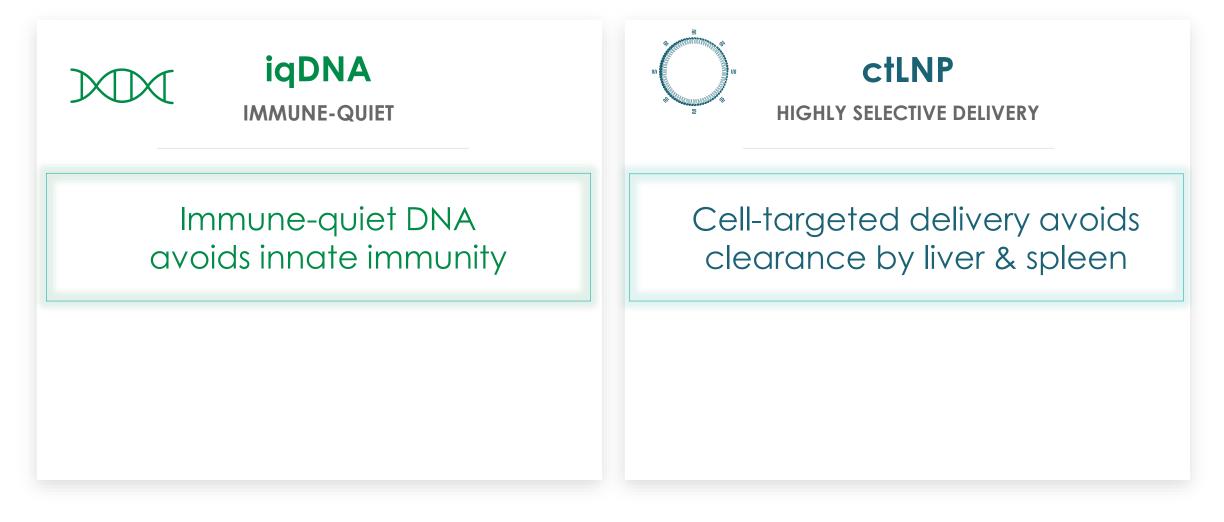
Immune-quiet DNA avoids all known DNA immune sensors



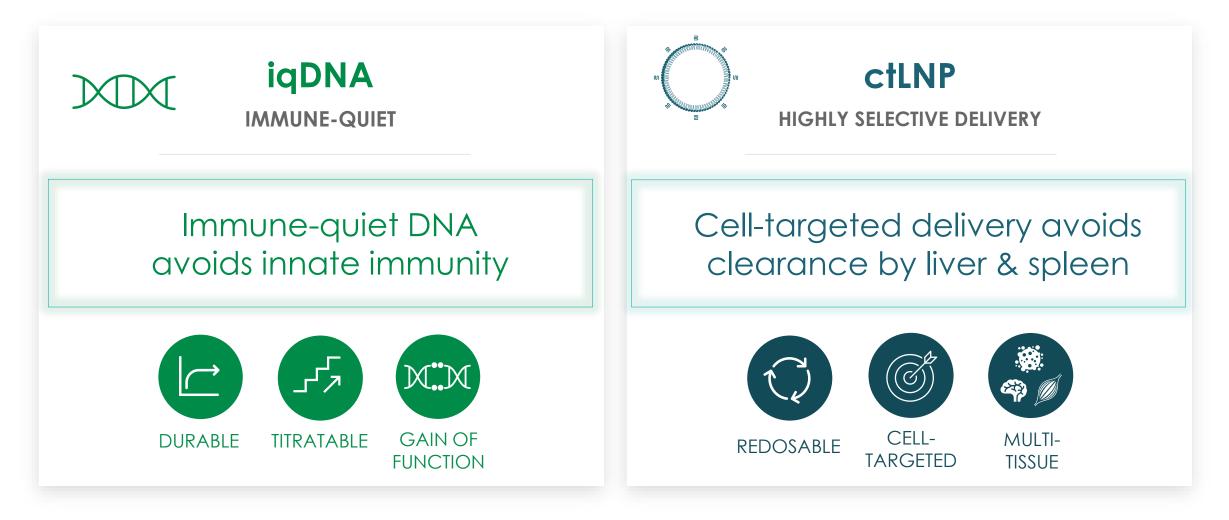
iqDNA platform opens unique therapeutic landscape

iqDNA IMMUNE QUIET Opens new indications by replacing or inserting large genes for life ∽∠ \mathbb{M} GAIN OF DURABLE TITRATABLE **FUNCTION**

GBIO has two proprietary solutions, two unique platforms



Our platforms have differentiated clinical attributes

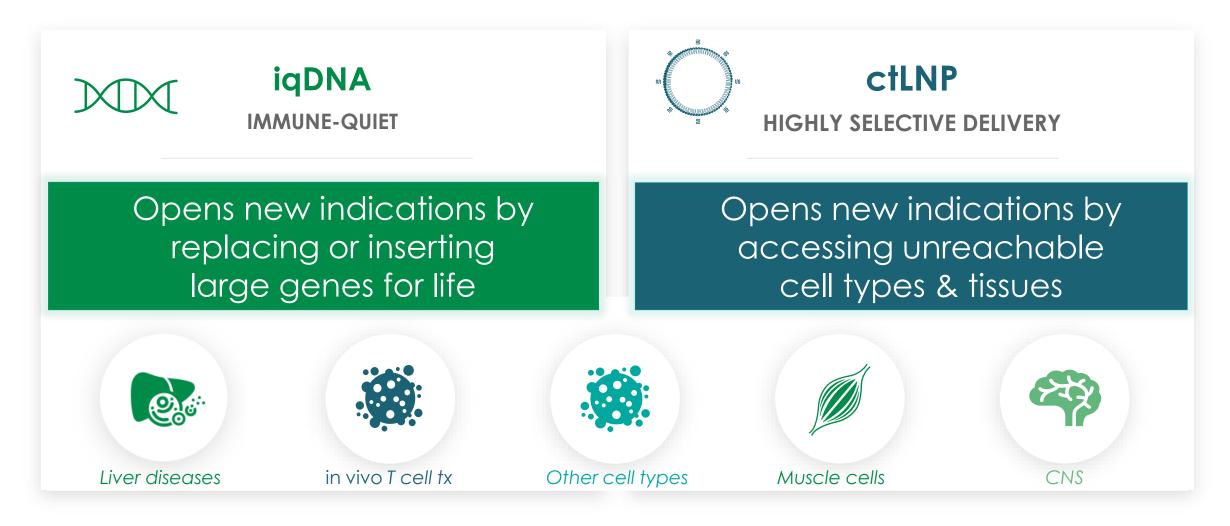


Our platforms open new large therapeutic opportunities

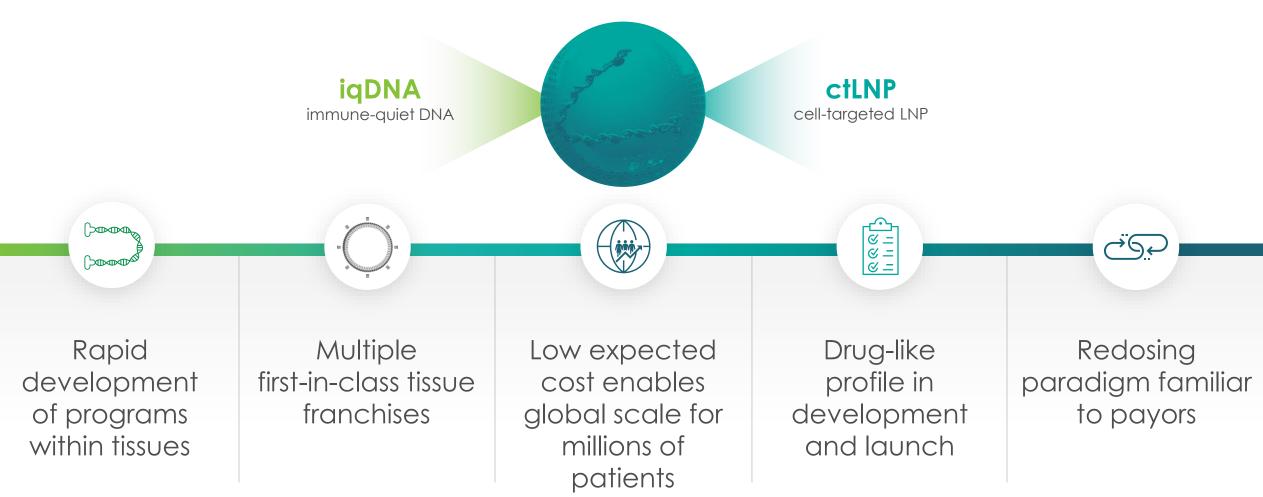


generation bio^{*}

We are developing a broad multi-tissue portfolio



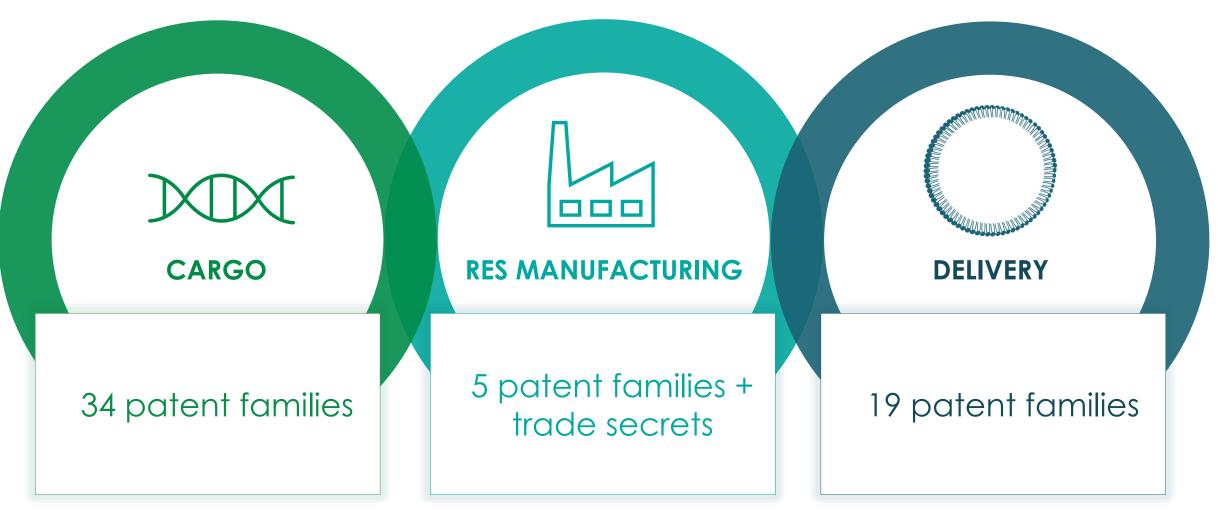
Our business model creates extraordinary leverage



