

generation bio™



Leading durable  
redosable scalable  
non-viral genetic medicines

FOR MILLIONS OF PATIENTS LIVING  
WITH RARE AND PREVALENT DISEASES

NASDAQ: GBIO

JANUARY 2022

## 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, 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 the timing and ability to complete the build-out of the company’s manufacturing facility and regarding the new 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; the impact of the COVID-19 pandemic on the company’s business and operations; 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.

# Generation Bio is unlocking the full potential of non-viral genetic medicines

Novel platform enables unique clinical profile...

...enabling access to a broad set of large therapeutic areas



**DURABLE**



**REDOSABLE**



**SCALABLE**



**MULTIPLE MODALITIES**



**GLOBAL SCALE**



**MULTIPLE TISSUES**

# Our proprietary non-viral genetic medicine platform

## THREE CORE PLATFORM TECHNOLOGIES

### Multiple Modalities



#### ceDNA

CLOSED-ENDED DNA

**29** PATENT FAMILIES

### Global Scale

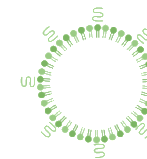


#### MFG

INTERNAL LARGE SCALE  
MANUFACTURING CAPACITY

**3** PATENT FAMILIES  
& TRADE SECRETS

### Multiple Tissues



#### ctLNP

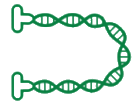
CELL-TARGETED  
LNP DELIVERY

**15** PATENT FAMILIES

# ceDNA – one construct, multiple modalities

ENABLES ACCESS TO BROAD THERAPEUTIC MECHANISMS

## Multiple Modalities



**ceDNA**

CLOSED-ENDED DNA

**29** PATENT FAMILIES



Gene transfer

**\$22.4bn**

total mkt cap

Durably express full transgene



Therapeutic antibodies

**\$47.2bn**

total mkt cap

Durably express and secrete full mAb



Vaccines

**\$142.5bn**

total mkt cap

Express target antigen(s)



Gene editing

**\$29.6bn**

total mkt cap

DNA template for genomic insertion/correction

# Rapid Enzymatic Synthesis - building internal capacity for rare and prevalent diseases

MFG TO MATCH SCALE, BREADTH OF PLATFORM POTENTIAL

## Global Scale



### MFG

INVESTING IN LARGE SCALE  
INTERNAL MANUFACTURING

**3** PATENT FAMILIES  
& TRADE SECRETS

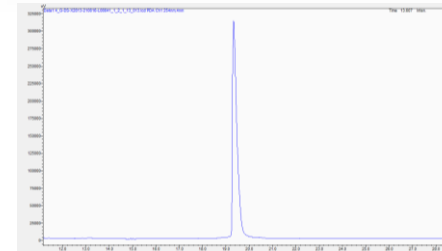
## Internal cGMP Capacity



104,000 sq. ft. facility in  
Waltham, MA

- State-of-the art facility to enable clinical and initial commercial supply for multiple potential launches

## Quality



IEX chromatography  
demonstrating high purity

- Consistently yields highly pure ceDNA

## Speed

28-day biologic production cycle



shortened to...



1-day enzymatic process

ENABLING

4-week research cycle



- Accelerates preclinical research and development



# ctLNP – each tissue-specific ctLNP creates modular access to a therapeutic area

LEADING PORTFOLIO OF ctLNP EXPERTISE AND ASSETS

## Multiple Tissues

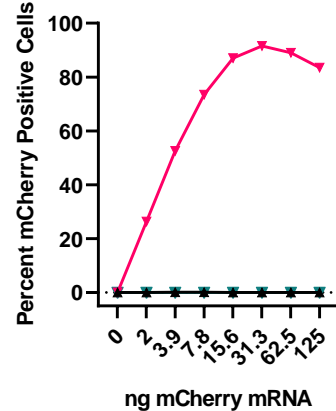


**ctLNP**  
CELL-TARGETED  
LNP DELIVERY

**15** PATENT FAMILIES

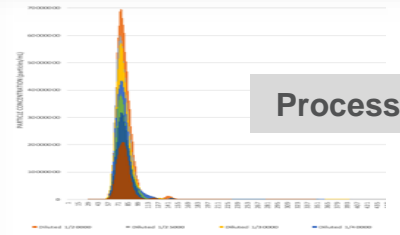
## Targeting

Specific LNP uptake

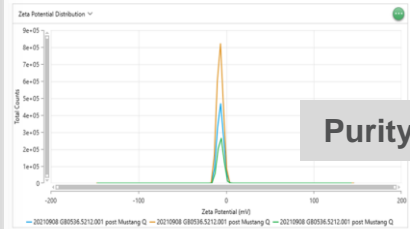


- Parental LNP
- Conjugated LNP
- Parental LNP (+ free ligand)

## Formulation Expertise



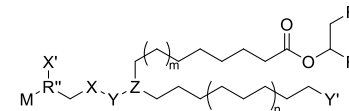
70-75 nm diam.  
Polydispersity <0.05



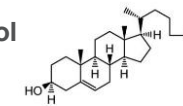
Uniform zeta,  
99% encapsulation

## Proprietary Lipids

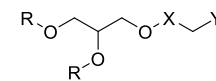
**Ionizable Lipids**  
Several Classes



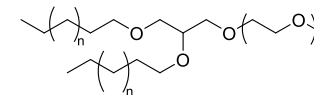
**Cholesterol & analogs**



**Helper lipids**





**Stabilizing polymer lipids**



## Modular Access

- LIVER
- RETINA
- VACCINES
- MUSCLE
- TUMOR
- CNS

# Broad portfolio of rare and prevalent indications in the liver and retina, enabled by modular ctLNP delivery

CORE AREAS OF DEVELOPMENT					
TISSUE	PREVALENCE	PROGRAM	RESEARCH	LEAD OPTIMIZATION	PRE-CLINICAL DEVELOPMENT
 <b>Liver</b>	Rare	Hemophilia A	<div style="width: 100%; height: 10px; background-color: #008000;"></div>		
		PKU	<div style="width: 80%; height: 10px; background-color: #008000;"></div>		
		Wilson Disease	<div style="width: 85%; height: 10px; background-color: #008000;"></div>		
		Gaucher Disease	<div style="width: 85%; height: 10px; background-color: #008000;"></div>		
	Prevalent	ETAP*	<div style="width: 40%; height: 10px; background-color: #004a7c;"></div>		
 <b>Retina</b>	Rare	Stargardt	<div style="width: 85%; height: 10px; background-color: #008000;"></div>		
		LCA10	<div style="width: 85%; height: 10px; background-color: #008000;"></div>		
	Prevalent	Wet AMD	<div style="width: 25%; height: 10px; background-color: #004a7c;"></div>		

