



NON-CONFIDENTIAL

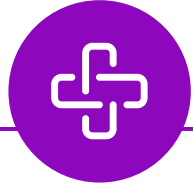
# Corporate Overview

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September 2024

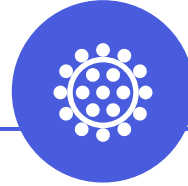


# Investment highlights



## Clinical Programs

- **Two clinical programs (cystic fibrosis and primary ciliary dyskinesia)**
- **>\$1B estimated peak sales** and no current treatments
- **Multiple near-term clinical value inflection points**



## Platform

- **Novel SORT LNP platform** engineered for higher potency delivery beyond the liver
- **Precision extrahepatic delivery** with tunable tissue specificity and cell tropism
- **Multiple routes** of administration



## Experienced Team & Syndicate

- **Deep expertise** in genetic medicine, LNP delivery and rare disease
- **\$370M raised** from **blue-chip financial and strategic investors**

Raising **\$50-75M Series C** ahead of planned 2025 IPO

# Experienced genetic medicines team and strong investor syndicate

Deep expertise in genetic medicine; \$370M raised from blue-chip financial and strategic investors

## Team



Shehnaaz Suliman,  
MD, MBA, MPhil  
CEO



David Lockhart, PhD  
President and CSO



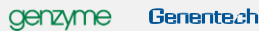
John Matthews, MD, PhD  
CMO



Marco Weinberg, PhD  
SVP, Head of Research



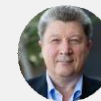
Jessica Couch, PhD, DABT  
SVP, Early Development



Ariel Kantor, PhD  
SVP, Business & Corporate  
Development



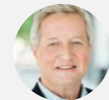
Erica Jefferson  
SVP, Corporate Affairs



Vladimir Kharitonov, PhD  
SVP, CMC



## Select Board Members



Dean Mitchell  
Board Chairman



Peter Thompson  
OrbiMed



Alan Colowick  
Matrix Capital



Oleg Nodelman  
EcoR1



Helen Kim  
Vida Ventures

## Investors



# Diverse clinical and research pipeline with first and best-in-class opportunities

RESPIRATORY

Indication	Modality	Target	Discovery	Preclinical	Phase 1/2
Cystic Fibrosis (CF)	mRNA	CFTR	RCT2100		
	Gene correction	CFTR	Intelia THERAPEUTICS		
Primary Ciliary Dyskinesia (PCD)	mRNA	DNAI1	RCT1100		
		CCDC39/40			
		DNAH5			
Other lung indications	Multiple	Undisclosed			
Other	mRNA	Undisclosed			
	Multiple	Undisclosed			
LIVER: Various	Multiple	Undisclosed	AskBio		
		Undisclosed			
CNS: Various	Multiple	Undisclosed			



**Delivery Method**

- Inhaled
- Inhaled IV
- IV
- Intrathecal

# 2024 progress in advancing to patients and partnerships



## Program Updates

- ✓ **Cleared INDs and ex-U.S. regulatory submissions** for CF and PCD
- ✓ **Dosed 120 healthy volunteers** across CF and PCD studies
- ✓ **Established therapeutic doses for CF and PCD patient studies** about to start
- ✓ **Completed PCD Ph1a SAD study** in PCD patients



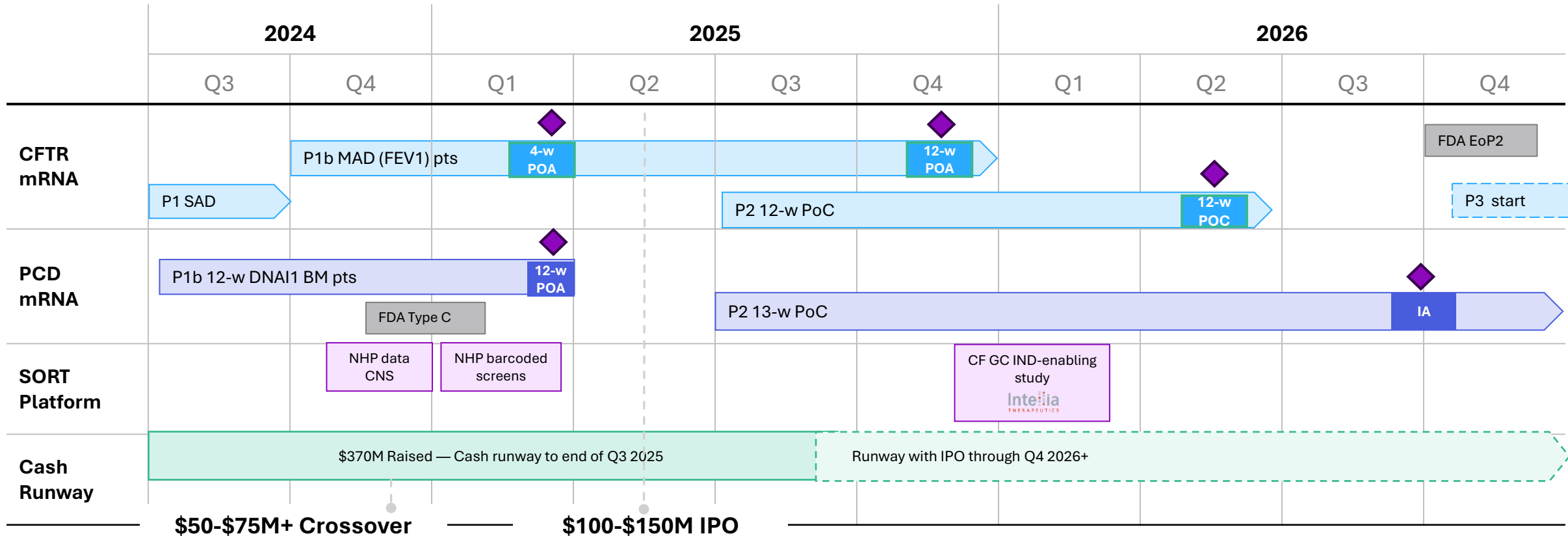
## Platform/Partnering Updates

- ✓ First demonstration of **durable and persistent editing of lung epithelial cells**, published in *Science*
- ✓ Demonstrated high levels of **hepatic and extrahepatic delivery with IV SORT** administration
- ✓ Executed **gene editing collaboration with Intellia Therapeutics** for CF gene writing

Cash runway through Q3 '25

# Significant opportunity with near-term, value-driving milestones

Clinical POA data anticipated across 2 clinical programs in 1H25



**Financing and key value-creating milestones**

- PCD and CF mRNA POA
- Platform NHP data
- 1 year of cash at IPO
- CF mRNA P2 PoC
- PCD P2 IA



Abbreviations: IND (investigational new drug application), IA (interim analysis to trigger start of confirmatory study for accelerated approval), GC (gene correction), MAD (multiple ascending dose), NHP (non-human primate), POA (proof of activity, e.g., convincing trend of clinically meaningful effect), PoC (proof of concept) and SAD (single ascending dose)



# Cystic Fibrosis (CF): RCT2100 inhaled mRNA program



# RCT-2100: Differentiated and potential best-in-class inhaled mRNA treatment being evaluated for Class 1 CFTR mutant CF patients

*Blockbuster opportunity supported by robust translational data with clinical POA anticipated in 1H25*



CF is a progressive, fatal genetic disease characterized by persistent lung infections and respiratory decline



CF patients with Class 1 (nonsense) mutations have **no effective therapeutic options**



Initially focused on **10% of CF patients** with Class 1 mutations, ~**13K** patients worldwide



RCT-2100 is a highly differentiated potentially disease-modifying treatment



**Ph1b SAD study** near completion (80 healthy volunteers dosed to date)



**4-week Ph1b MAD study** in patients to initiate in Q3'24

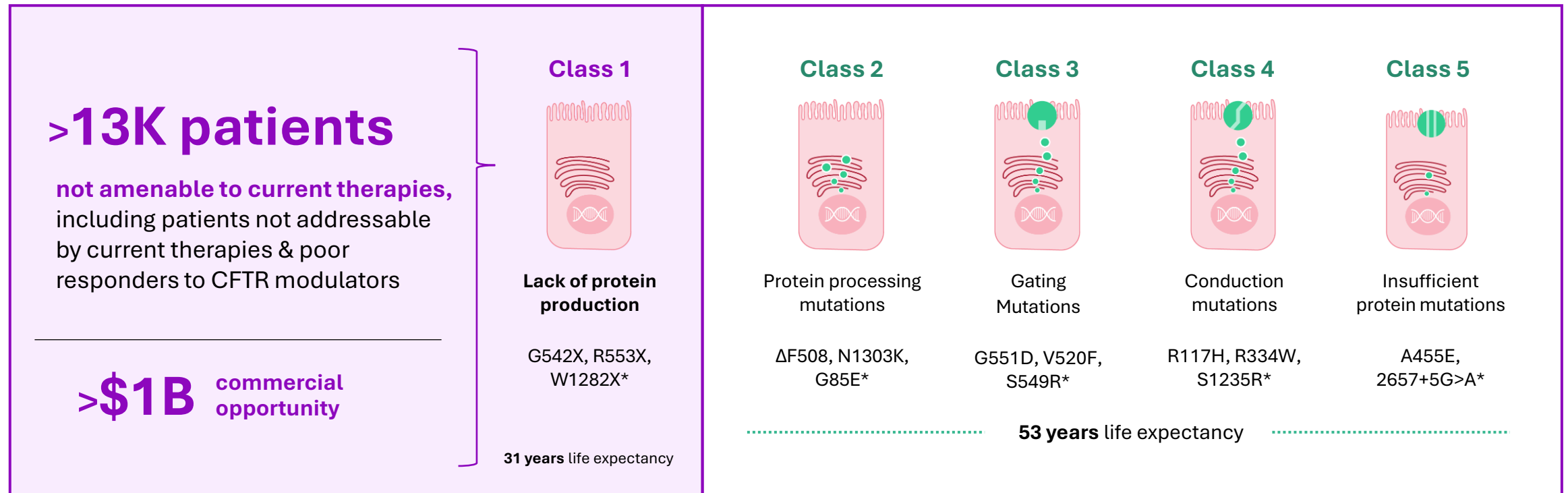


Preclinical data demonstrates **significant potency and efficacy in human bronchial epithelial cell (hBE) assay and ferret model**