Platform Capabilities

Matt Stanton

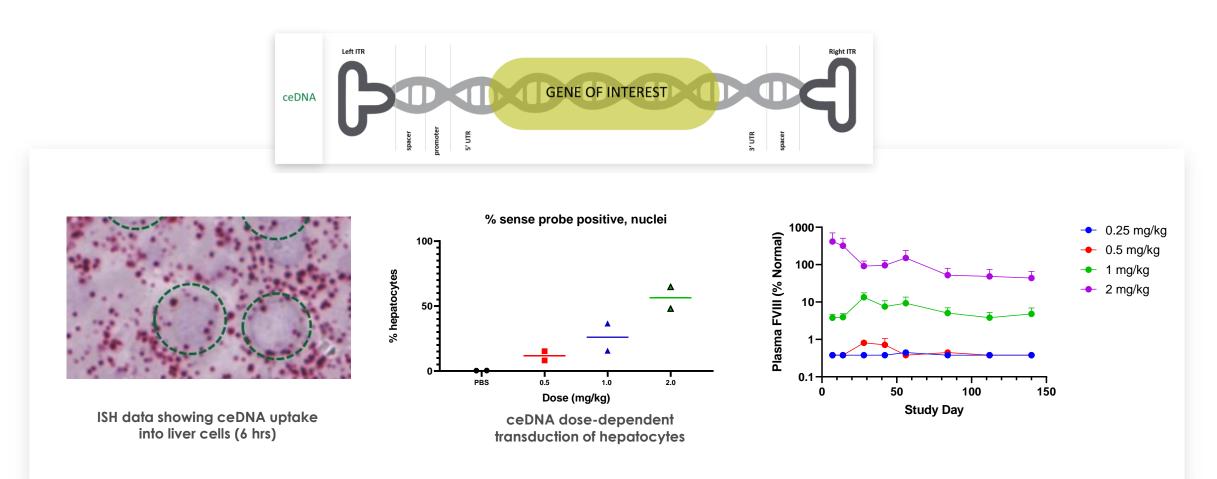
We have made deep investments in our platform to solve the challenges for non-viral gene therapy



generation bio*

As of September 24, 2023

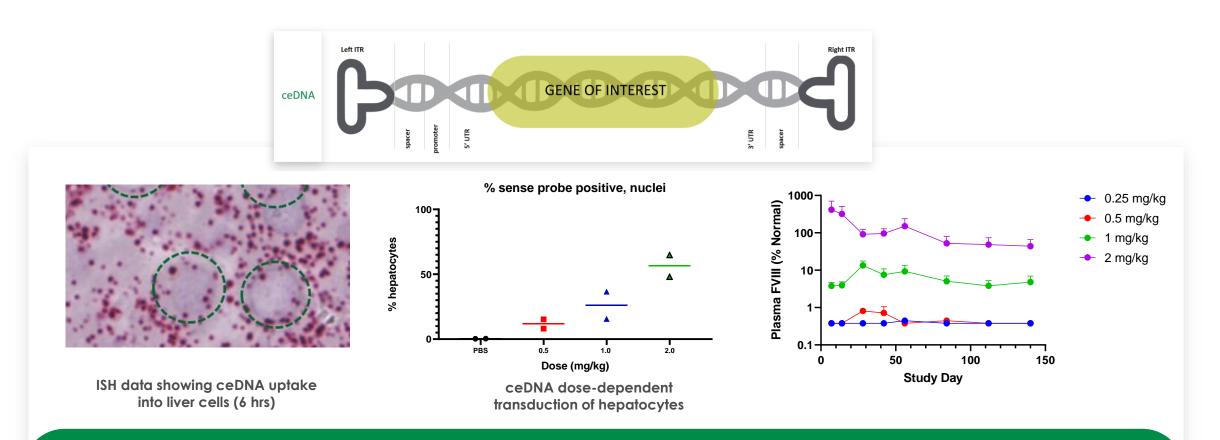
We have made deep investments in our platform to solve the challenges for non-viral gene therapy



generation bio

CARGO

We have made deep investments in our platform to solve the challenges for non-viral gene therapy



iqDNA is a variant of ceDNA that maintains these critical features

generation bio

CARGO

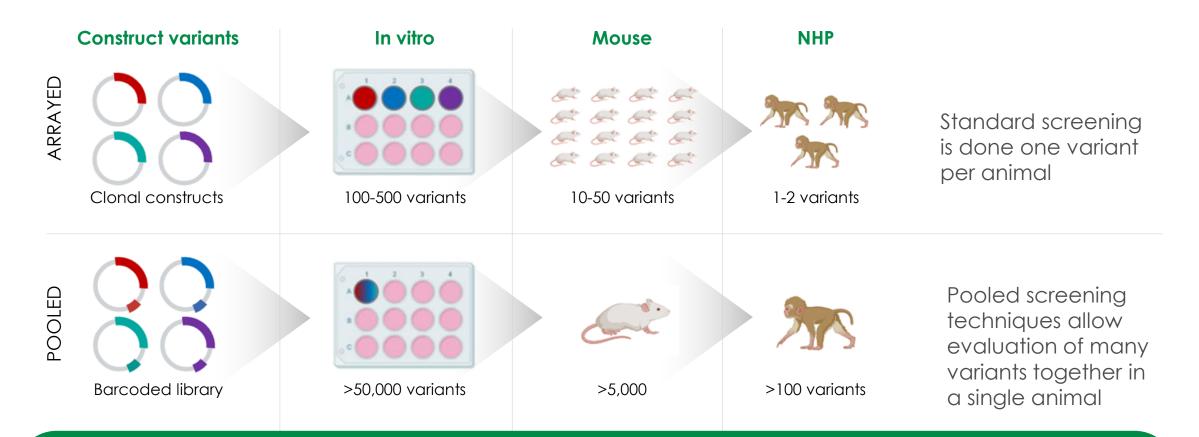
Advantages of increased capacity of iqDNA for large constructs

1	2	3	4
Improved Expression	Large transgenes	Multiple transgenes	Regulatable expression
 Larger promoters/ enhancers and/or UTRs for genes such as Factor VIII (FVIII) 	 Full length ATP7B gene for Wilson Disease as example 	 Single constructs that encode for both heavy and light chain for antibody secretion 	 Large enhancer and promoter regions that are responsive to physiological fluctuations
 Routinely >6 kb for FVIII Drives improved expression relative to AAV constrained constructs 		 KD and replace opportunities such as alpha-1 antitrypsin (hairpin for KD of dominant negative; replace with full native alpha-1 antitrypsin) 	 Example is promoters that are active only in presence of high levels of TNFa

generation bio

CARGO

Pooled screening techniques speed the path to discovery & development



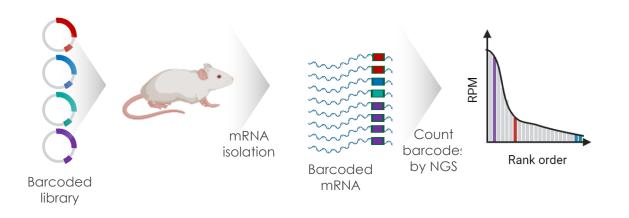
Pooled screening approaches can be used to accelerate optimization of nucleic acid cargo or LNP delivery

generation bio

CARGO

Pooled screening in a single animal identifies improved promoters from a complex library of 6000 variants

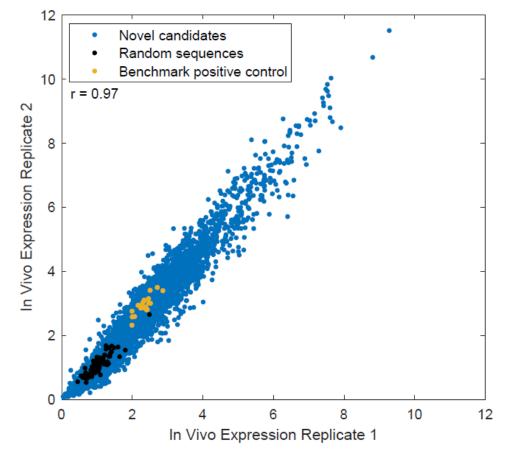
Schematic of mRNA barcoding method used to track promoter strength for 6000 variants



- Numerous promoter variants identified that perform better than "best-in-class" liver promoter control
- High reproducibility observed for replicate animals in study
- High performers are being recombined and screened for additional gains

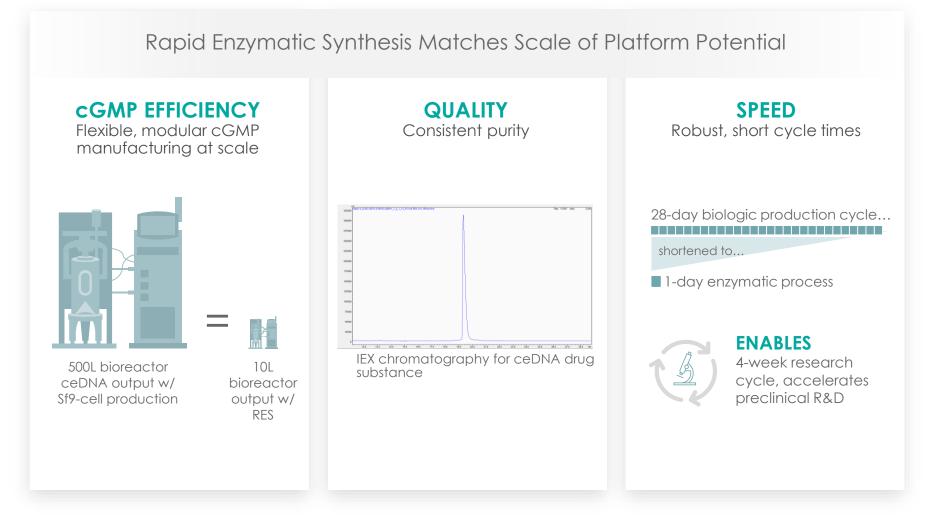
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Normalized mRNA levels for each promoter plotted relative to negative & positive controls





We have made deep investments in our platform to solve the challenges for non-viral gene therapy

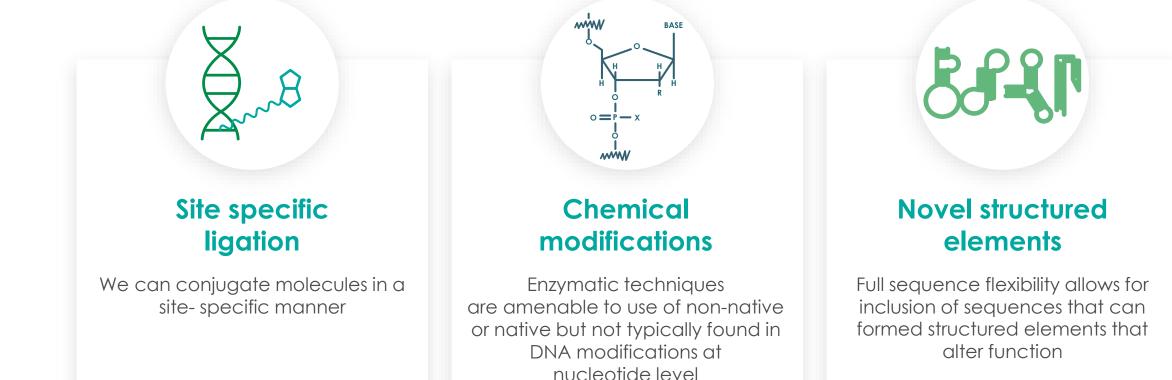


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MANUFACTURING



Enzymatic manufacturing opens up a myriad of ways to alter structure



This structural and chemical flexibility led to the discovery of iqDNA



Ambr[®] 250 system

- Demonstrates production from small tube
 to stir tank reactor scale
- High throughput, automated bioreactor system for process development
- 12 fully featured single-use 250 mL bioreactors allow scientists to evaluate multi-factor optimizations in a single experiment
- Process parameters translate directly to 2L+ reactors to be used for larger scale