## EARLY RESEARCH



Vaccines

## EXPANSION AREAS



Skeletal Muscle



Oncology



CNS

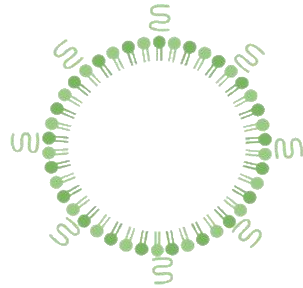


# ctLNP enables modular access to tissues and therapeutic areas

## PRIMARY FOCUS

### Liver

SYSTEMIC ctLNP DELIVERY



RARE LIVER DISEASES

**100K**

U.S. PATIENTS

PREVALENT DISEASES

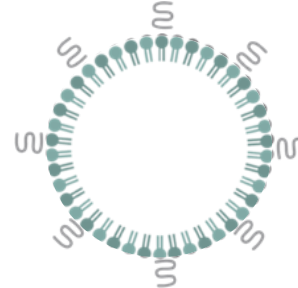
**>10M**

U.S. PATIENTS

## SECONDARY DEVELOPMENT AREAS

### Retina

LOCAL ctLNP DELIVERY



RETINAL DISEASES

**>1M**

U.S. PATIENTS

### Vaccine

LOCAL vLNP DELIVERY



INFECTIOUS DISEASES

**>100M**

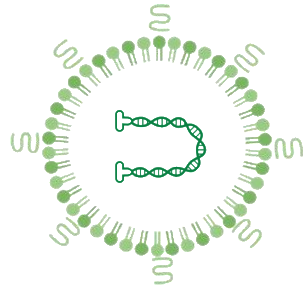
U.S. PATIENTS

# ctLNP enables modular access to tissues and therapeutic areas; cargo options

## PRIMARY FOCUS

### Liver

SYSTEMIC ctLNP DELIVERY



RARE LIVER DISEASES

**100K**

U.S. PATIENTS

PREVALENT DISEASES

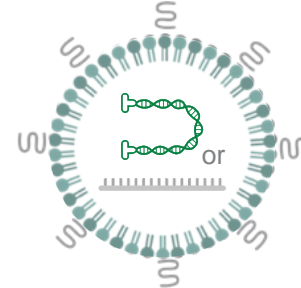
**>10M**

U.S. PATIENTS

## SECONDARY DEVELOPMENT AREAS

### Retina

LOCAL ctLNP DELIVERY



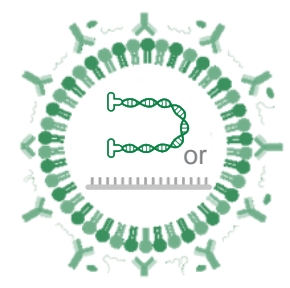
RETINAL DISEASES

**>1M**

U.S. PATIENTS

### Vaccine

LOCAL vLNP DELIVERY



INFECTIOUS DISEASES

**>100M**

U.S. PATIENTS

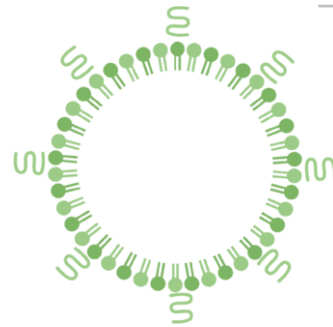
# ctLNP enables redosable, biologically driven cell and tissue targeting

## ctLNP builds on the success of clinically-validated redosable LNP systems



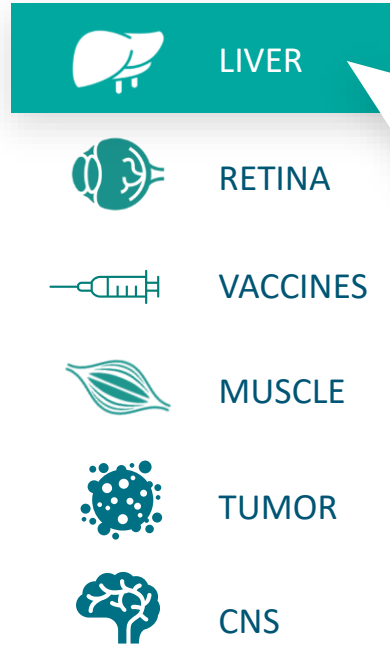
LNP (mRNA)

- 1:1 NHP → human translation
- Biodegradable lipids
- Application expanded from liver to immune cells for vaccines

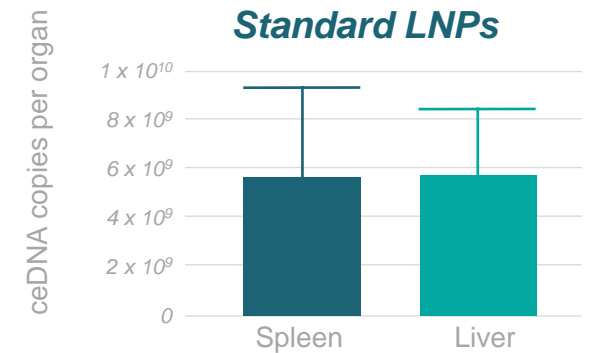
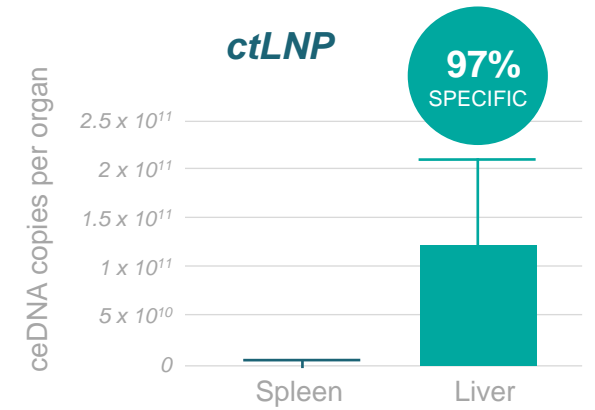


ctLNP

- Actively targeted for cell selectivity
- Minimal off-target distribution
- Applicable to cells/tissues beyond the liver