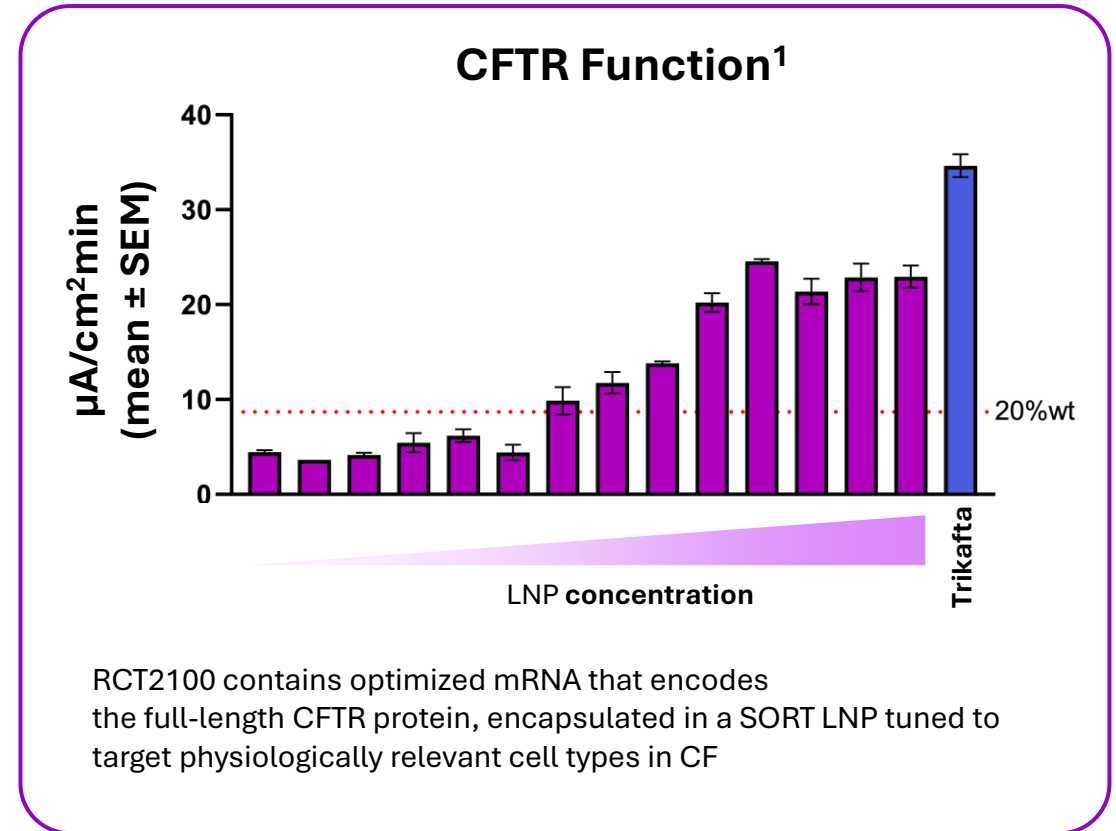
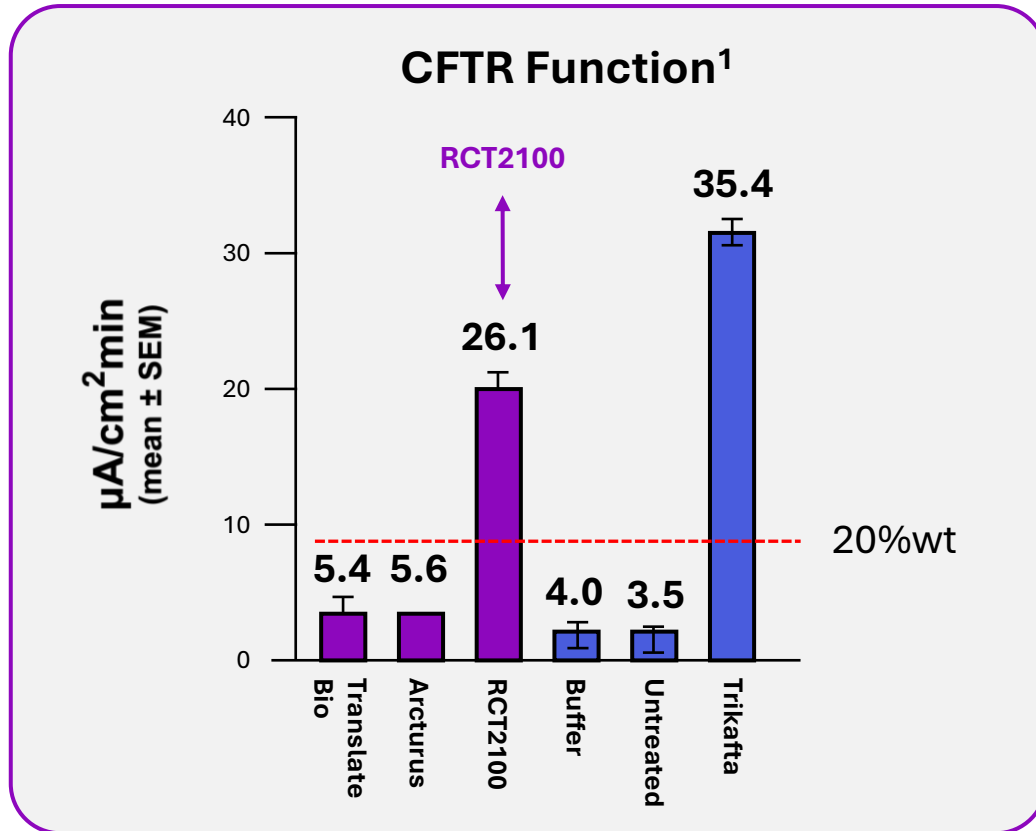
# RCT2100 targets 10%+ of CF patients with no treatments

130K patients worldwide with 10% of patients without a disease modifying treatment



# RCT2100 restores CFTR function more potently than competitor formulations

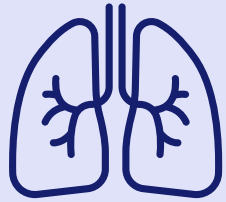
5X+ greater potency in gold-standard hBE model



RCT2100 contains optimized mRNA that encodes the full-length CFTR protein, encapsulated in a SORT LNP tuned to target physiologically relevant cell types in CF

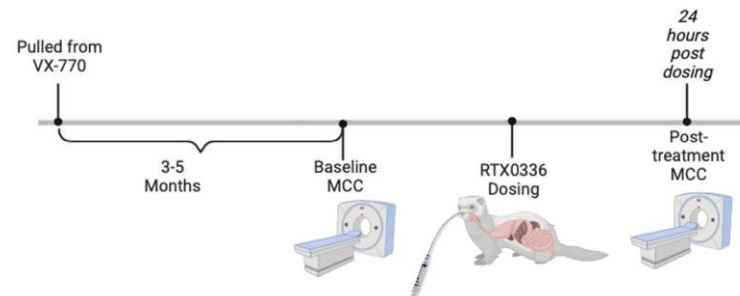
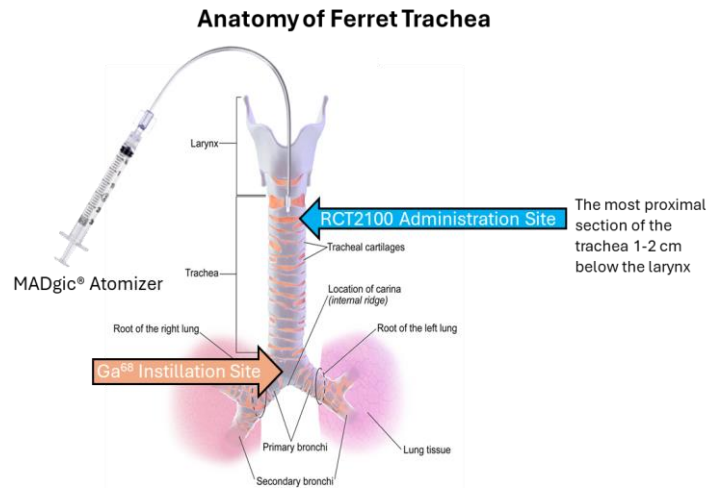
RCT2100 demonstrates potent efficacy in CF patient-derived, fully differentiated bronchial epithelial cells via apical delivery in the presence of mucus

# RCT2100 efficiently delivers to target cell types and penetrates through G551D CF ferret mucus



Genetic similarities and airway physiology of ferrets make them helpful predictors of human activity

CF ferret tracheal mucociliary clearance assay is the gold standard *in vivo* model



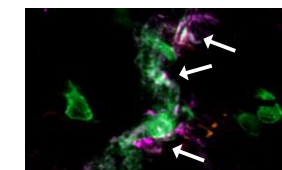
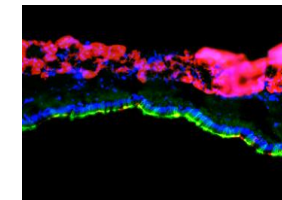
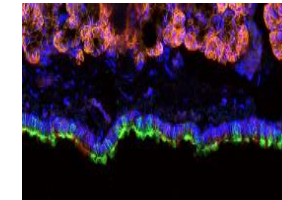
## G551D CF Ferret Mucus