generation bio

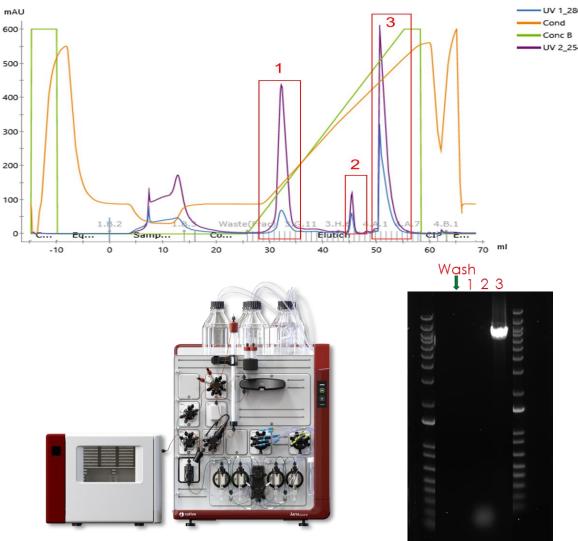
MANUFACTURING



Resin screening and optimization processes to deliver a pure Drug Substance

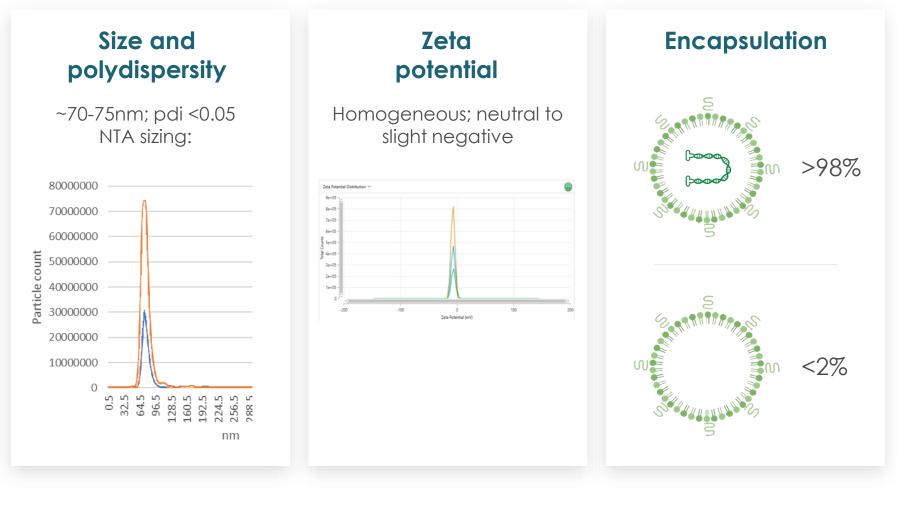
Chromatography Resin Screening and Optimization

- Various column chemistries and resin types are screened for overall performance
- Focus on product purity, consistent recovery, and scalability
- Example chromatogram shown at right demonstrates impurity removal (peaks 1 and 2) and product elution (peak 3)
- ÄKTA™ chromatography systems used throughout development lifecycle
- Scalable from benchtop to large scale





We have made deep investments in our platform to solve the challenges for non-viral gene therapy



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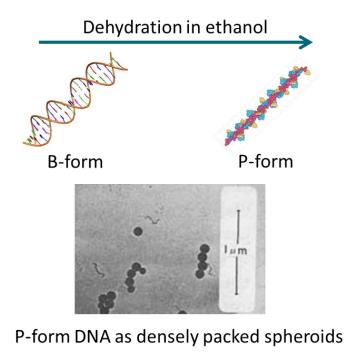
DELIVERY



Example – dehydrating and solubilizing ceDNA into ethanol – pDNA conformation

Conformation of P-Form DNA

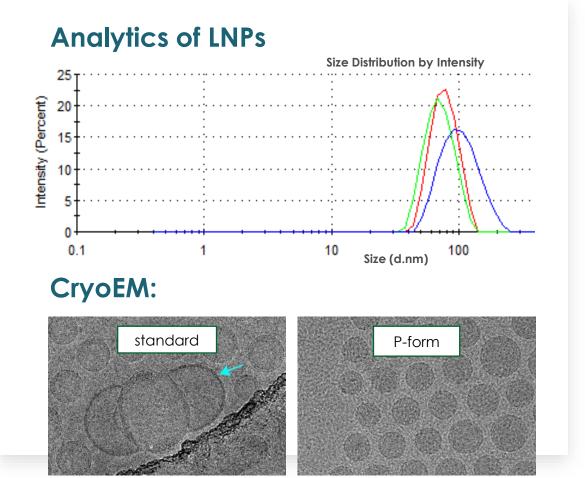
MICHEAL H. ZEHFUS and W. CURTIS JOHNSON, JR., Department of Biochemistry and Biophysics, Oregon State University, Corvallis, Oregon 97331



QUESTION

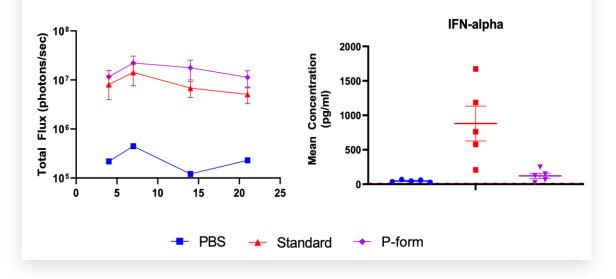
Can we dehydrate ceDNA in ethanolic LNP input stream (with lipids), favor P-form DNA in densely packed spheroids and use to create smaller, more homogeneous LNPs?

Adaptation of P-form DNA formation to LNP manufacturing process led to smaller, more homogeneous particle sizes, which leads to better expression and tolerability



Profile in mice

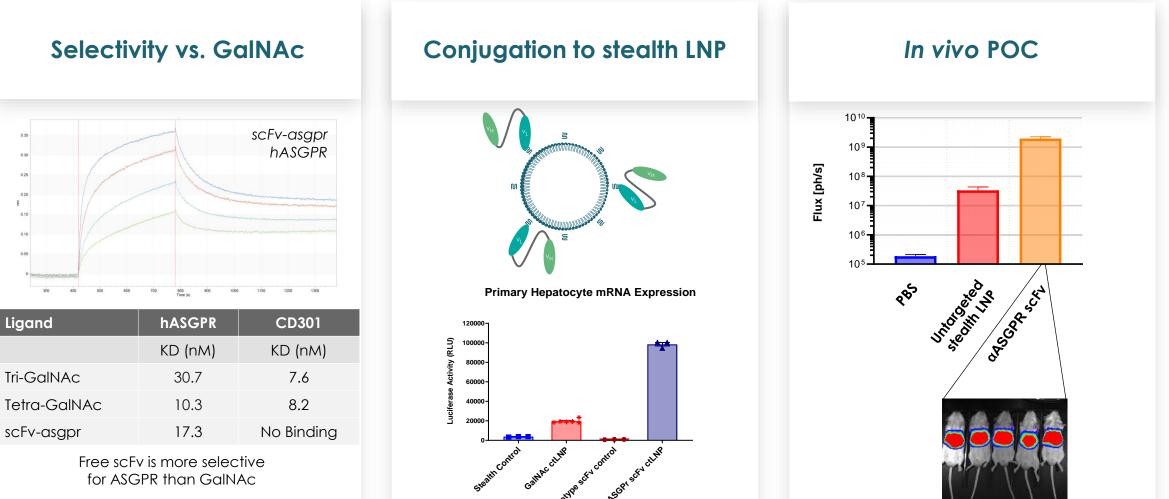
- Mice dosed IV at 0.25 mg/kg
- LNP compositions identical; same ceDNA lot
- Improvement in tolerability correlates with higher liver/spleen ratio (~30:1 liver:spleen copies/dg)



generation bio

DELIVERY

Working towards more selective ligands: scFv targeting to ASGPr provides improved alternative to GalNAc