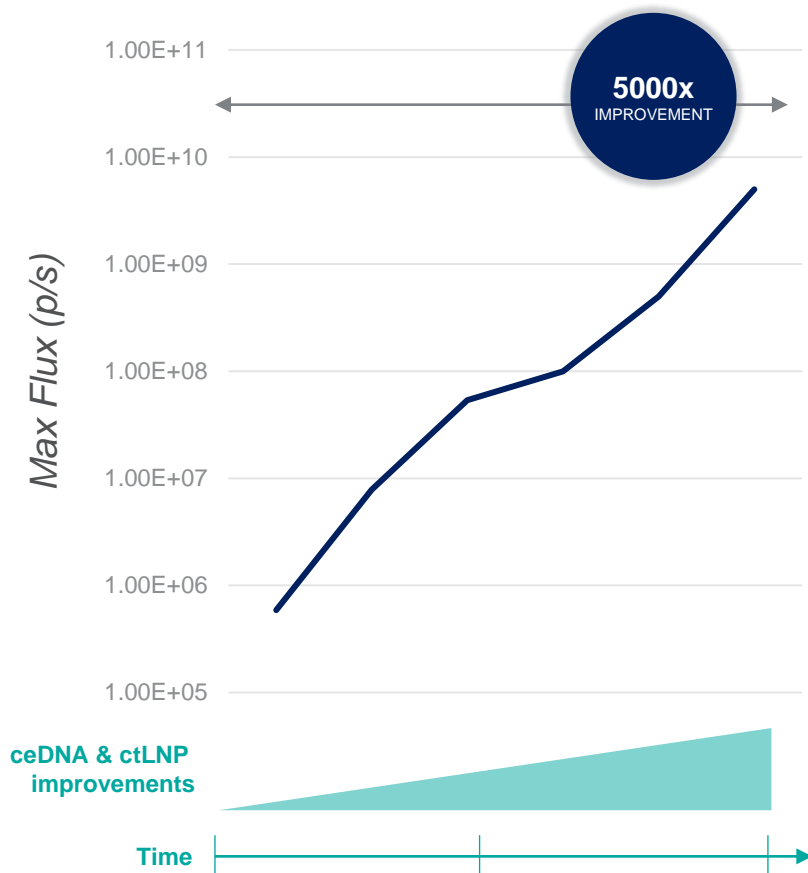
## GaINAc-targeted ctLNP Highly specific hepatocyte delivery



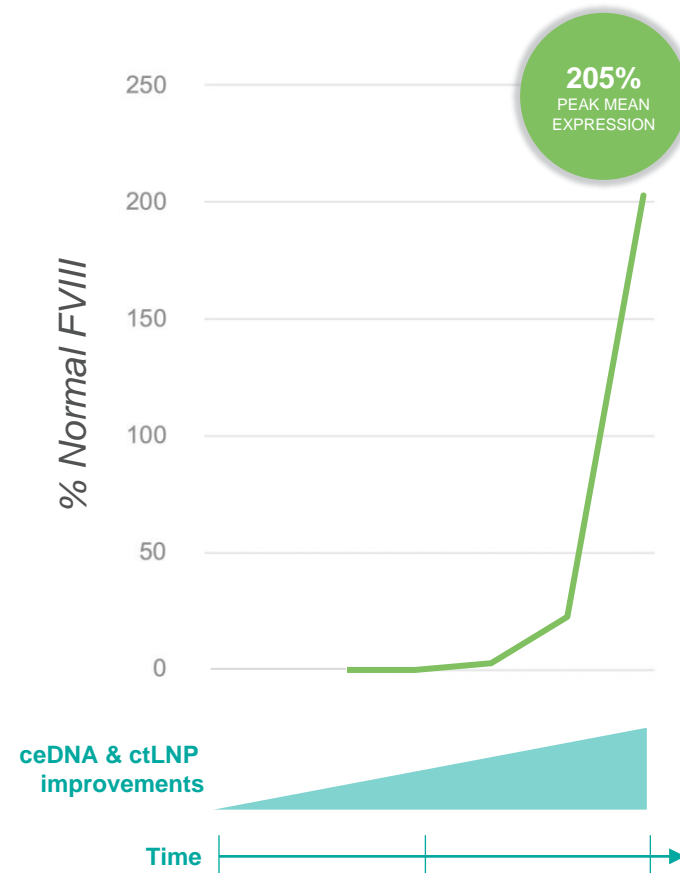
# Substantial platform progress with leading profile for non-viral DNA delivery and expression in liver



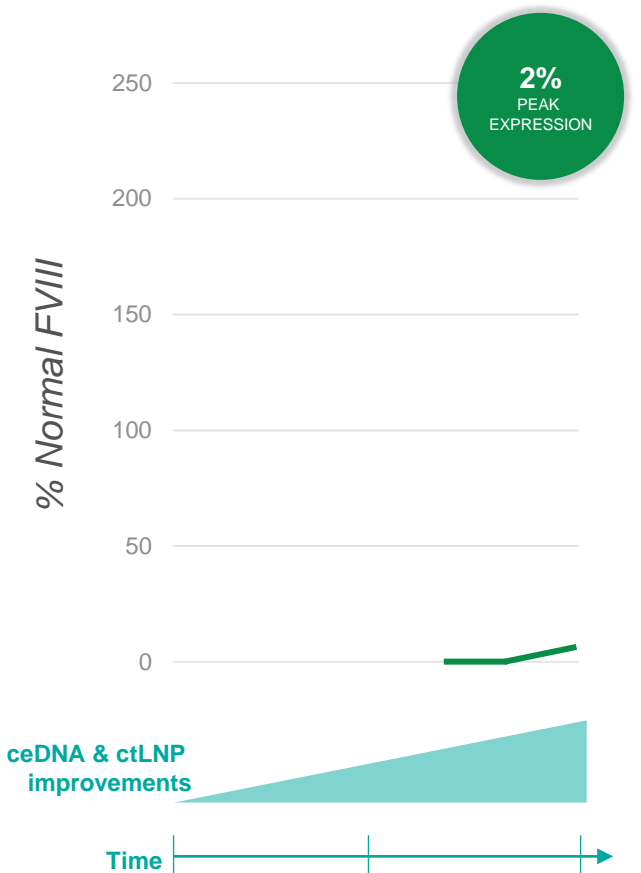
## Initial optimization with luciferase in mice