## RCT21000 LNPs

Encapsulating Cre mRNA

CF Trachea

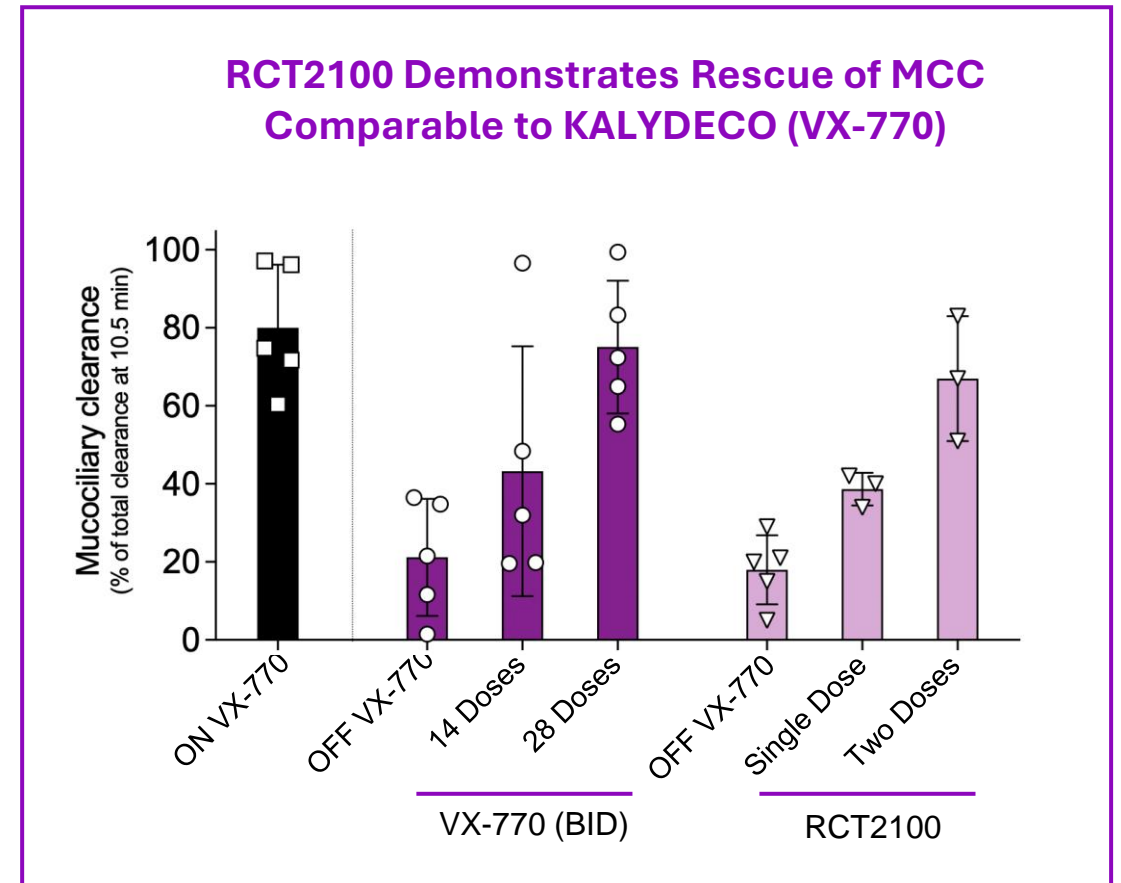
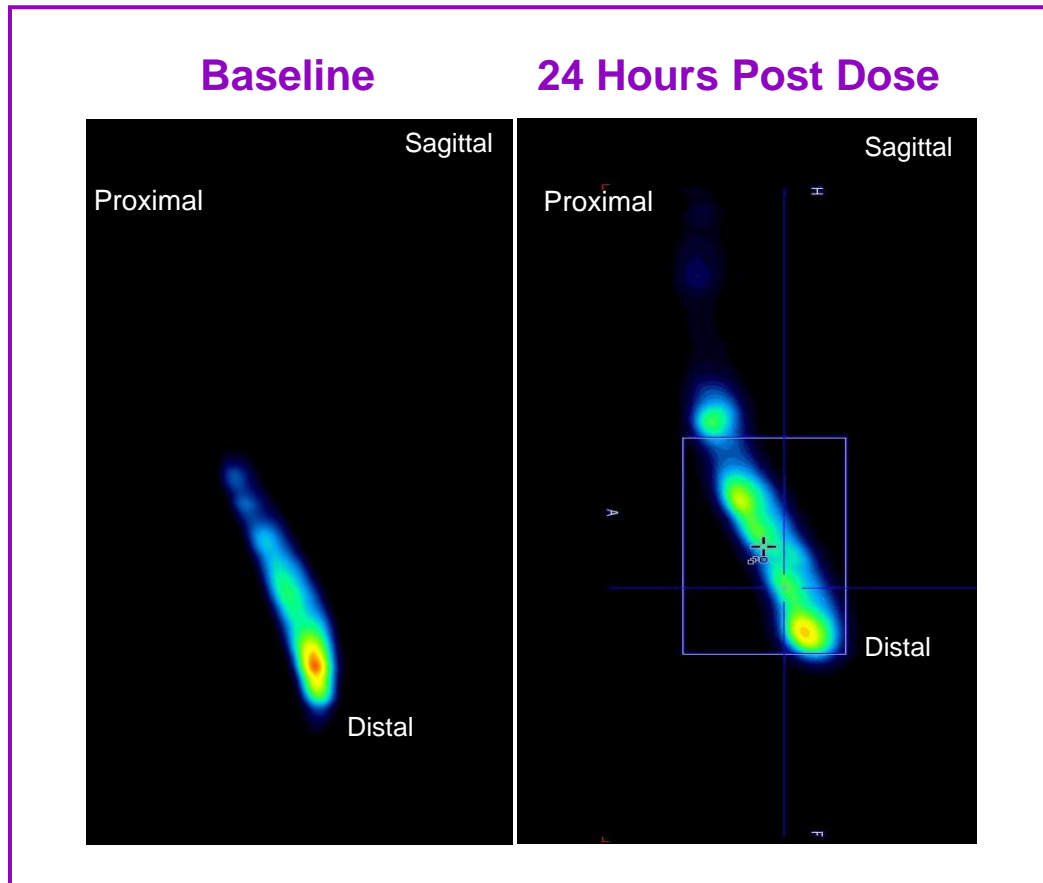


- CRE Induced GFP
- tdTomato
- Nuclei (DAPI)

- CRE Induced GFP
- CFTR
- Ionocytes (BSND)

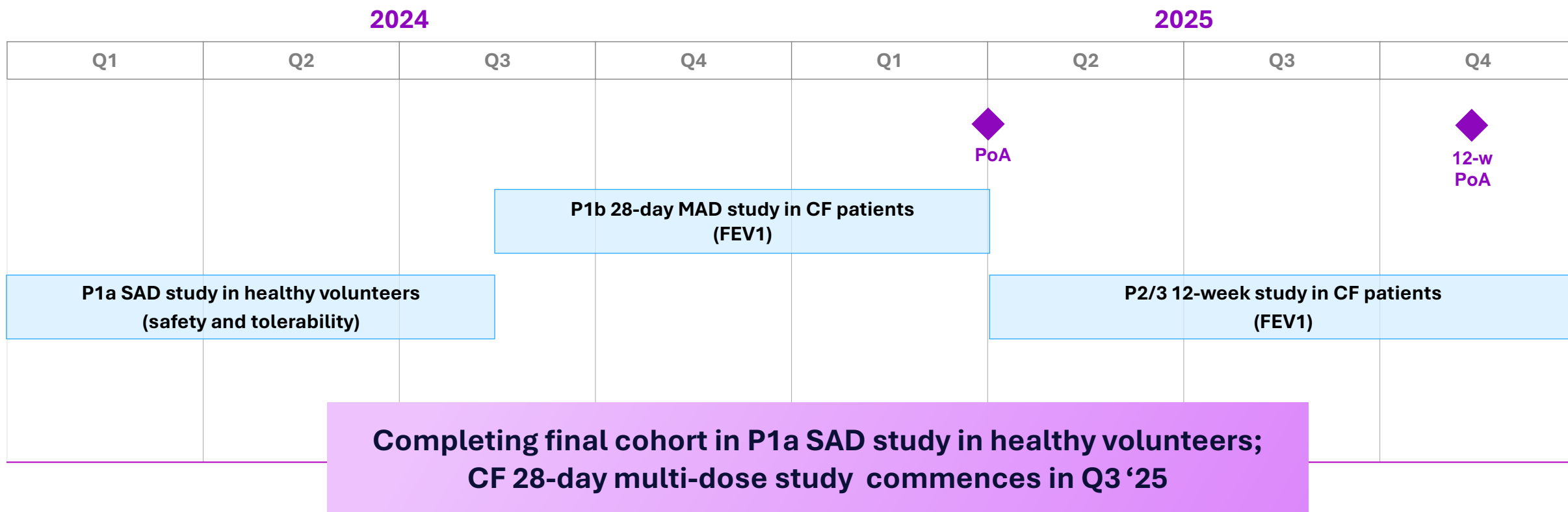
# High level of CFTR-dependent mucociliary clearance observed within 24 hours

Robust delivery and efficacy in gold-standard in vivo model (CF ferret); delivery confirmed in NHPs



# P1/2 program designed to deliver rapid clinical POA

Pending supportive P1b clinical POA data in 1H25, P2/3 study planned to initiate mid-2025



# Primary Ciliary Dyskinesia (PCD): RCT1100 inhaled mRNA program





# RCT-1100: First-in-class inhaled mRNA therapeutic for PCD with DNAI1 mutations

*Blockbuster franchise opportunity supported by robust translational data with clinical POA anticipated in 1H25*



**PCD is a rare genetic disorder that leads to chronic lung disease and bronchiectasis**



**RCT-1100 is a potential first-in-class treatment**



PCD is caused by loss of function mutations in cilia cells causing **recurrent respiratory infections**



Orphan lung disease with **no competition**



**SAD study nearly complete** (40 healthy volunteers and 9 PCD patients dosed to date)



**12-w biomarker studies to initiate 3Q24 and produce clinical POA data 1H25**



Designed to support **P2/3 study initiation mid-2025**



FDA granted **Orphan Drug Designation (ODD)** for treatment of PCD

# PCD is a high-morbidity orphan respiratory disease with no approved treatment

Primary Ciliary Dyskinesia caused by genetic mutations that **impair ciliary function**, resulting in **deficient mucociliary clearance (MCC)**, leading to chronic respiratory infections, bronchiectasis and loss of lung function