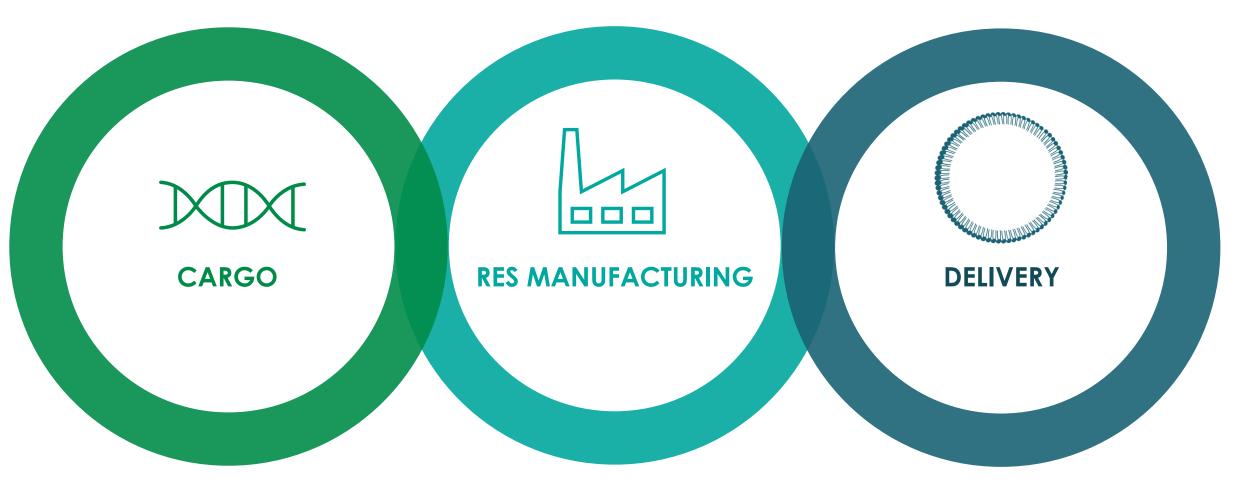


for ASGPR than GalNAc

Data presented at ESGCT 2023 meeting

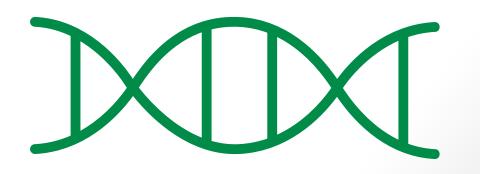
DELIVERY

Three critical elements to solving the challenges for non-viral genetic medicine





iqDNA Tracy Zimmermann

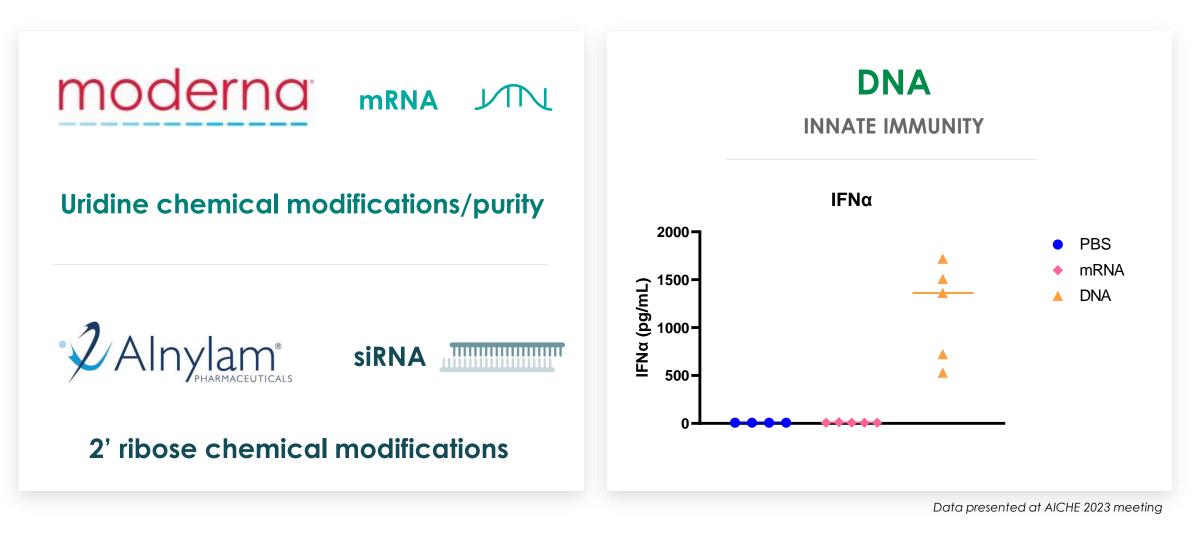


iqDNA avoids innate immunity

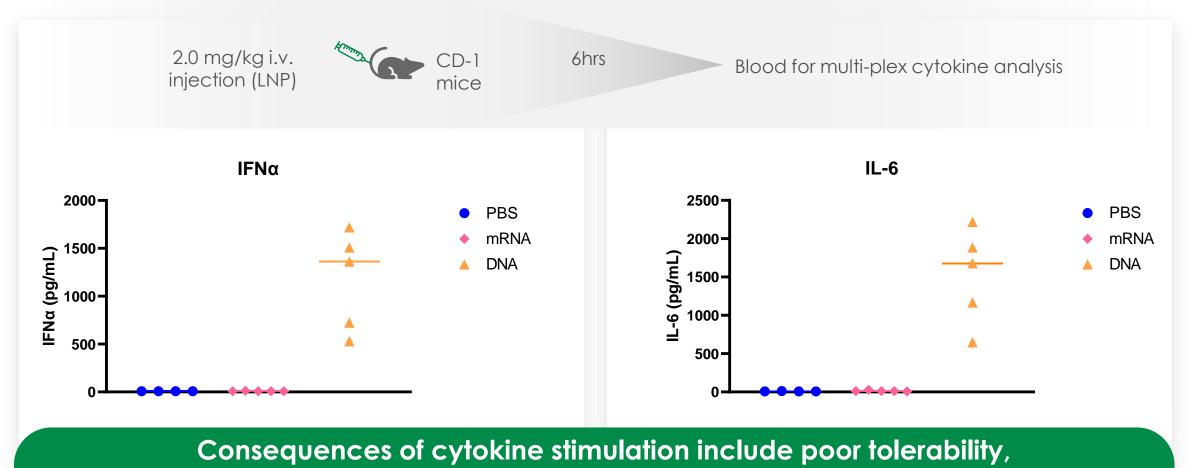
opening new indications by replacing or inserting large genes

iqDNA

Unlike RNA platforms, we started with no known chemistry solutions to DNA innate immunity



Cytokine elevation limits therapeutic index of DNA based genetic medicines



limited dose range and limited expression

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Data presented at AICHE 2023 meeting

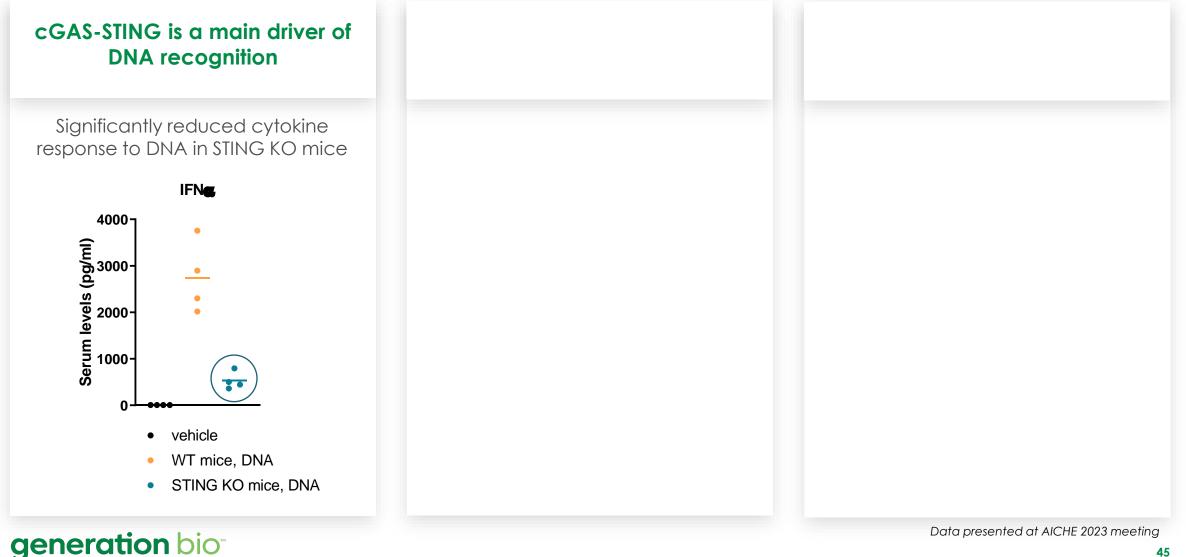
Multiple DNA-sensing receptors reside in cytoplasm and endolysosomal compartment of cells

cGAS-STING is a main driver of DNA recognition

TLR9 also contributes to inflammation in response to DNA

Inflammasome response to DNA is independent of cGAS-STING/TLR9

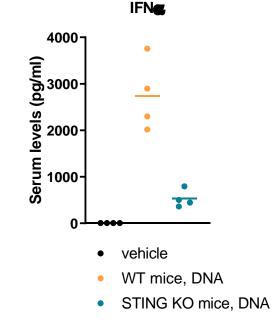
Innate immune responses to DNA driven predominantly by cGAS-STING, with contributions from TLR9 & the inflammasome



Innate immune responses to DNA driven predominantly by cGAS-STING, with contributions from TLR9 & the inflammasome

cGAS-STING is a main driver of DNA recognition

Significantly reduced cytokine response to DNA in STING KO mice



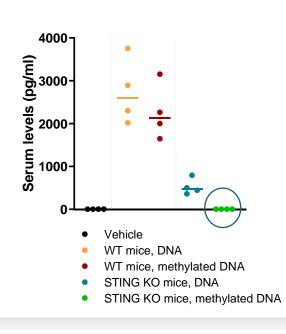
generation bio

inflammation in response to DNA

TLR9 also contributes to

CpG methylation to prevent TLR9 activation also reduces cytokines

IFNe



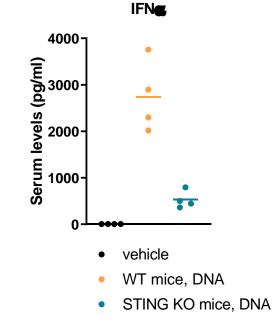
Data presented at AICHE 2023 meeting

46

Innate immune responses to DNA driven predominantly by cGAS-STING, with contributions from TLR9 & the inflammasome

cGAS-STING is a main driver of DNA recognition

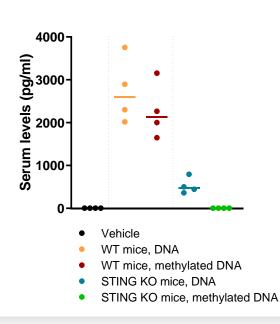
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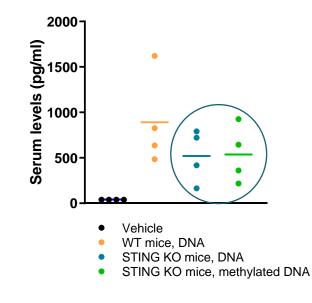
IFNe



Inflammasome response to DNA is independent of cGAS-STING/TLR9

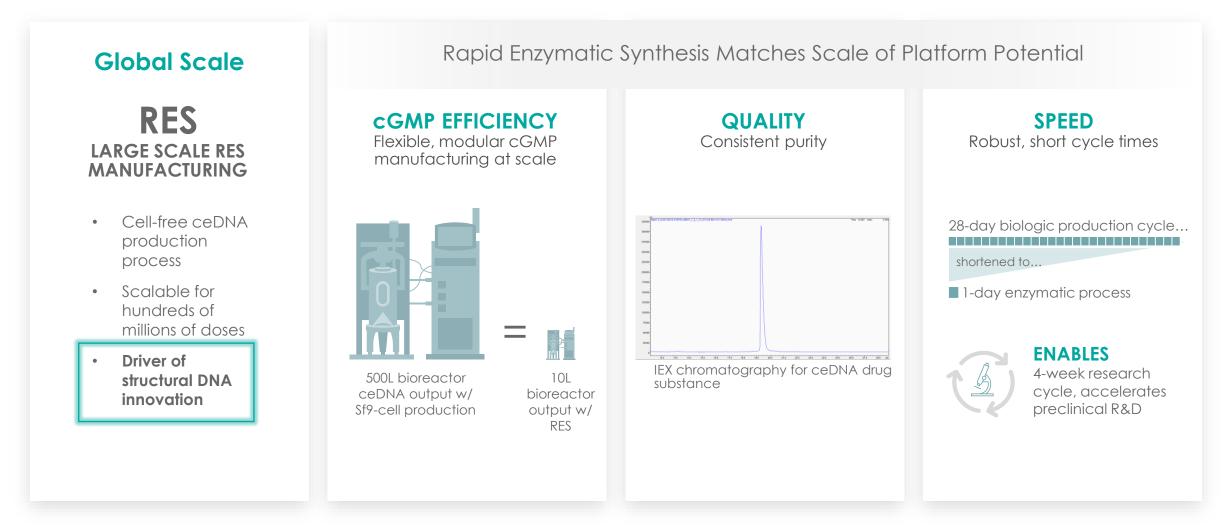
Elevation of IL-18 indicates Inflammasome activation