## Rapid progress with Factor VIII in mice

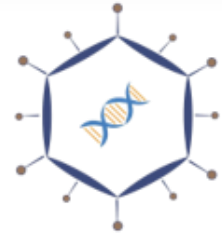


## Current translation with Factor VIII in NHP



# Developing novel ctLNP to enable broad access to photoreceptors and RPE

## ctLNP aiming for best-in-class non-viral delivery to the retina



### AAV

Current gold standard for retinal gene therapy

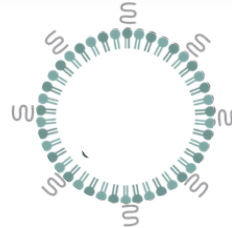
#### Limitations:

- Cargo size
- May require dual AAV, increasing possibility for off-target tox
- Sub-optimal retina transduction



### Standard LNPs

- Theoretically address AAV limitations, but...
- Poor tolerability and severe retinal degeneration
- Low expression



### ctLNP

- Minimal distribution to immune cells
- Preservation of photoreceptors in outer nuclear layer (ONL)
- Unique broad retinal transduction



LIVER



RETINA



VACCINES



MUSCLE

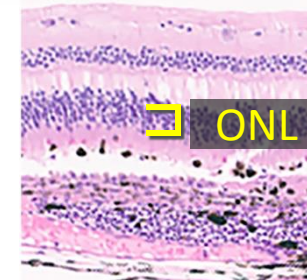


TUMOR

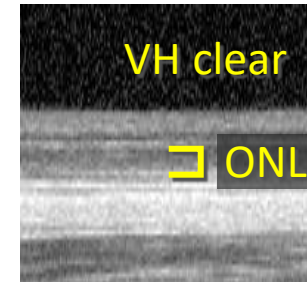


CNS

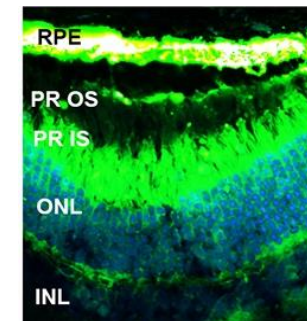
## Target subretinal ctLNP profile: stable ONL, broad expression



Tolerability (H&E)



Tolerability (OCT)

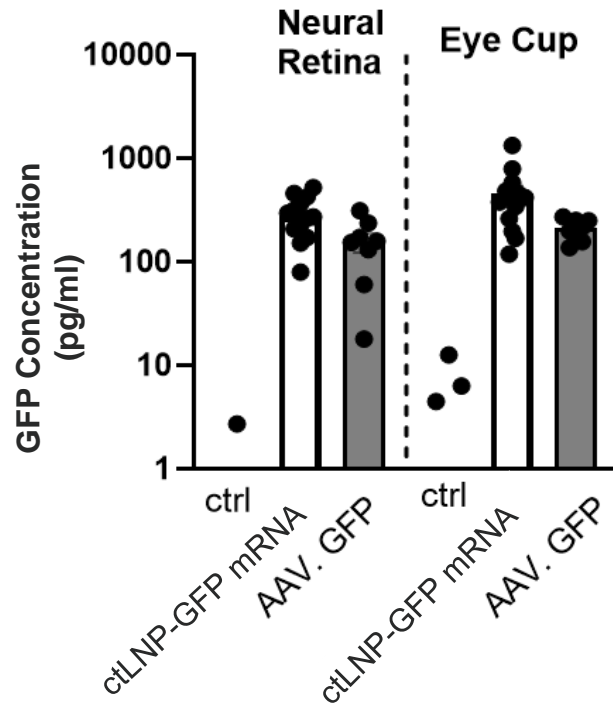


Biodistribution (IHC)

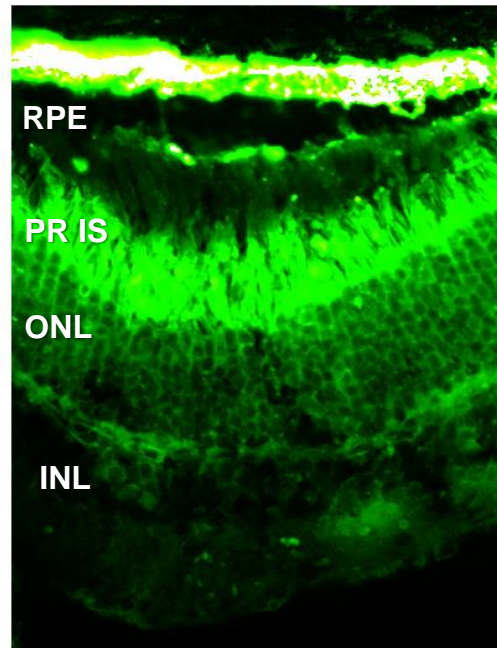
# ctLNP-mRNA shows broad photoreceptor distribution versus AAV5 which appears punctate



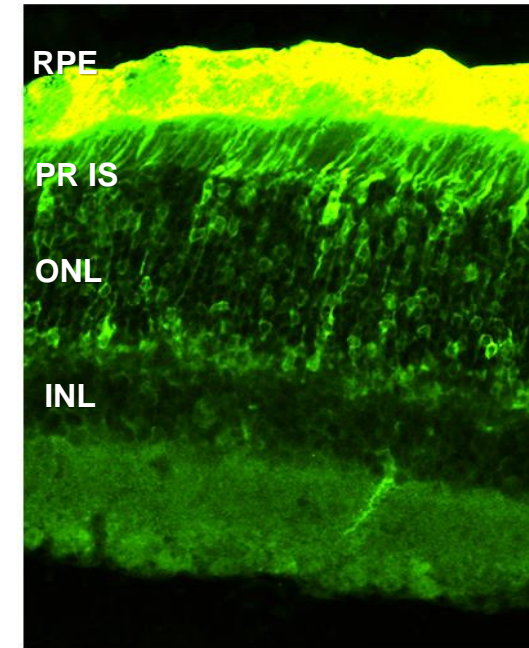
## ctLNP-mRNA shows total expression in photoreceptors comparable to AAV5