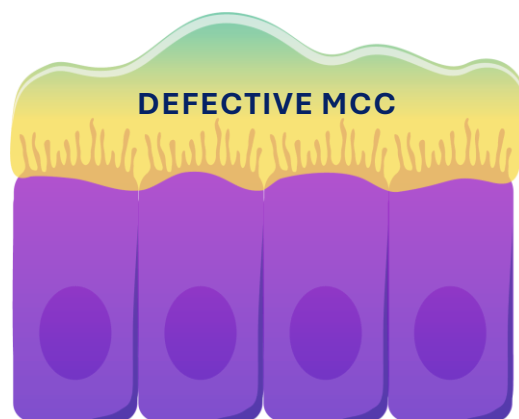
**>100K patients**

estimated prevalence across mutations in the U.S., UK and EU5<sup>1</sup>

**No approved treatments**

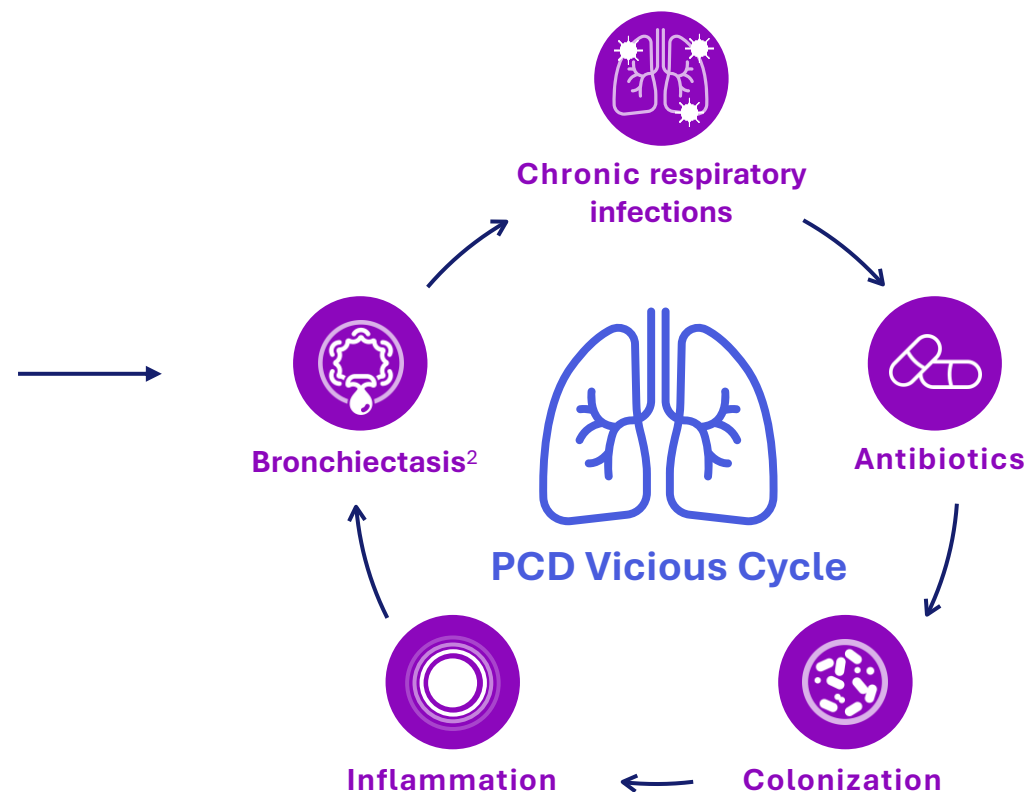
**\$2B market**

for most prevalent genes (DNA1, DNAH5, CCDC39/40)



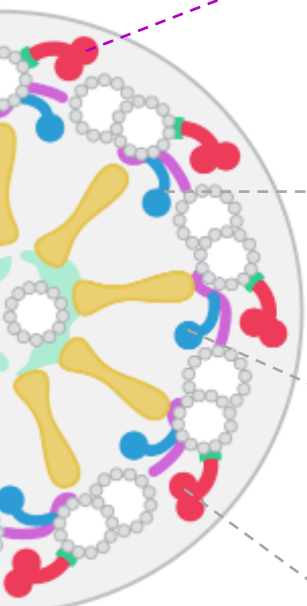
Mutations in genes cause dysfunctional cilia\*

\*Hair-like structures that line the upper and lower airways



<sup>2</sup>Permanent lung damage in **100%** of patients

# PCD is a ~\$2B franchise opportunity with no competition



		Patients, U.S. & EU5	Estimated Sales
<b>RCT1100</b>	~7% Outer dynein arm defects <b>DNAI1</b>	~7K	~\$440M
	~7% Inner dynein/MTD defects <b>CCDC39</b>	~7K	~\$440M
	~3-4% Inner dynein/MTD defects <b>CCDC40</b>	~3-4K	~\$200M
	~20% Outer dynein arm defects <b>DNAH5</b>	~20K	~\$900M

**31-45K**  
patients  
with mutations  
in the 4 most prevalent  
PCD genes

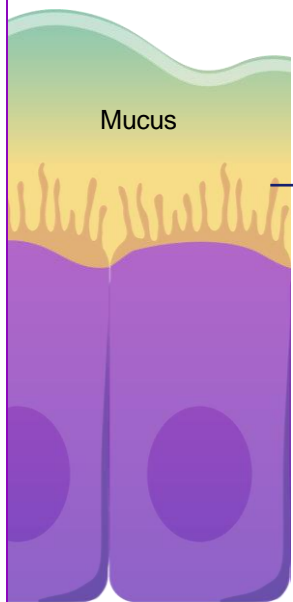
# RCT1100 is an inhaled mRNA therapeutic targeting DNAI1 mutations

*SORT LNP-encapsulated DNAI1 mRNA designed to restore MCC*

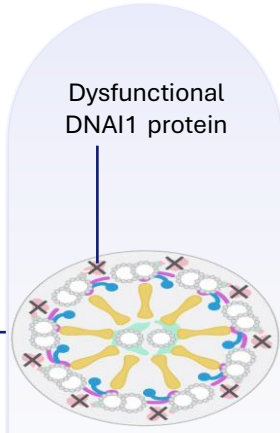


## PCD

PCD is caused by pathogenic mutations in **DNAI1**, a gene that encodes a protein essential for ciliary movement.



Mucus



Dysfunctional DNAI1 protein

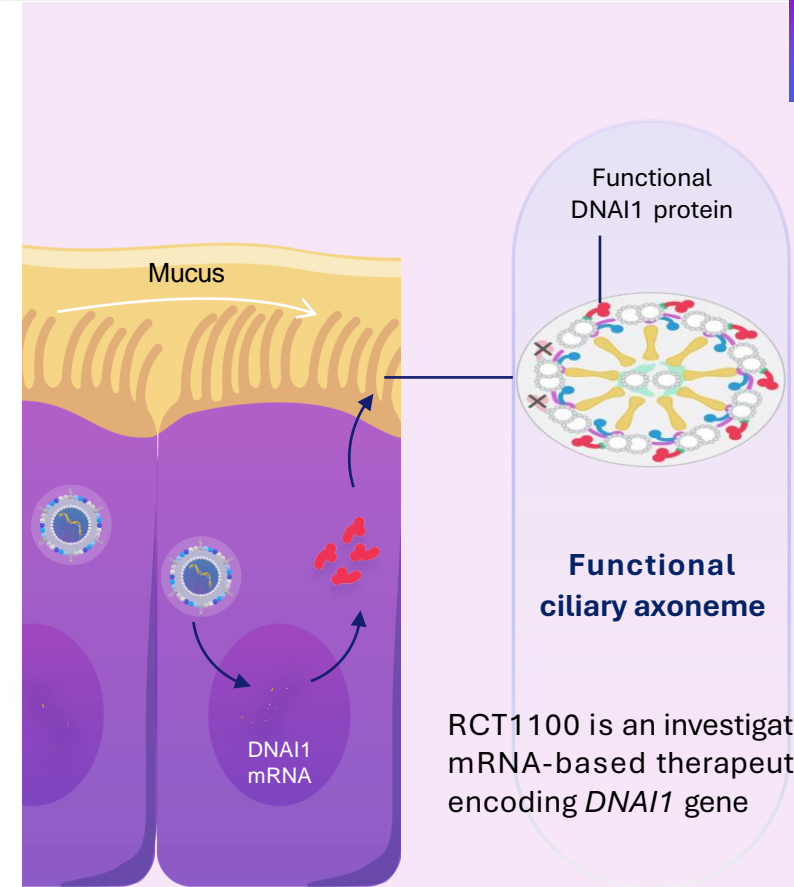
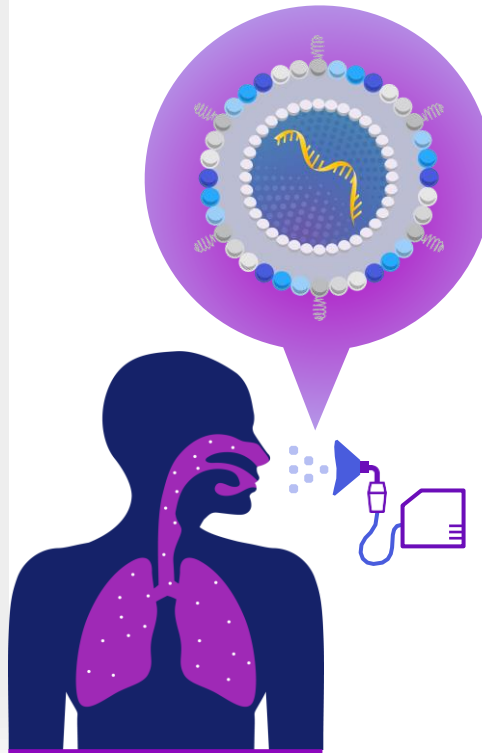
**Dysfunctional ciliary axoneme**