IL-18

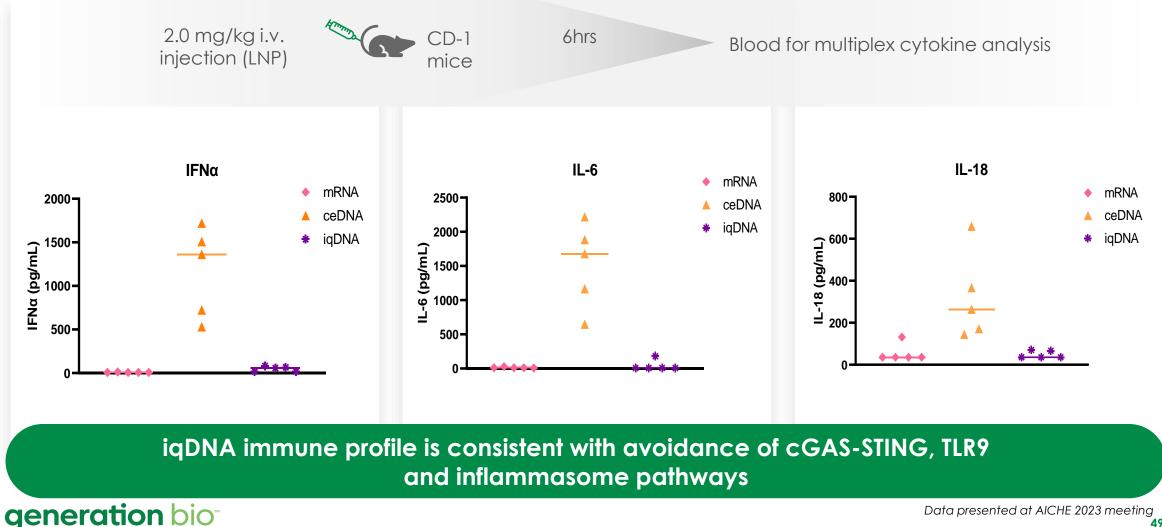


Data presented at AICHE 2023 meeting

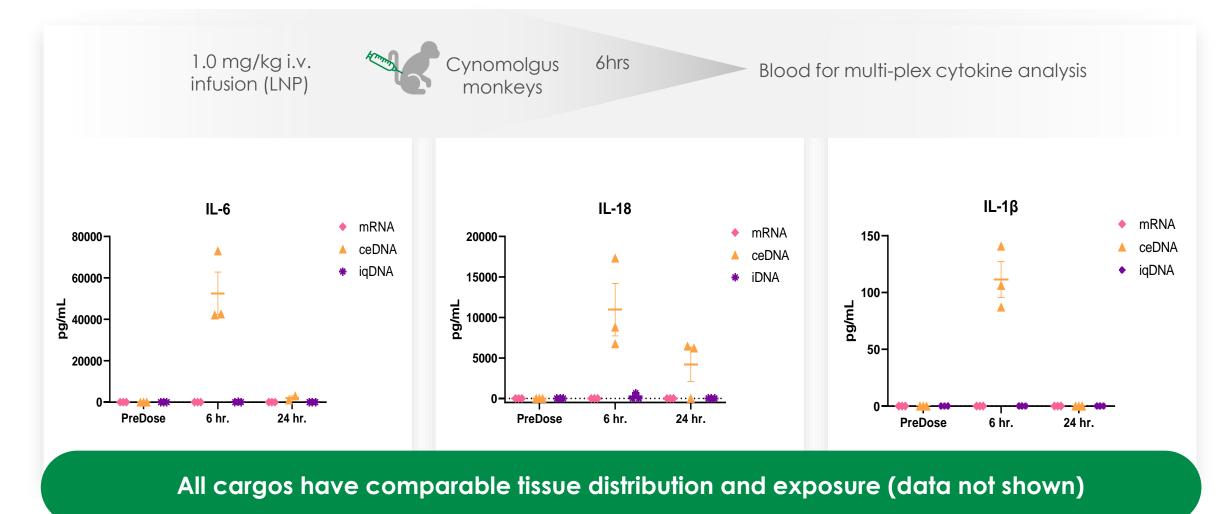
Unique RES process builds scale and is a driver of structural DNA innovation



We have identified a RES-enabled solution to innate immunity we call immune-quiet DNA (iqDNA)



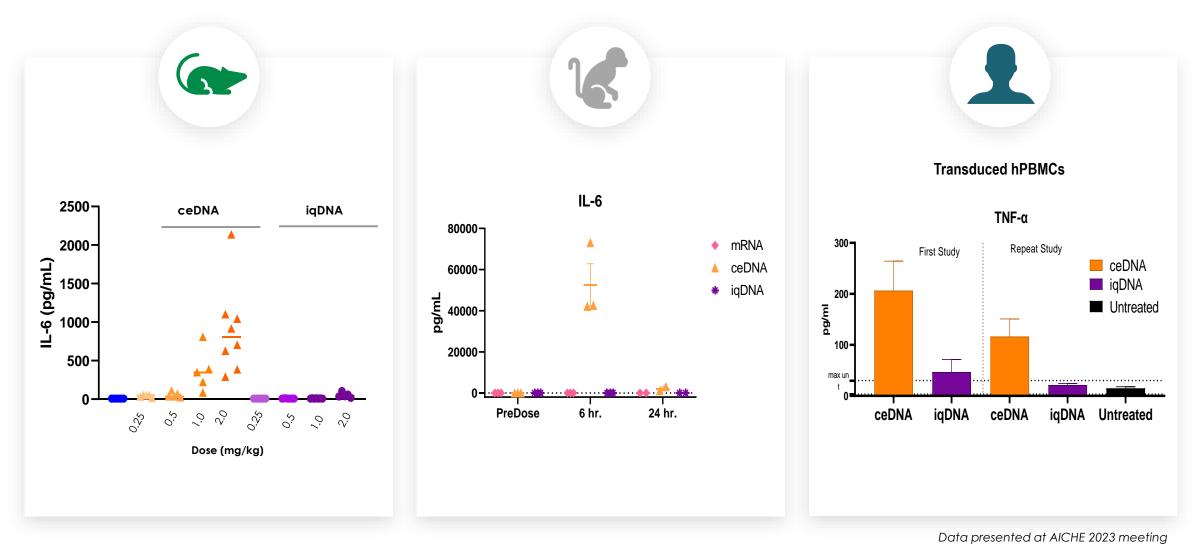
iqDNA profile is not limited to mice: Clear differentiation in nonhuman primates



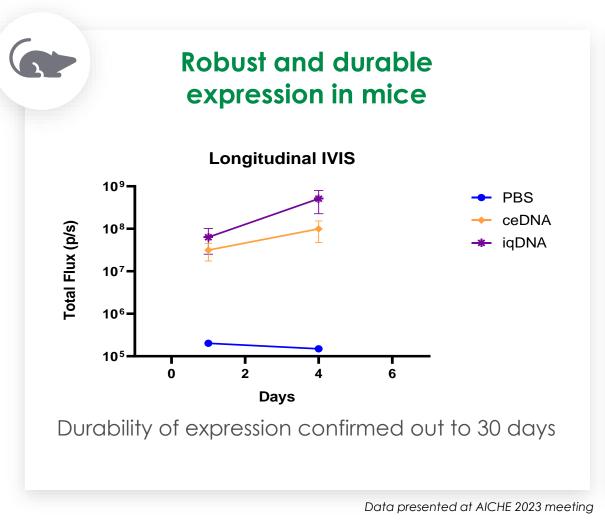
generation bio^{*}

Data presented at AICHE 2023 meeting

iqDNA profile is conserved across species, including human PBMCs



Importantly, iqDNA has demonstrated robust and durable expression with reporter luciferase gene



Next steps are focused on therapeutic translation of iqDNA platform for *in vivo* proof of concept





Phillip Samayoa

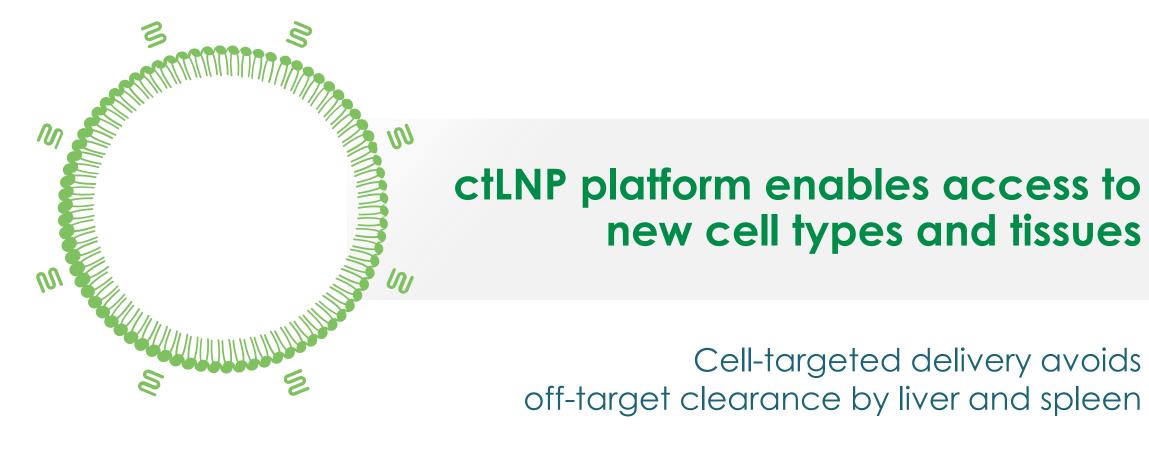
050-37

DMAE POS

DSD-373-

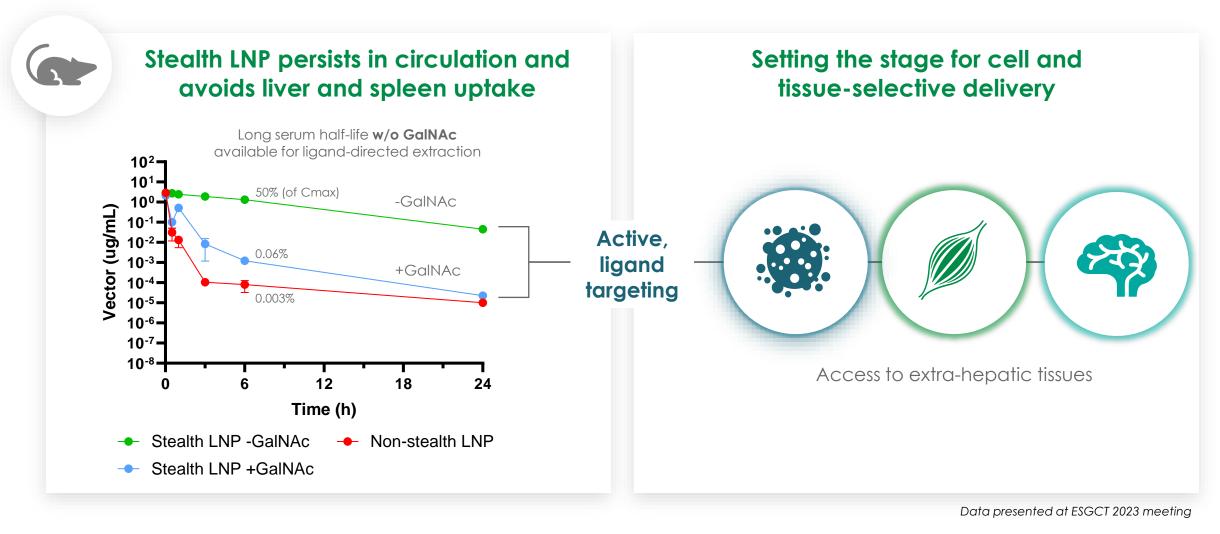
25 mL.