ctLNP-GFP mRNA at 24 h



AAV5.GFP at Day 28



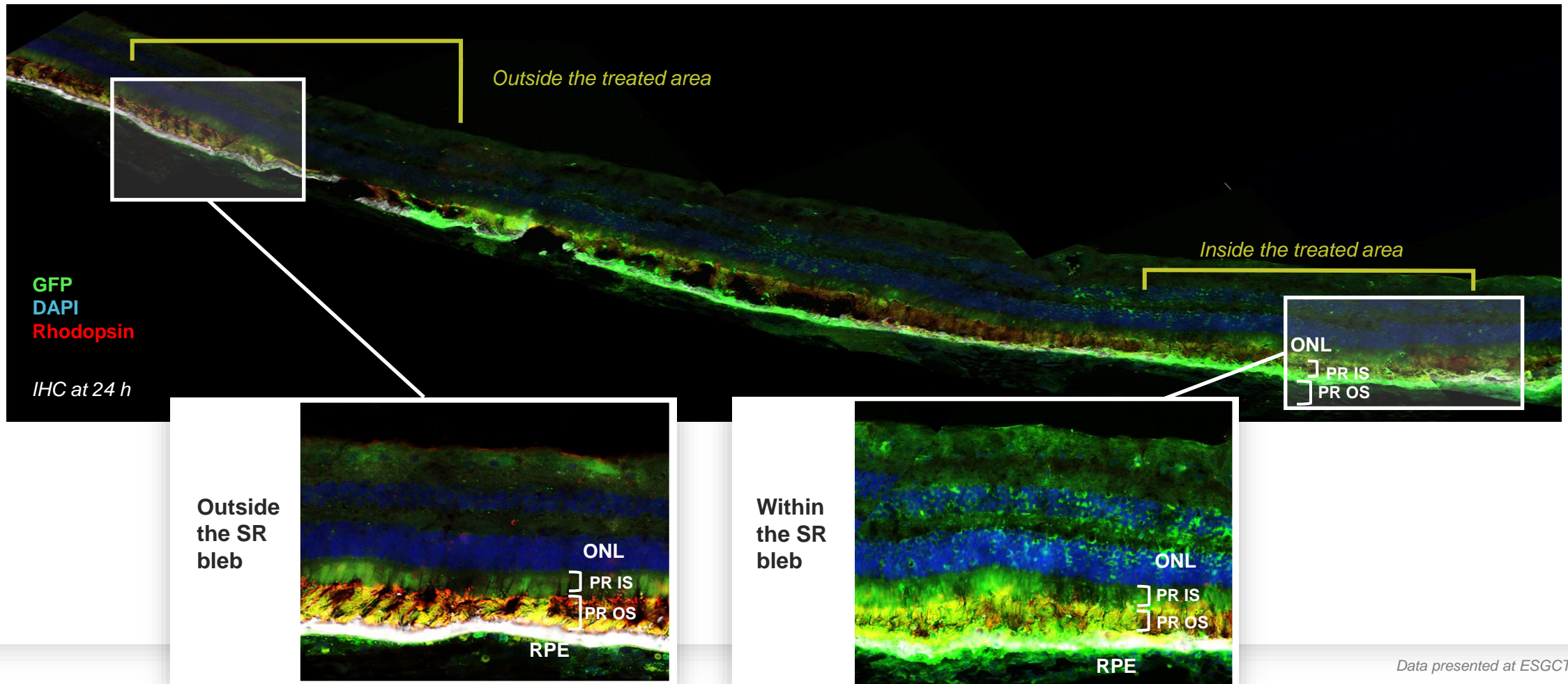
Expression data from mouse

Data presented at ESGCT 2021



# ctLNP-GFP mRNA transduces NHP photoreceptors and RPE

 Preserved photoreceptor layer (ONL) and broad GFP expression in treated area (SR injection)

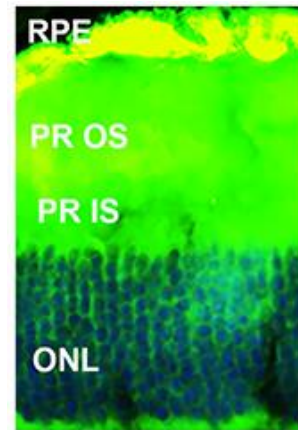
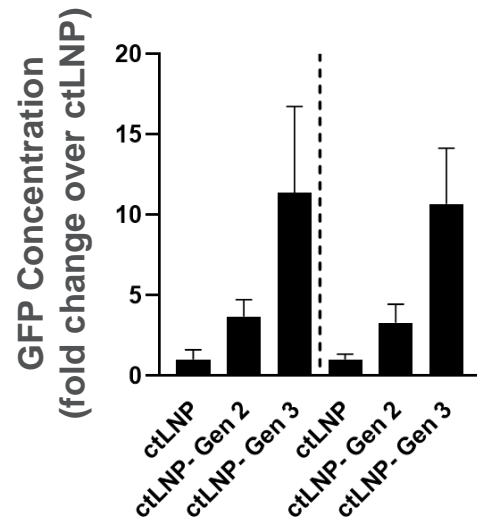
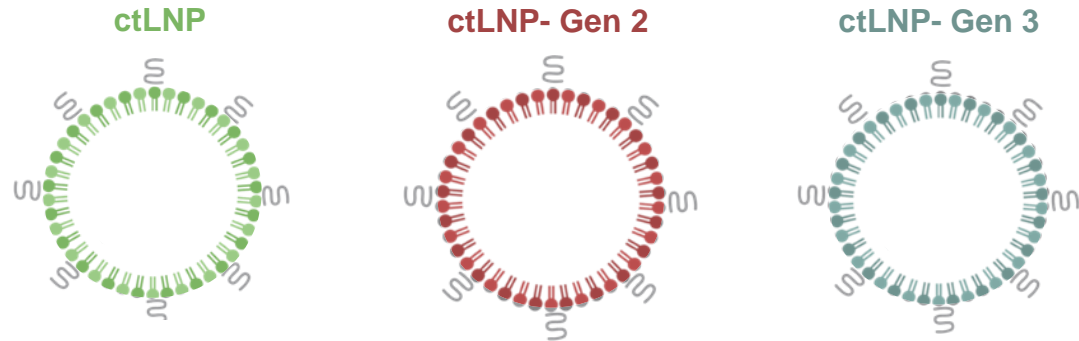