Missing DNAI1 protein and outer dynein arm structure

Ciliated cell

## Treatment

**SORT LNP with DNAI1-mRNA**



Mucus

Functional DNAI1 protein

**Functional ciliary axoneme**

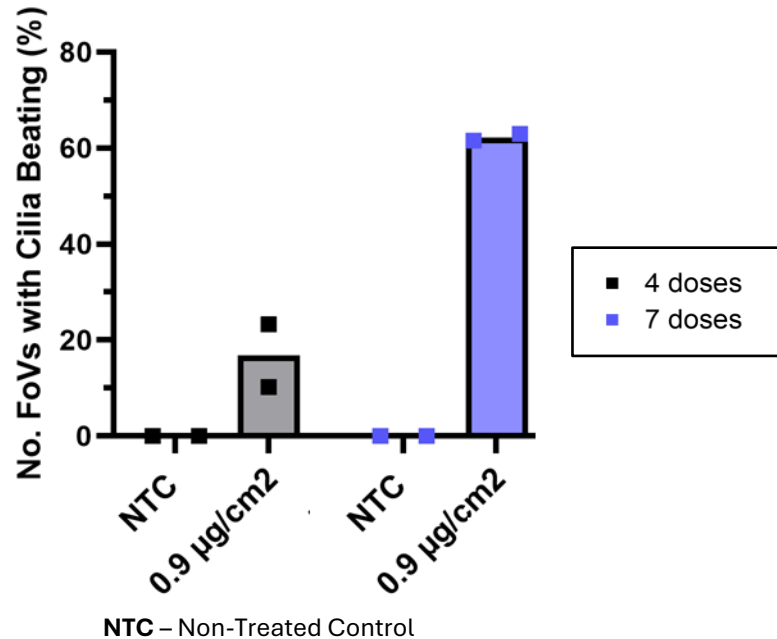
RCT1100 is an investigational mRNA-based therapeutic encoding *DNAI1* gene

Ciliated cell



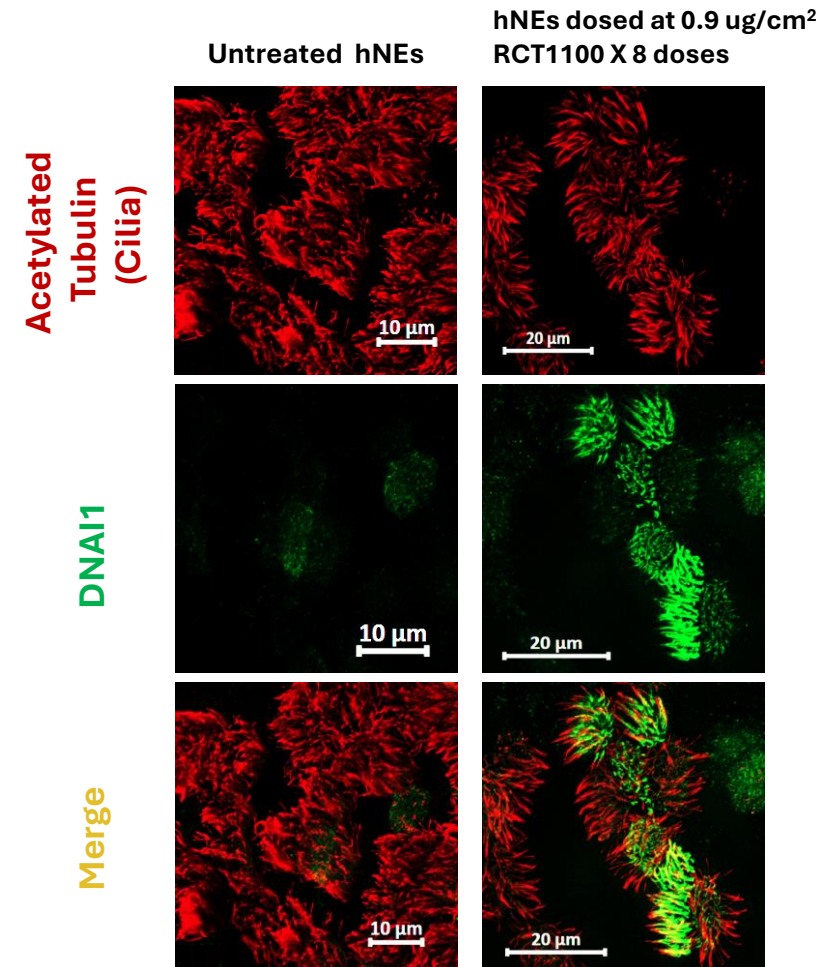
# RCT1100 restores DNAI1 protein and ciliary activity in patient nasal epithelial cells (hNEs)

Increased Ciliary Activity Achieved with Repeated Nebulized Administrations



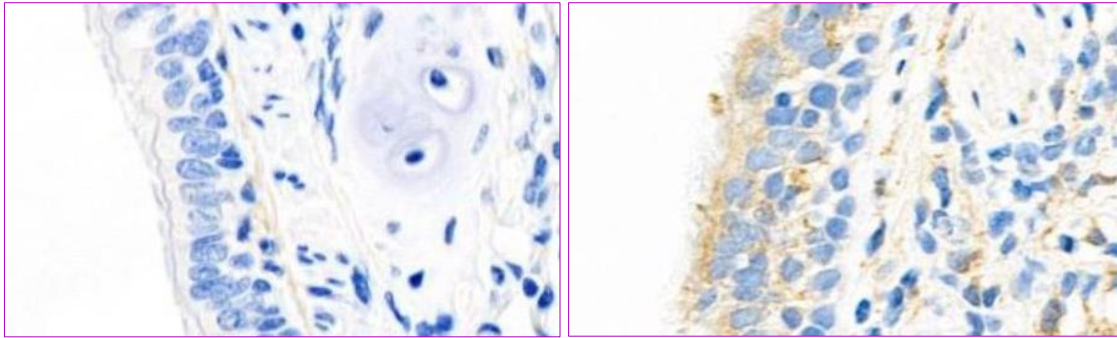
- Up to 60% of fields of view show ciliary beating
- 0.9 µg/cm<sup>2</sup> corresponds to ~3 mg nebulized dose

DNA1 Protein Expression Demonstrated in Cilia with Repeated Nebulized Administrations



# Non-human primate data demonstrates increased expression of DNAI1 protein in target cells with repeated dosing

Protein level derived from mRNA delivered via nebulization increases with repeated administration and is dose-dependent

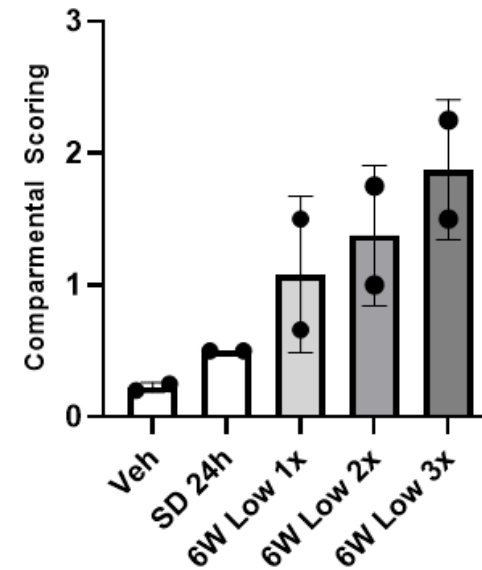


Vehicle Control

Low Dose (3x/week)

- Signal accumulation
- High protein expression detected in airway epithelial cells and cilia of NHPs after 6-week repeat-dose studies
- Detectable at low dose (0.14 mg/kg)

## Semi-quantitative Scoring of DNAI1-HA in the NHP lung



Key -

0 = no signal

1 = mild signal, some epithelial cells

2 = 50% of airways indicate epithelial-specific signal

3 = intense signal in more than 50% of airways, with cilia specific localization several regions

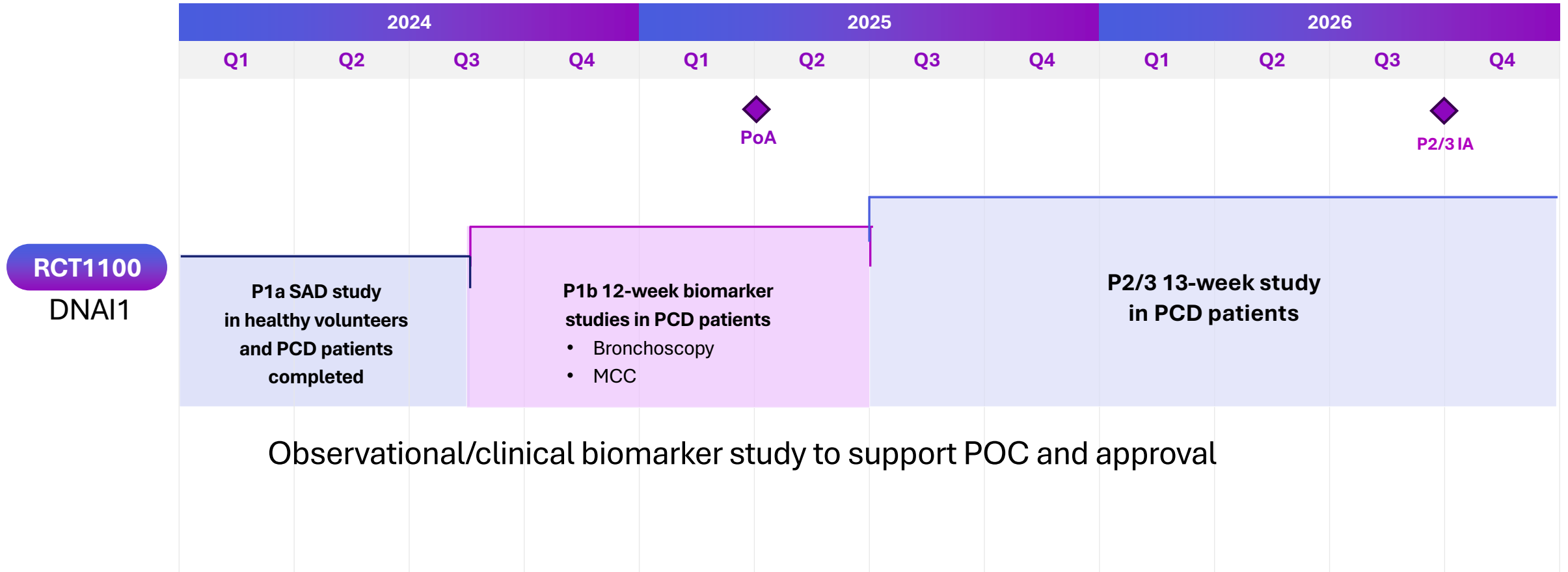
4 = intense signal in all airways, with clear cilia localization in most regions