1-3

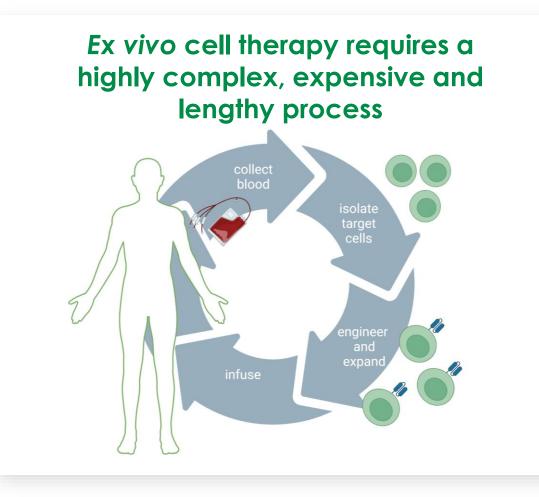


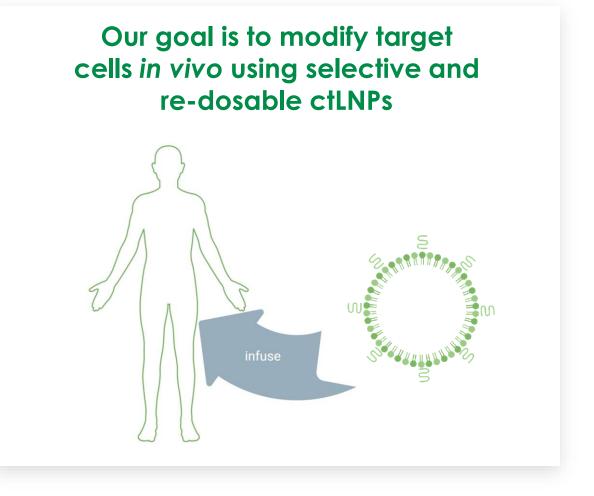
ctLNP

Stealth LNP profile supports targeting to cell types and tissues beyond the liver

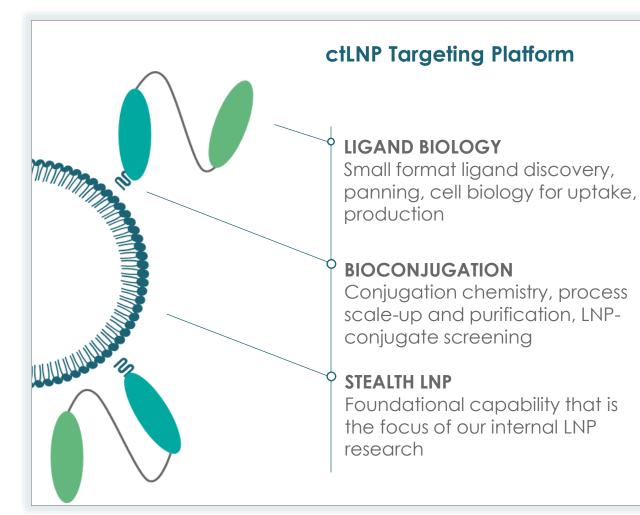


In vivo targeted delivery could transform access to cell therapies

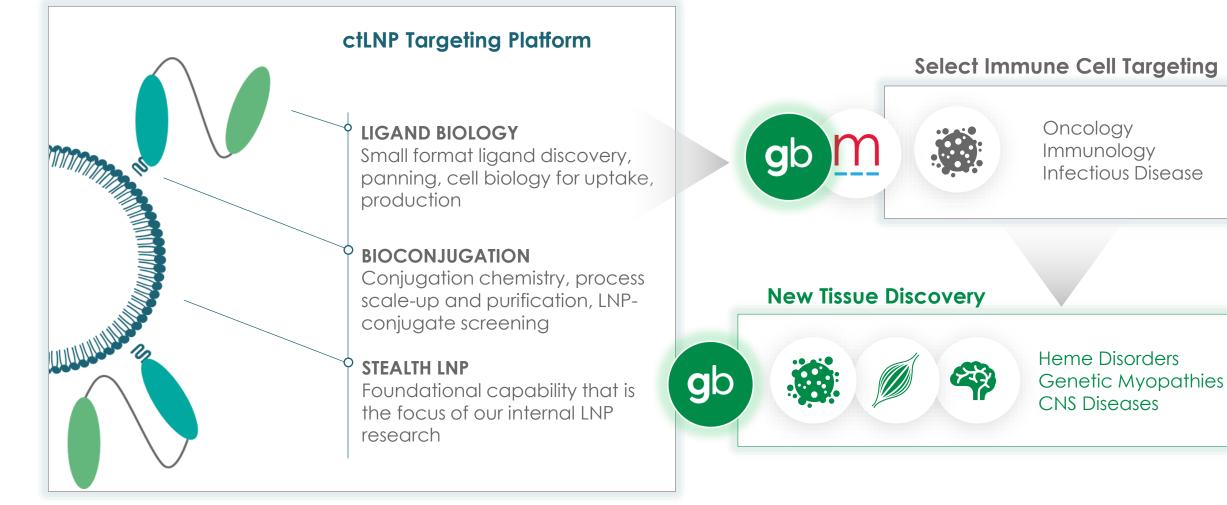




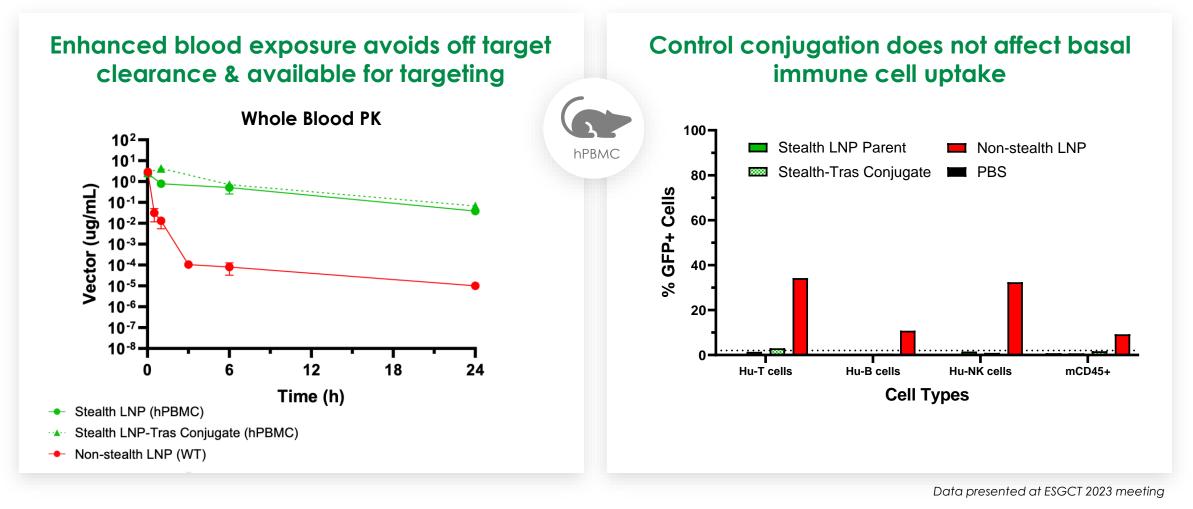
Targeting platform is a modular system built on our foundational stealth LNP technology, capable of targeting a wide variety of extra-hepatic tissues



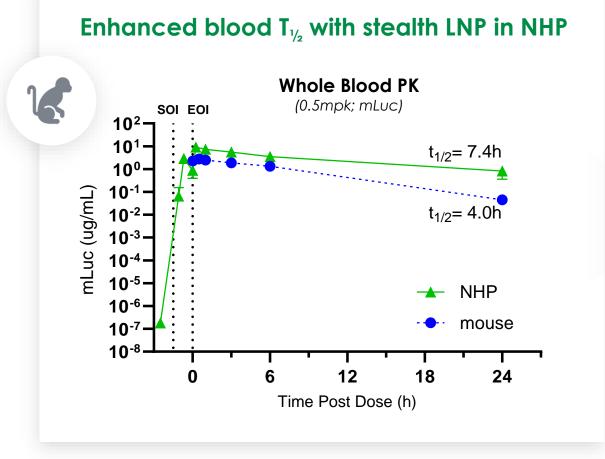
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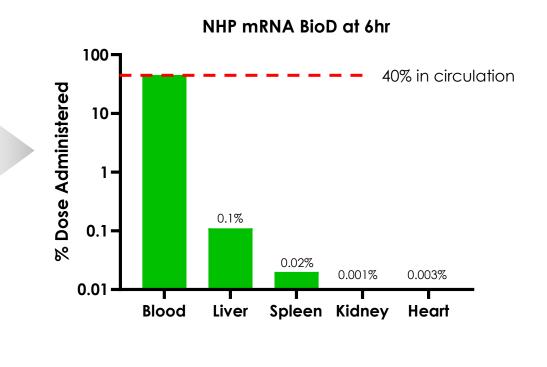
Stealth LNP controls show low/no uptake and expression in human immune cells in hPBMC mice (mRNA cargo)



Stealth LNP carrying mRNA maintains prolonged PK profile and avoids clearance by liver and spleen in NHP

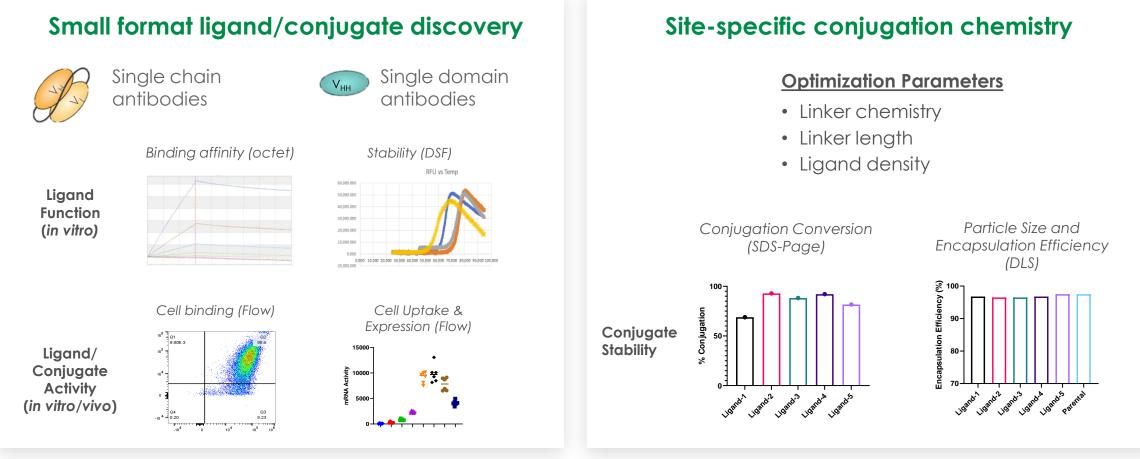


Majority of drug remains in circulation, avoiding biodistribution to the liver or spleen



Data presented at ESGCT 2023 meeting

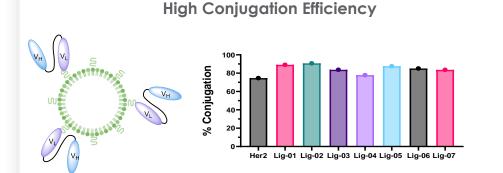
Validated bioconjugation platform to discover and characterize cell targeted LNP conjugates



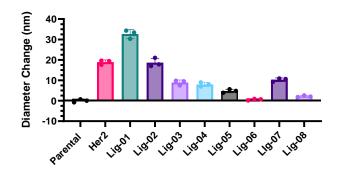
Data presented at ESGCT 2023 meeting

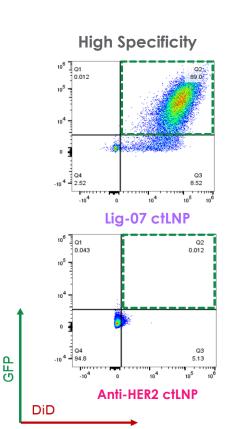
Stealth LNP conjugates targeting human T cells demonstrate dose dependent, receptor specific uptake *in vitro*