Data presented at ESGCT 2021

# ctLNP optimization shows improved BioD and potency in photoreceptors and RPE



## Optimization of ctLNP composition



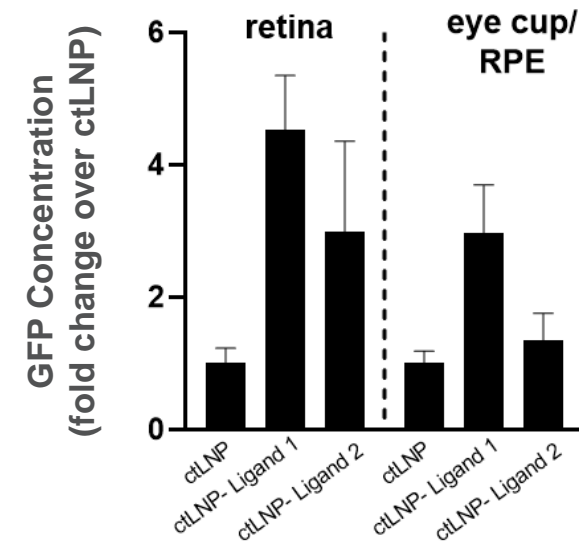
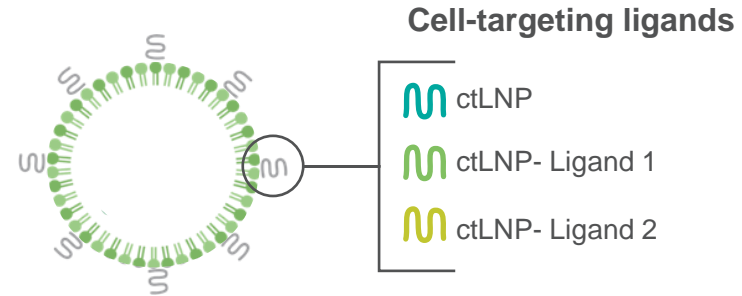
ctLNP- Gen 3

*In vivo mouse expression*  
ctLNP-GFP mRNA

Data presented at ESGCT 2021



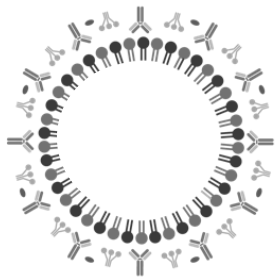
## Optimization of ctLNP targeting ligands



*In vivo mouse expression*  
ctLNP-GFP mRNA

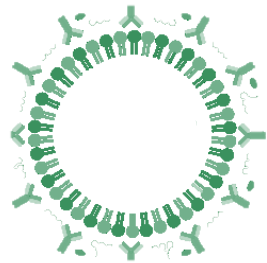
# Expanding our LNP technology from cell-targeted to vaccine-optimized compositions

## Novel proprietary LNPs tailored to nucleic acid vaccines



### LNP (mRNA)

- 1:1 NHP → human translation
- Biodegradable lipids
- Application expanded from liver to immune cells for vaccines



### vLNP

- Proprietary vaccine optimized LNP (vLNP)
- Optimized for immune cell distribution and expression
- Utilizes proprietary lipid estate



LIVER



RETINA



VACCINES



MUSCLE

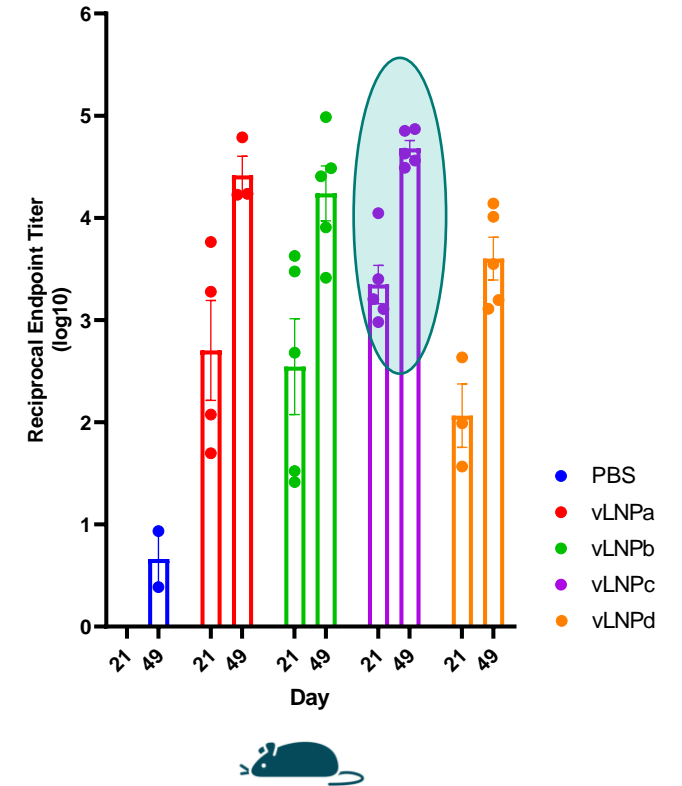


TUMOR



CNS

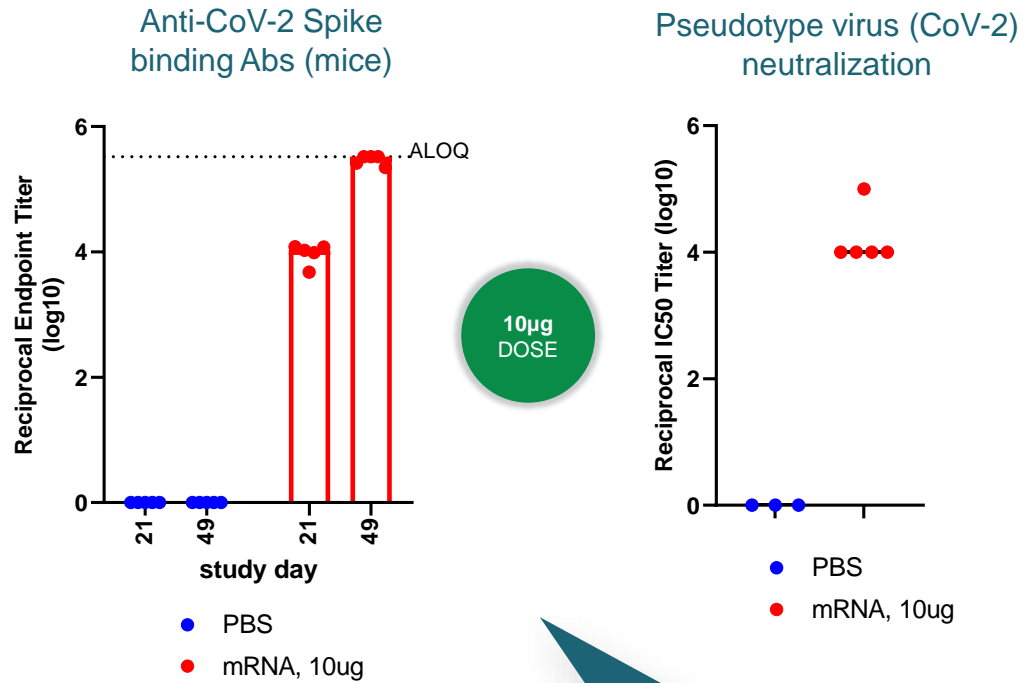
## Screening of LNPs to directly identify those with optimal immunogenicity profile