- Semi-quantitative scoring of the bronchial epithelium shows frequency-dependent accumulation of *DNAI1* protein following repeat-dose administration over 6 weeks (each score represents avg of 3-4 lung regions)
- Single dose (SD) study: 0.34 mg/kg; 6-week repeat-dose: 0.14 mg/kg; 24h post-dose timepoint for all groups



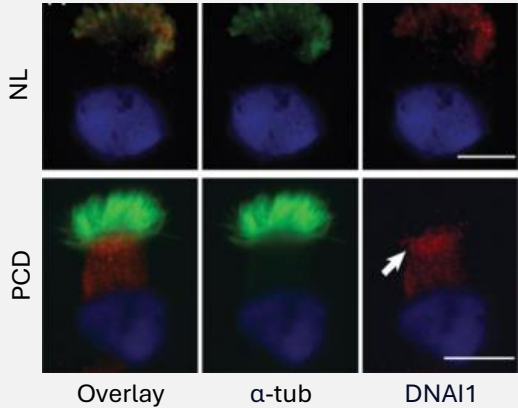
# P1/2 program designed to deliver rapid clinical POA

*P2/3 study planned to initiate mid-2025*



# P1b studies designed to show evidence of restoration of mucociliary function

*Designed to demonstrate rescue of protein expression, ciliary structure and function, and mucociliary clearance*

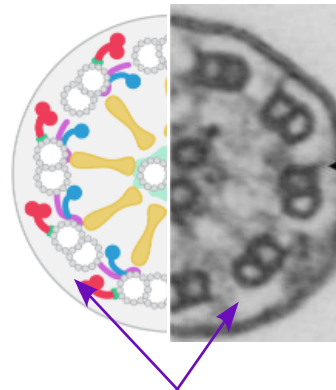


## Immunofluorescence (IF)

showing protein expression in disease-relevant cells

*PLoS One 8 (2013) e59436*

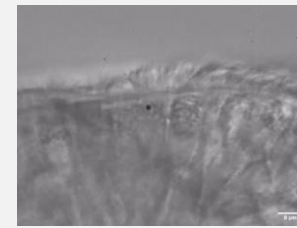
Normal vs Defective ODA Structure (e.g. DNAI1)



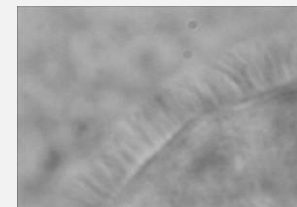
## Transmission electron microscopy (TEM)

showing rescue of the ciliary axoneme structure

*Clin Chest Med 43 (2022) 127–140*



Healthy Normal; Cilia beat at approximately 10 Hz



DNAI1; (This is a video, the cilia are not moving)

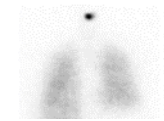
## High-speed video microscopy

showing rescue of ciliary beat frequency and beat pattern

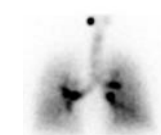
*Clin Chest Med 43 (2022) 127–140*

Baseline

2hrs



Normal



Abnormal

## Mucociliary clearance (MCC)

Inhaled radio-aerosol showing whole lung mucociliary clearance

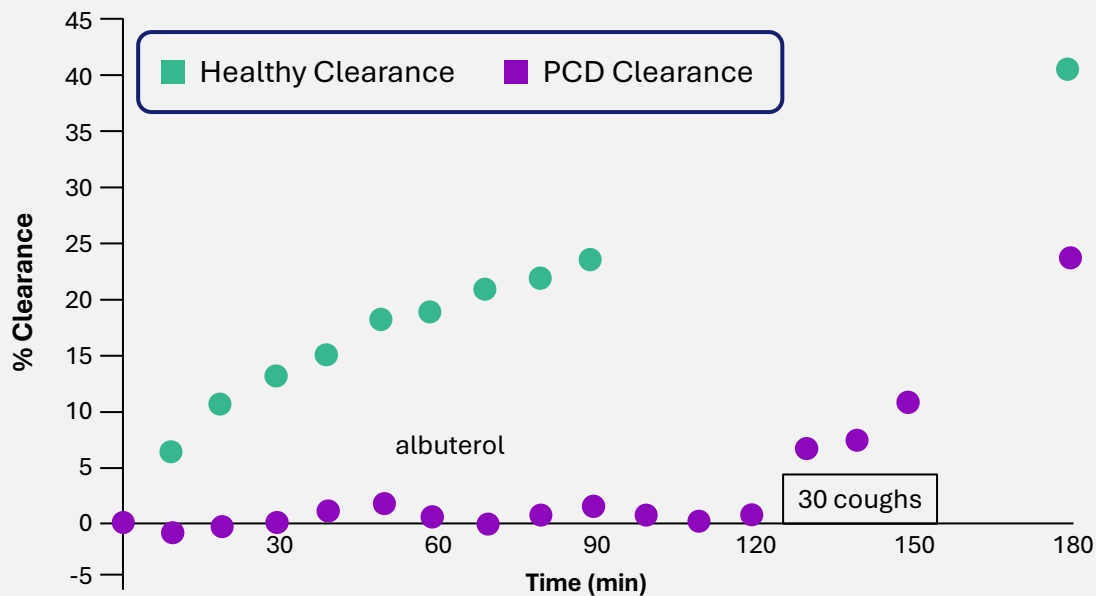
*ERJ Open Research 9 (2023) 00865–2023*

Patient data anticipated Q1 '25

# Pulmonary radioaerosol MCC is a sensitive assay likely to predict clinical benefit

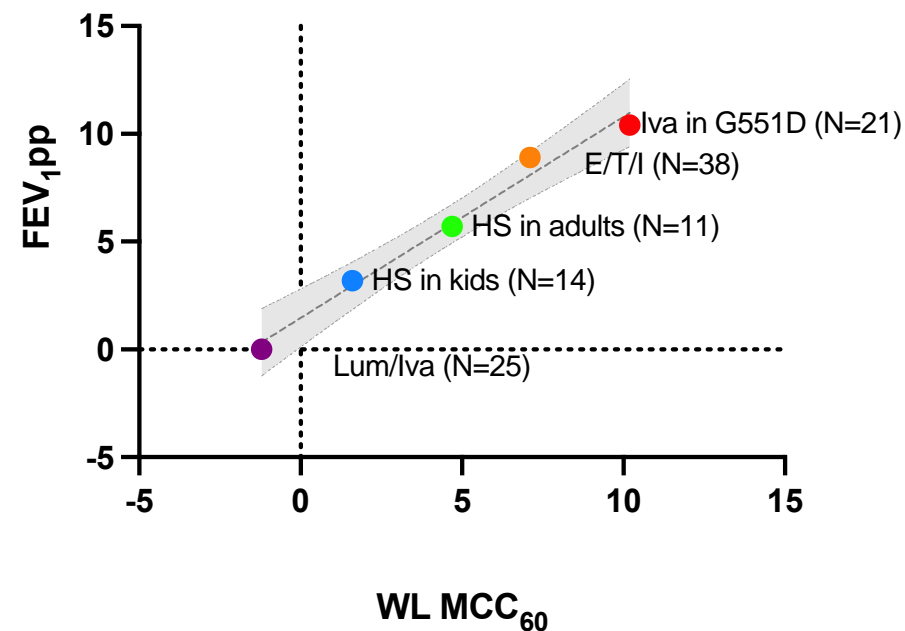
*Distinguishes PCD from healthy lung function and correlates with clinical improvement*

## Comparison of MCC in PCD patients vs. Healthy Controls



Whole lung MCC in adult PCD (n=4) vs. healthy non-smokers (n=12). PCD patients received 4 puffs of albuterol MDI w/ spacer at 60 min and performed 30 voluntary coughs between 120-150 minutes