Efficient conjugation of protein ligands maintains LNP stability

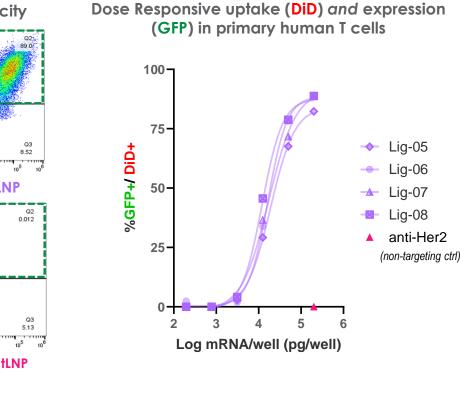


Pre/Post Conjugation Particle Size Stability



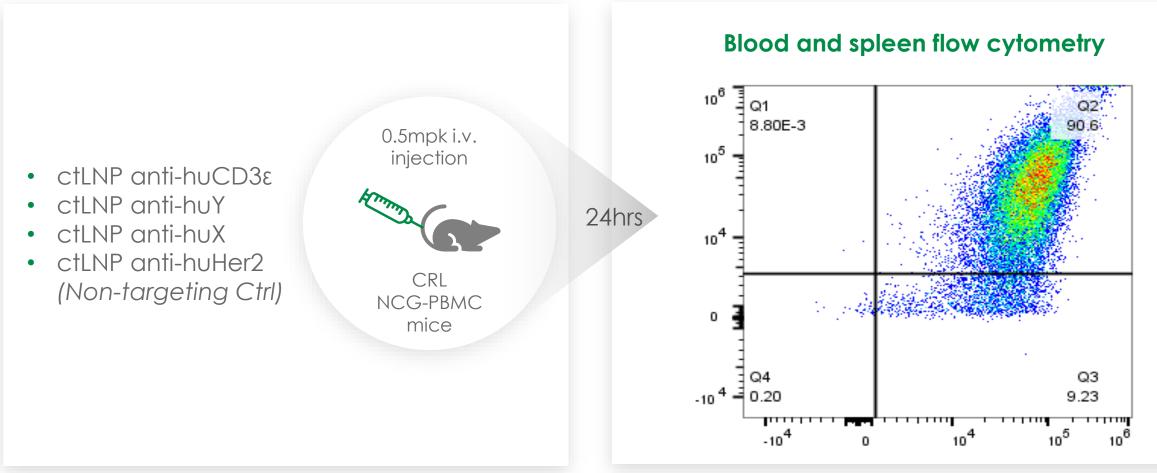


Conjugated LNP uptake and expression is dose dependent and target specific



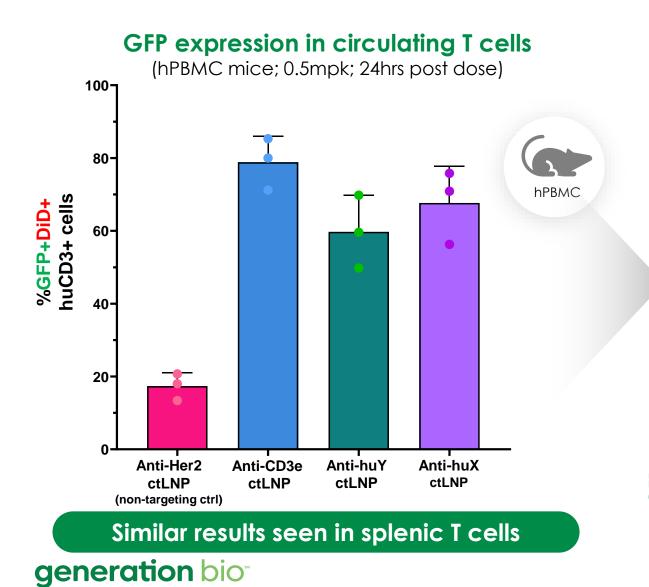
Data presented at ESGCT 2023 meeting

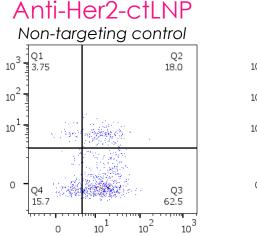
Validation of T cell targeted ctLNPs for analytical quality and *in* vitro uptake/expression sets stage for *in vivo* POC experiment in hPBMC mice



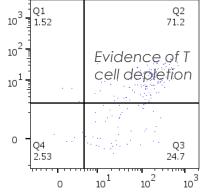
Data presented at ESGCT 2023 meeting

T cell targeting LNP conjugates induce uptake and expression of mRNA cargo in vivo

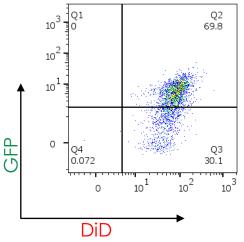




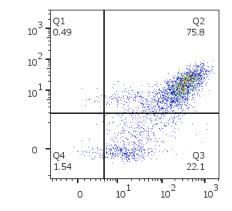
Anti-CD3E-ctLNP



Anti-huY-ctLNP

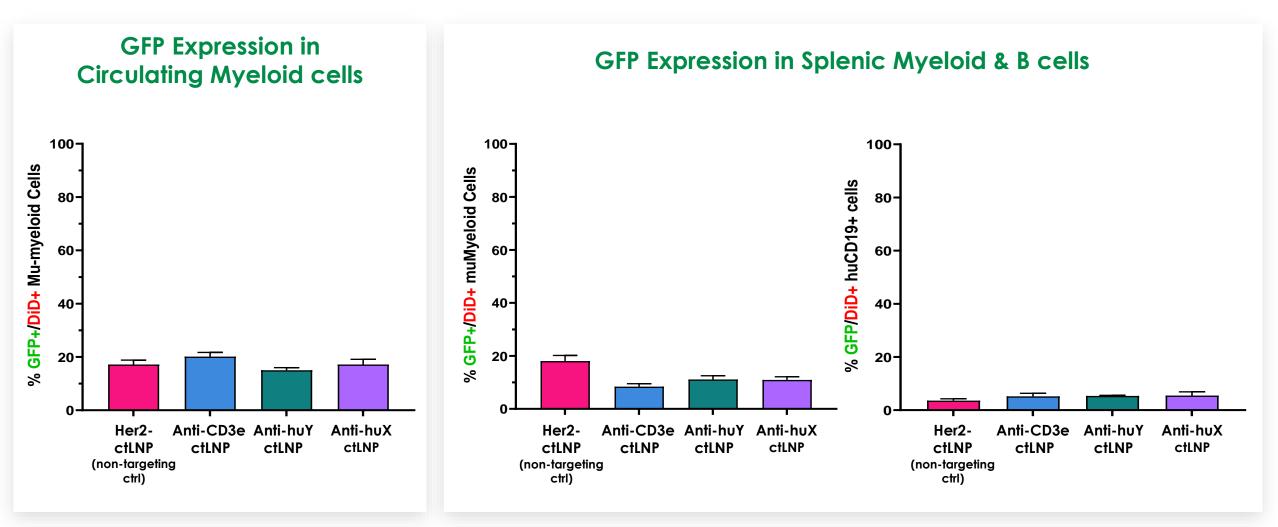


Anti-huX-ctLNP



Data presented at ESGCT 2023 meeting

Off-target cell type uptake & expression remains at baseline with successful T cell engagement

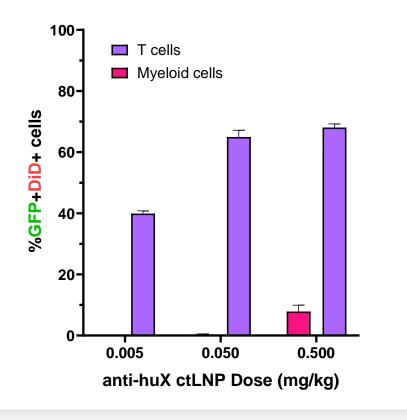


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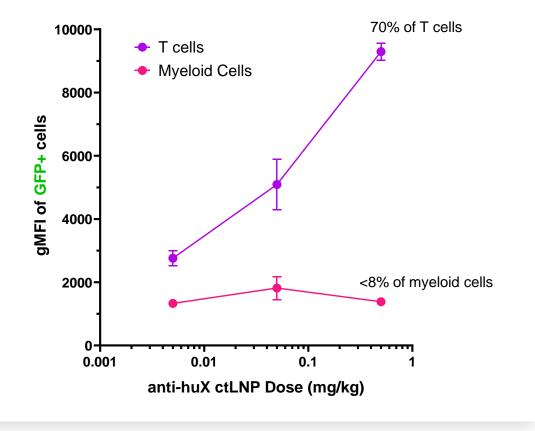
Data presented at ESGCT 2023 meeting

T cell targeted ctLNP demonstrates selective uptake and expression across a dose range *in vivo*

Efficient T cell transduction across dose range



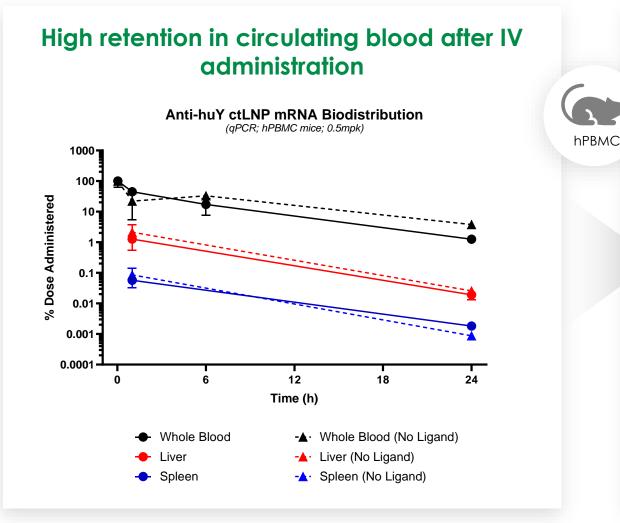
Minimal off target cell uptake and expression



Data presented at ESGCT 2023 meeting

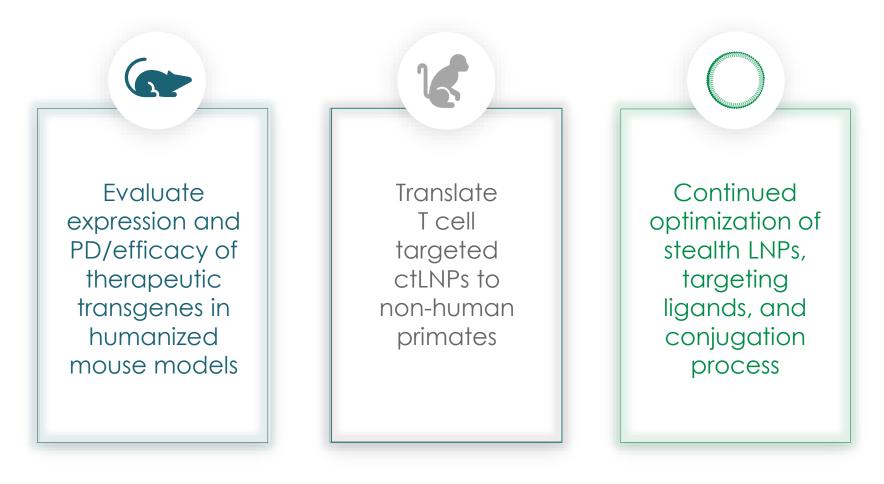
generation bio^{**}

Majority of ctLNP cargo remains in circulation, with little off-target biodistribution