# vLNP-mRNA achieves benchmark antibody levels and neutralization across species



## Strong neutralizing antibody response

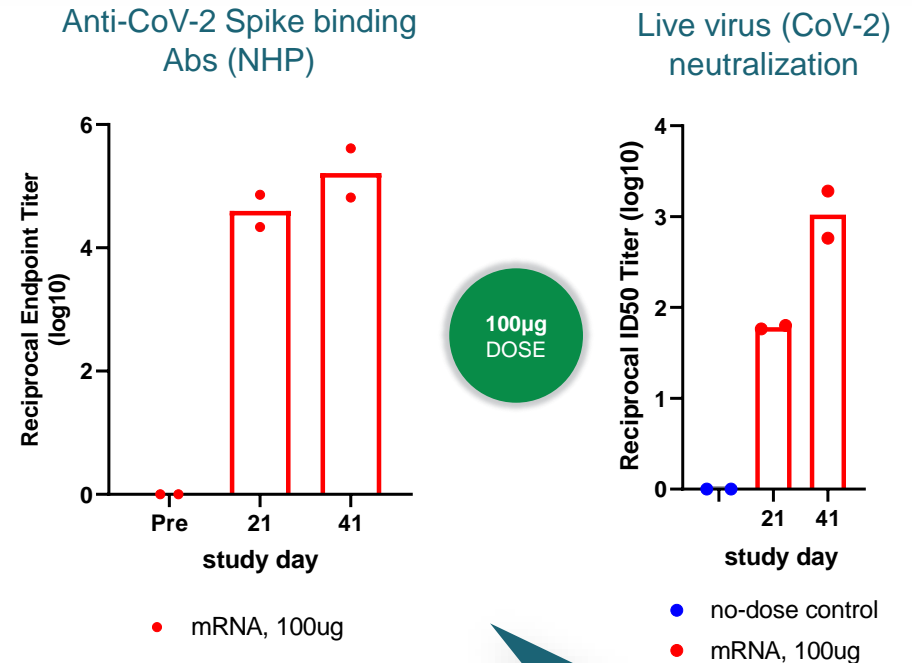


Prime day 0, boost day 28

*vLNP-mRNA benchmark on par with Moderna's mRNA-1273 in Balb/c mice (Corbett Nature 2020)*



## Consistent species translation to NHP



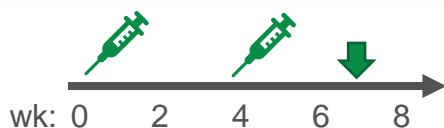
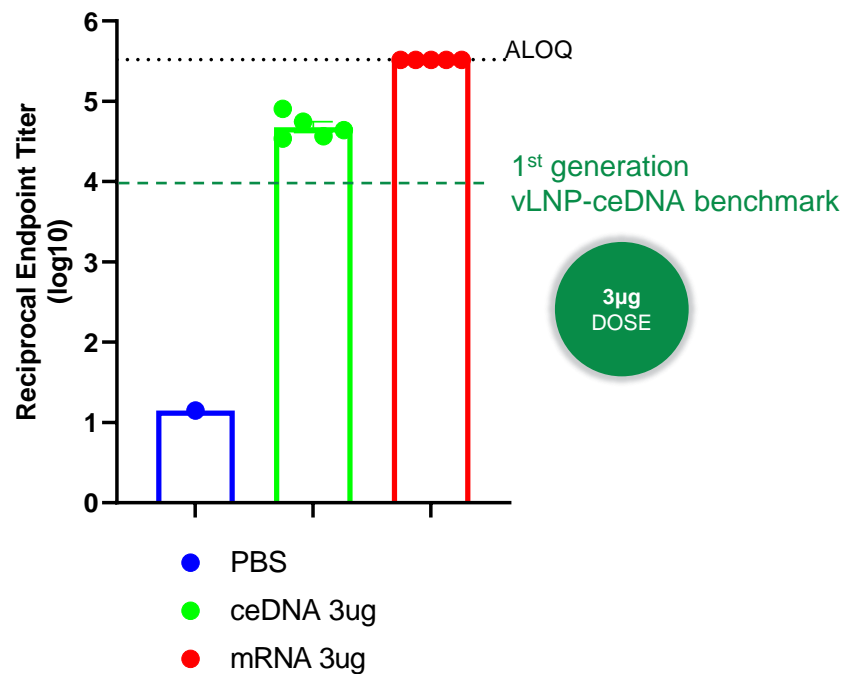
Prime day 0, boost day 28

*vLNP-mRNA benchmark on par with Moderna's mRNA-1273 in cynomolgus monkeys (Corbett NEJM 2020)*