## Absolute Change in Whole Lung MCC vs. FEV<sub>1</sub> in CF<sup>1</sup>

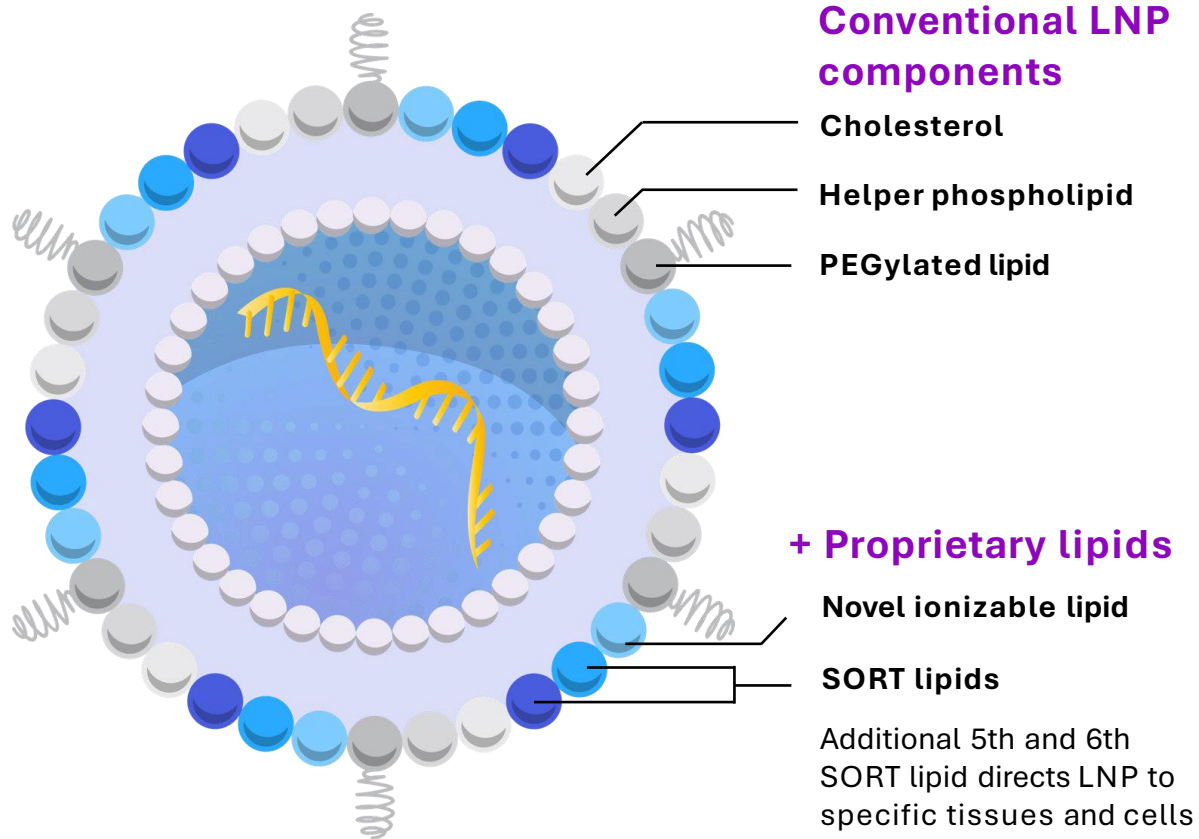


# Novel Selective Organ Targeting (SORT) Lipid Nanoparticle (LNP) Platform



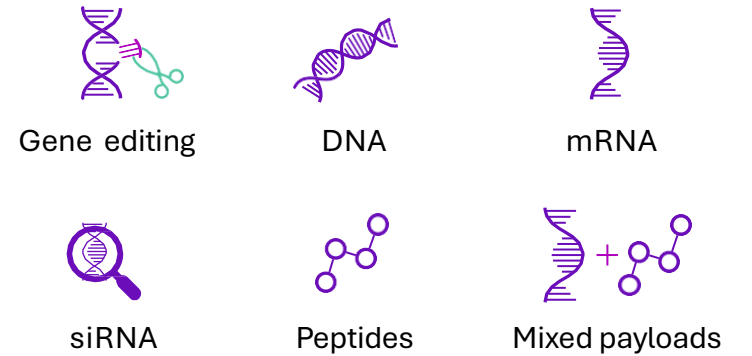
# SORT LNP platform delivers diverse genetic payloads beyond the liver

## Sort LNP architecture

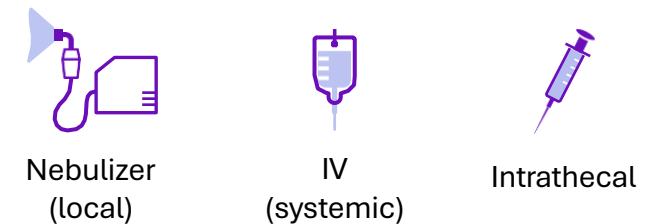


Proprietary LNP platform compatible with wide range of payloads and routes of administration

## POSSIBLE PAYLOADS



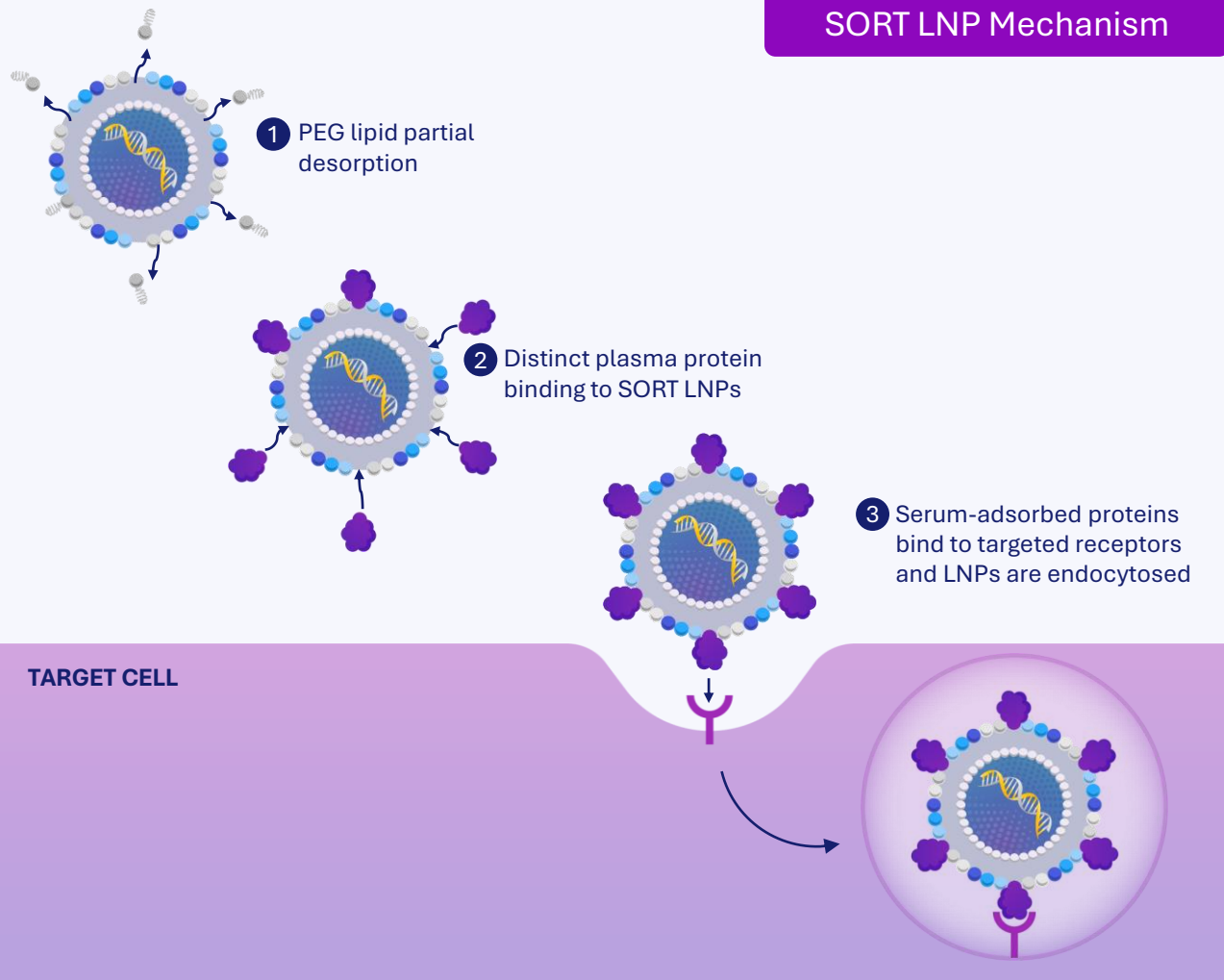
## ADMINISTRATION METHODS



# Endogenous targeting MOA enables tissue-selective and cell-tropic delivery

*SORT LNPs designed to absorb specific plasma proteins that mediate tissue-selective delivery*

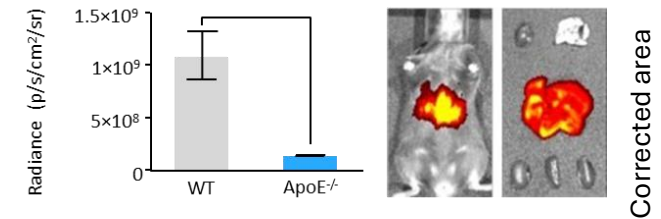
## SORT LNP Mechanism



**Extrahepatic delivery of SORT LNPs occurs via an ApoE-independent mechanism**

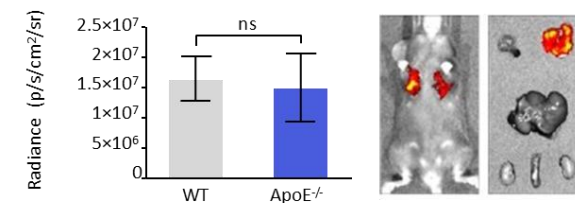
### Liver SORT LNP

**ApoE for Liver**



### Lung SORT LNP

**Vitronectin for Lung**

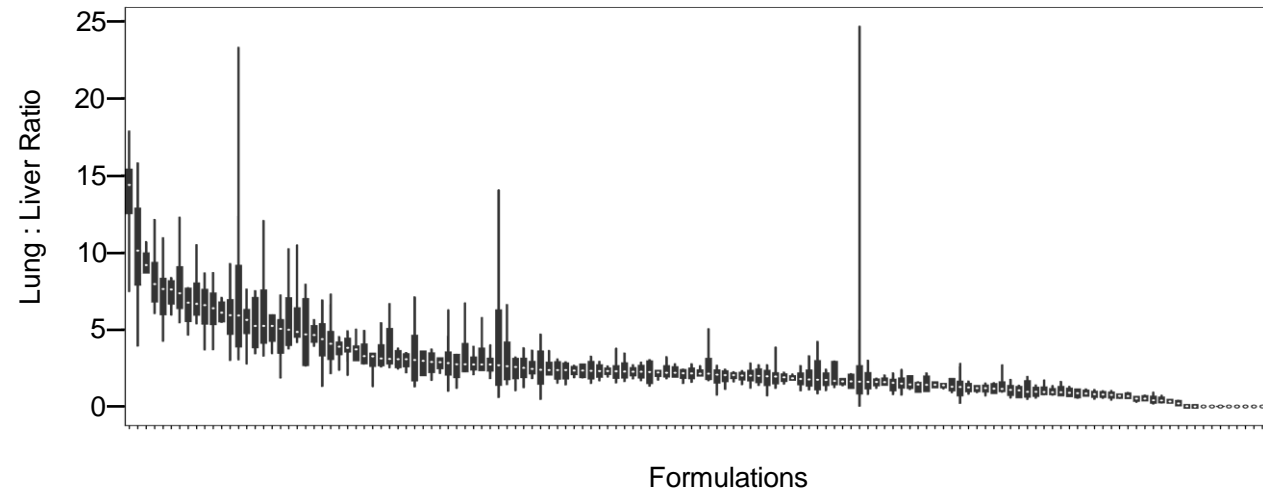




# IV SORT LNPs are optimized for extrahepatic selectivity

SORT LNPs leverage multiple routes of administration, including IV, for targeted delivery and biodistribution