Ligand targeting does not drive additional off-target distribution **1hr Biodistribution** 100 45% in circulation % Dose Administered 10 1% 1. <0.1% 0.1 0.0 Whole Blood Liver Spleen Anti-huX ctLNP Anti-huY ctLNP

Next steps are focused on therapeutic translation of extra-hepatic targeting platform



ctLNP platform poised to broadly unlock extra-hepatic delivery

Foundational proof points in place for ctLNP platform

- ✓ ctLNPs avoid clearance organs and remain available for systemic targeting
- Targeting ligands drive highly selective, dose-responsive delivery beyond the liver
- Streamlined process for ligand discovery and bioconjugation
- ✓ Compatible with DNA and RNA cargos

Positioned to bring genetic medicines to previously unreachable cell types and tissues

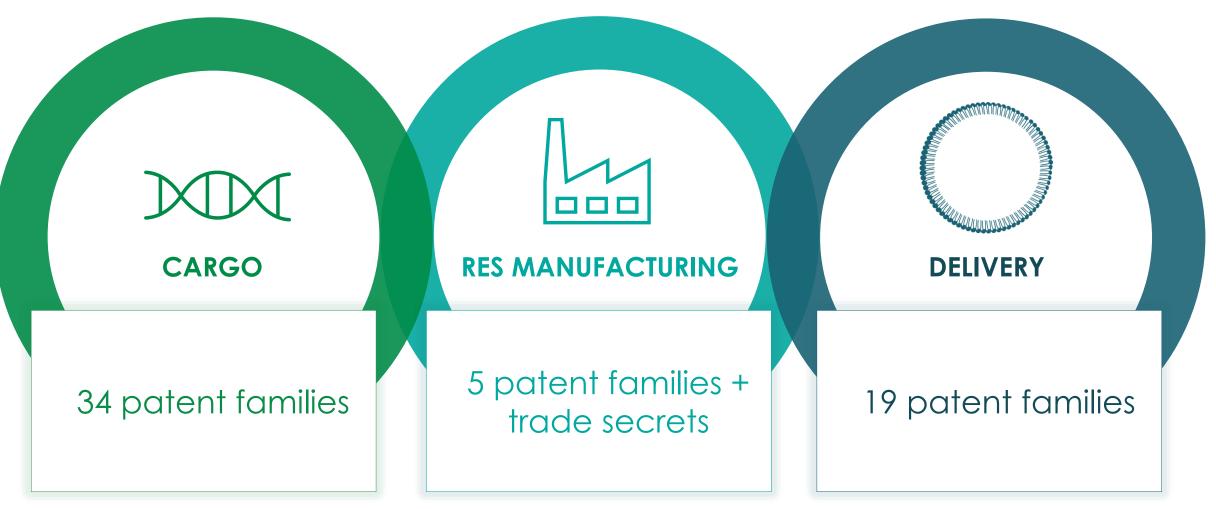


Access to extra-hepatic tissues

Closing Geoff McDonough



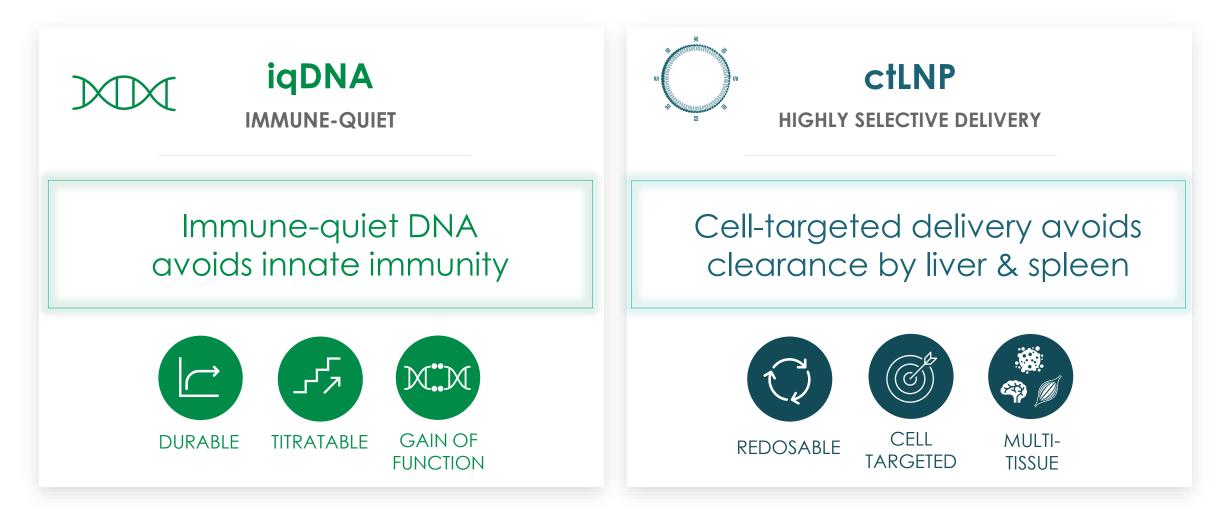
We have made deep investments in our platform 425 pending applications, 58 patent families



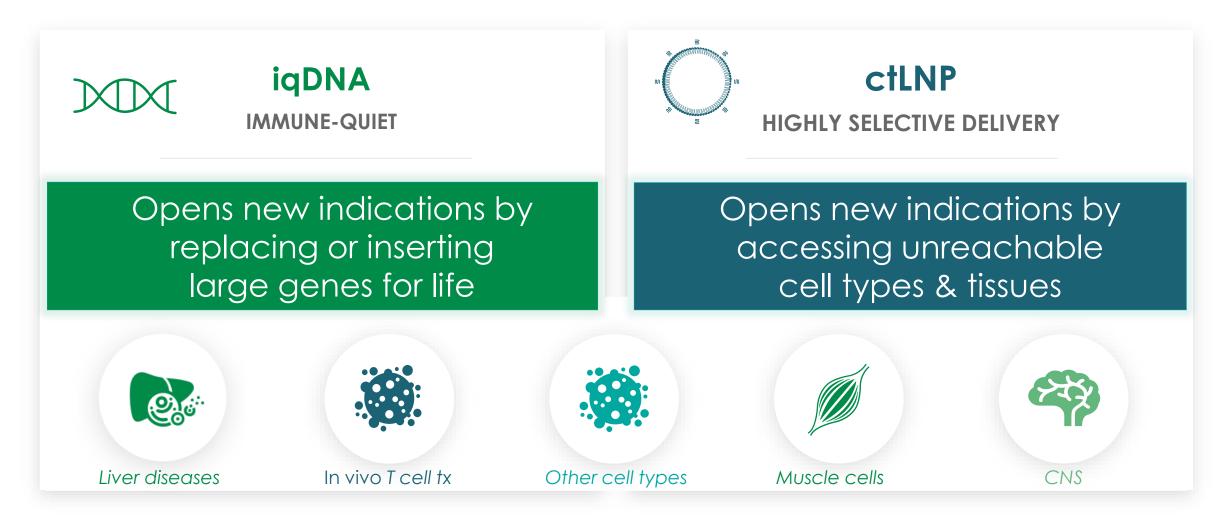
generation bio

As of September 24, 2023

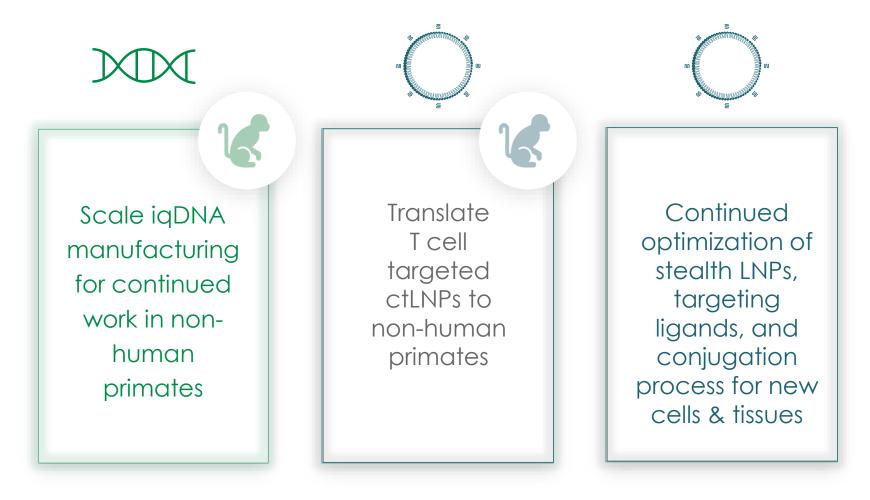
Our platforms have differentiated clinical attributes



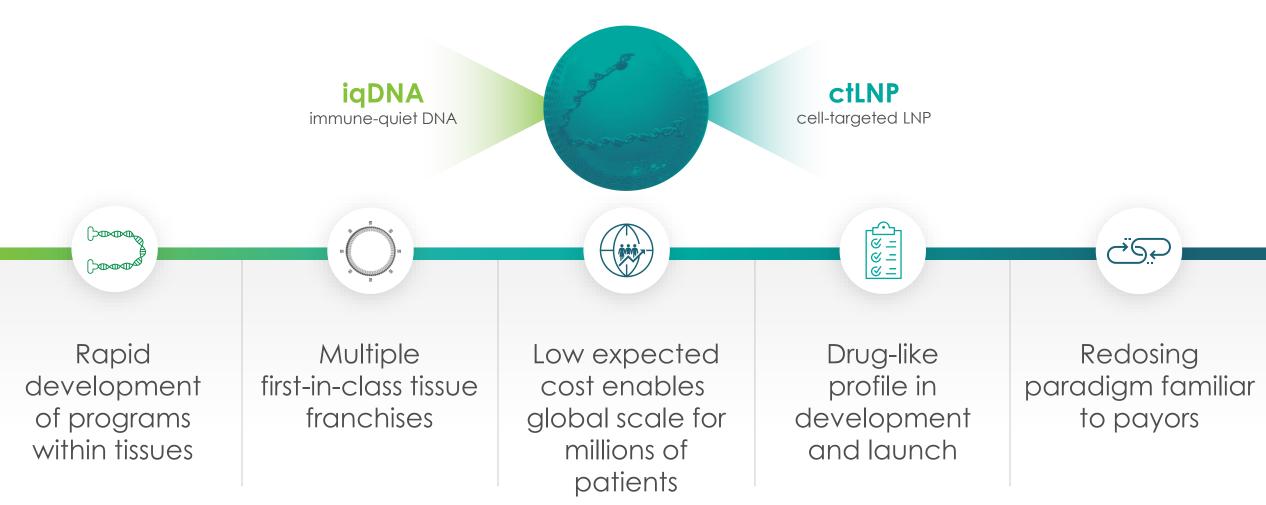
We are developing a broad multi-tissue portfolio



Building momentum in NHP for both platforms



The GBIO platform creates extraordinary leverage



generation bio

Thank you!