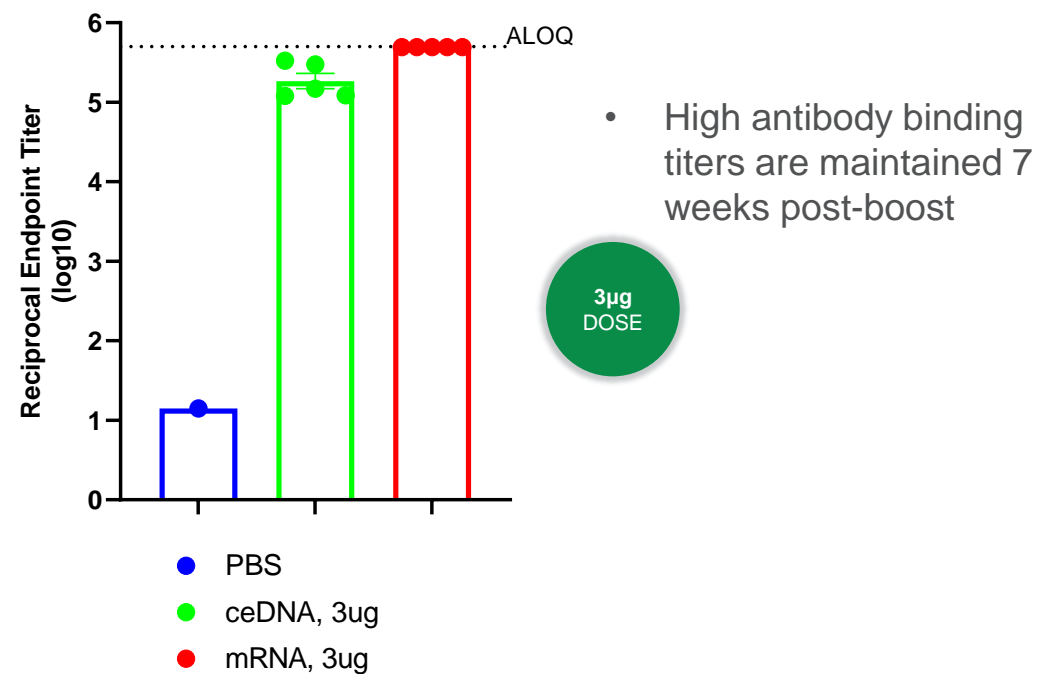
# vLNP optimization further increases vaccine potency



## Next-generation vLNP-ceDNA demonstrates enhanced antibody response



## Antibody response further enhanced by longer prime-boost spacing



# World class team and strong balance sheet



## PROVEN TEAM TRACK RECORD

40+ IND filings, 20 approved products



## \$400M CASH BALANCE\*

to fund innovation



## RUNWAY

Into 2024

### LEADERSHIP TEAM



GEOFFREY  
**MCDONOUGH, MD**  
President & CEO



MATTHEW  
**NORKUNAS, MD, MBA**  
Chief Financial Officer



MATT  
**STANTON, PHD**  
Chief Scientific Officer



JENNIFER  
**ELLIOTT, PHD, JD**  
Chief Legal Officer



DOUG  
**KERR, MD, PHD**  
Chief Medical Officer



TRACY  
**ZIMMERMANN, PHD**  
Chief Development Officer



ANTOINETTE  
**PAONE**  
SVP, Regulatory Affairs  
& Quality



ZHONG  
**ZHONG, PHD**  
SVP, DNA Sciences



SARA  
**DEN BESTEN**  
Chief People Officer



PHILLIP  
**SAMAYOA, PHD**  
SVP, Head of Corporate  
Development



LESLIE  
**WOLFE, PHD**  
SVP, Head of CMC

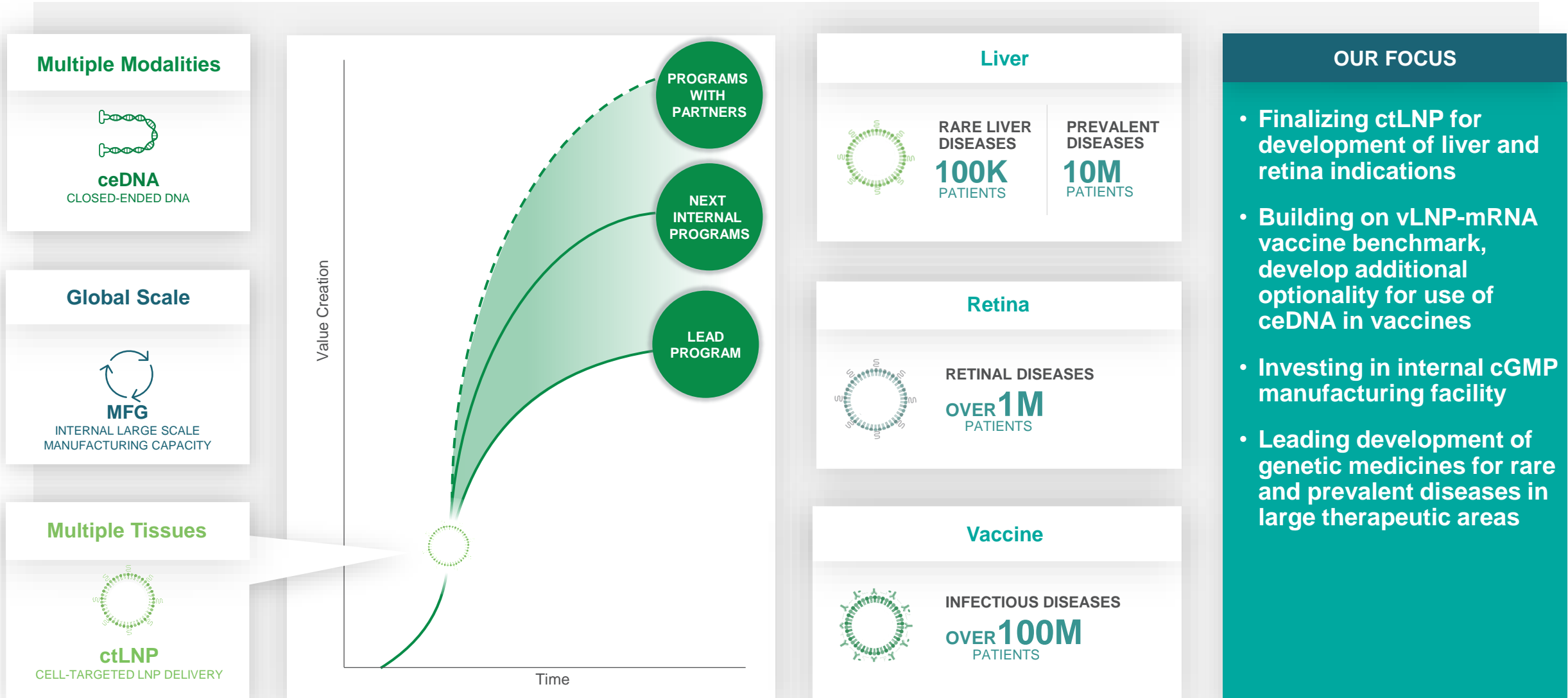


SONIA  
**RAZZETI**  
VP, Quality Assurance





# Generation Bio is unlocking the full potential of non-viral genetic medicines



E  
2  
2

generation bio™



Thank you

QUESTIONS & ANSWERS

JP MORGAN

JANUARY 2022