## Distribution of Lung: Liver Ratios for LNPs



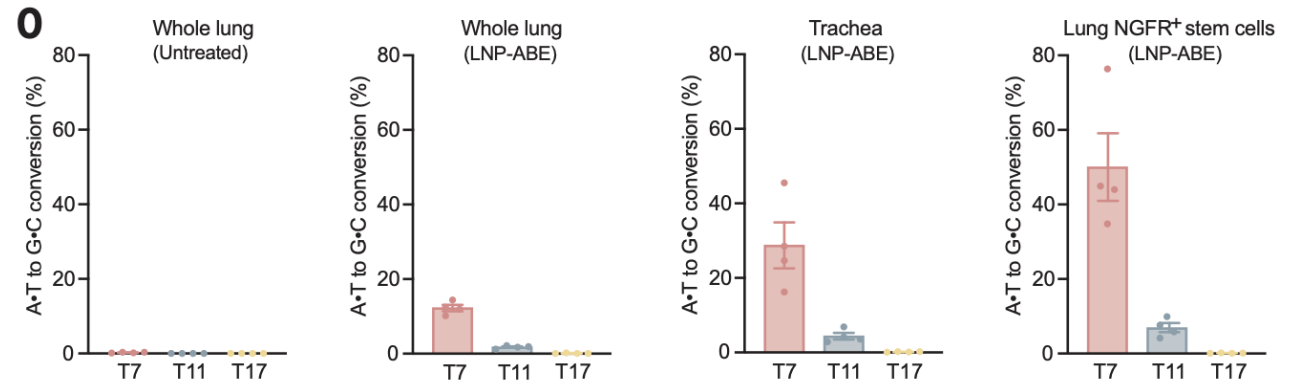
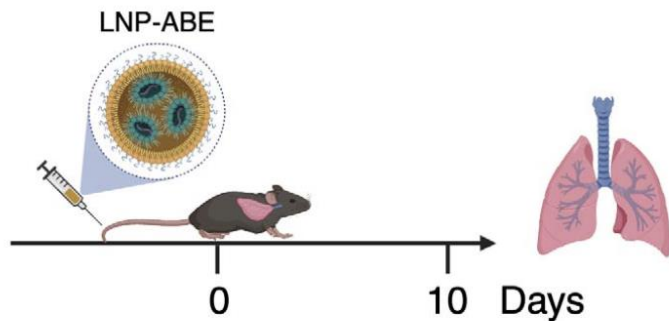
- ~200 unique IV SORT LNP formulations screened in rats
- Identified SORT LNPs with high lung expression relative to benchmark LNPs
- Leads differentiated from established benchmarks and validated via orthogonal protein readouts

# Demonstrated direct and persistent *in vivo* gene editing of mouse lung epithelial cells

Science

GENE EDITING

## In vivo editing of lung stem cells for durable gene correction in mice

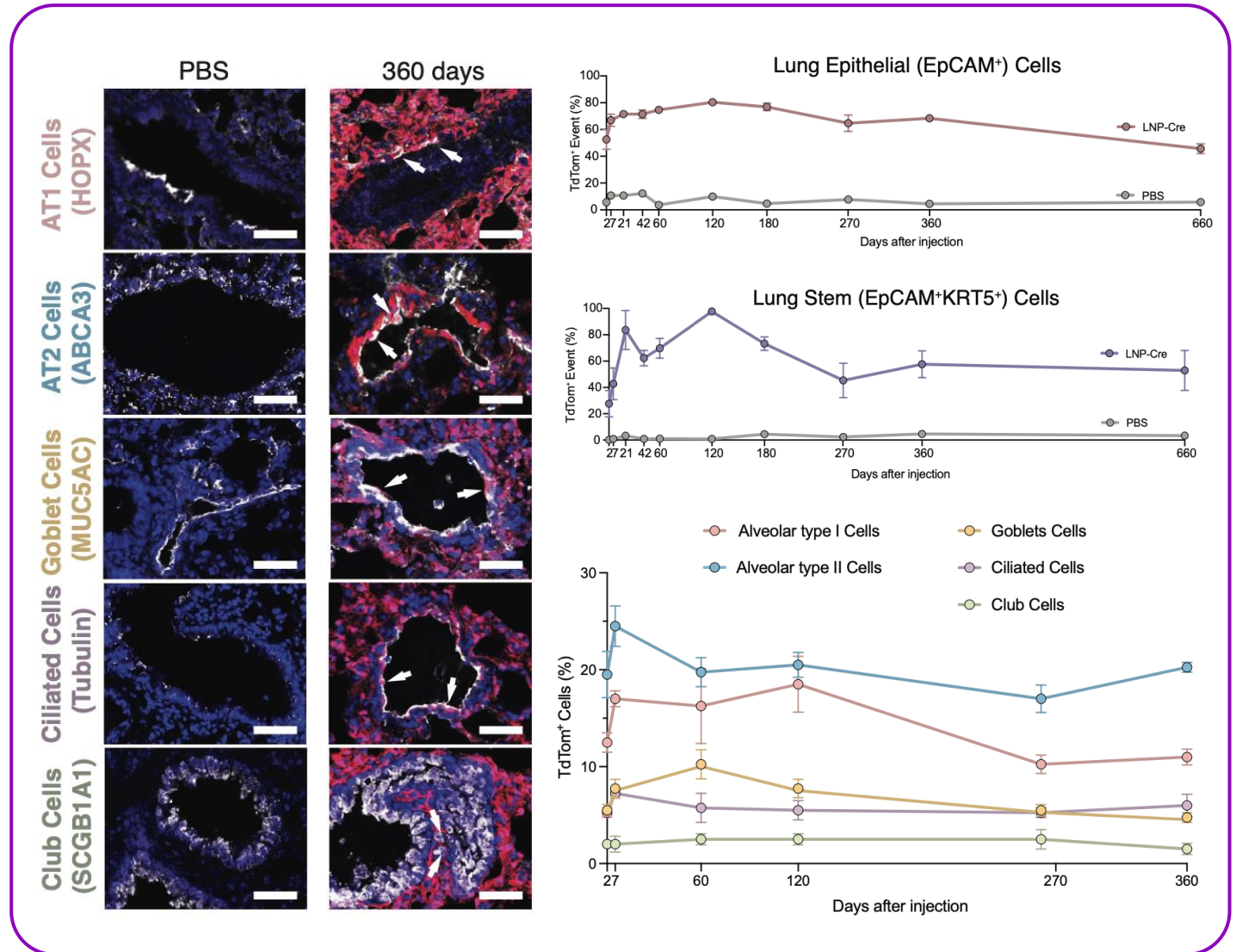


ABE Gene Correction of CFTR hR553X Mouse Lung Basal Cells After a Single Administration\*

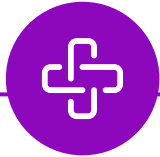
# Durable *in vivo* gene editing of mouse lung epithelial cells for ~ 2 years

## Importance of Findings

- First direct evidence of genetic edit of lung epithelial cells, including stem cells, following IV SORT LNP administration
- High editing efficiency *in vivo*, with persistence for nearly 2 years



# Significant opportunity with near-term data milestones

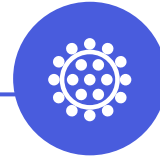


## Ph1b

### studies for first two mRNA-therapeutics programs imminent

- **Q1 2025:** Demonstrate human proof-of activity for RCT1100 and RCT2100
- **Q3 2025:** Initiate Ph2 proof-of-concept studies for RCT1100 and 2100

● → Path to registration for RCT1100 expected by **1H 2025**



## Launch next wave of in vivo genome editing programs

- Demonstrate preclinical proof-of-concept of editing for CF GC program
- CF ferret data (in 2H '25)



## Partnering

- Leverage business development to accelerate pipeline and extend reach of SORT LNP platform across novel genome and epigenome engineering payloads
- Explore program deals for RCT1100 and RCT2100 post-data to enhance and globalize market potential

**Cash runway to end of Q3 '25;** Crossover & IPO proceeds support runway through '26 & registrational readouts in PCD & CF

# Only LNP platform that provides FTO with a large and chemically diverse library

*Other platforms require stacked licenses from multiple parties*

### Library

ReCode LNPs are designed & optimized by adjusting the ionizable & SORT lipids and their relative molar ratios

**SORT**

**Ionizable cationic lipids**

### Patients

**New lipids, SORT LNPs, formulations, MOAs, therapeutics, manufacturing**

<b>150+</b> applications	<b>40+</b> issued patents	<b>30+</b> patent families	<b>300+ classes</b> novel 1 <sup>st</sup> & 2 <sup>nd</sup> gen ionizable, SORT and PEG lipids
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### WW Coverage

✓ Distinct LNPs in a crowded and litigious space	✓ WW and exclusive IP rights	✓ One license
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### Know-How

✓ Therapeutic-grade LNP manufacturing	✓ MOAs & optimization	✓ Composition identification & optimization
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NON-CONFIDENTIAL

# Corporate Overview

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September 2024

