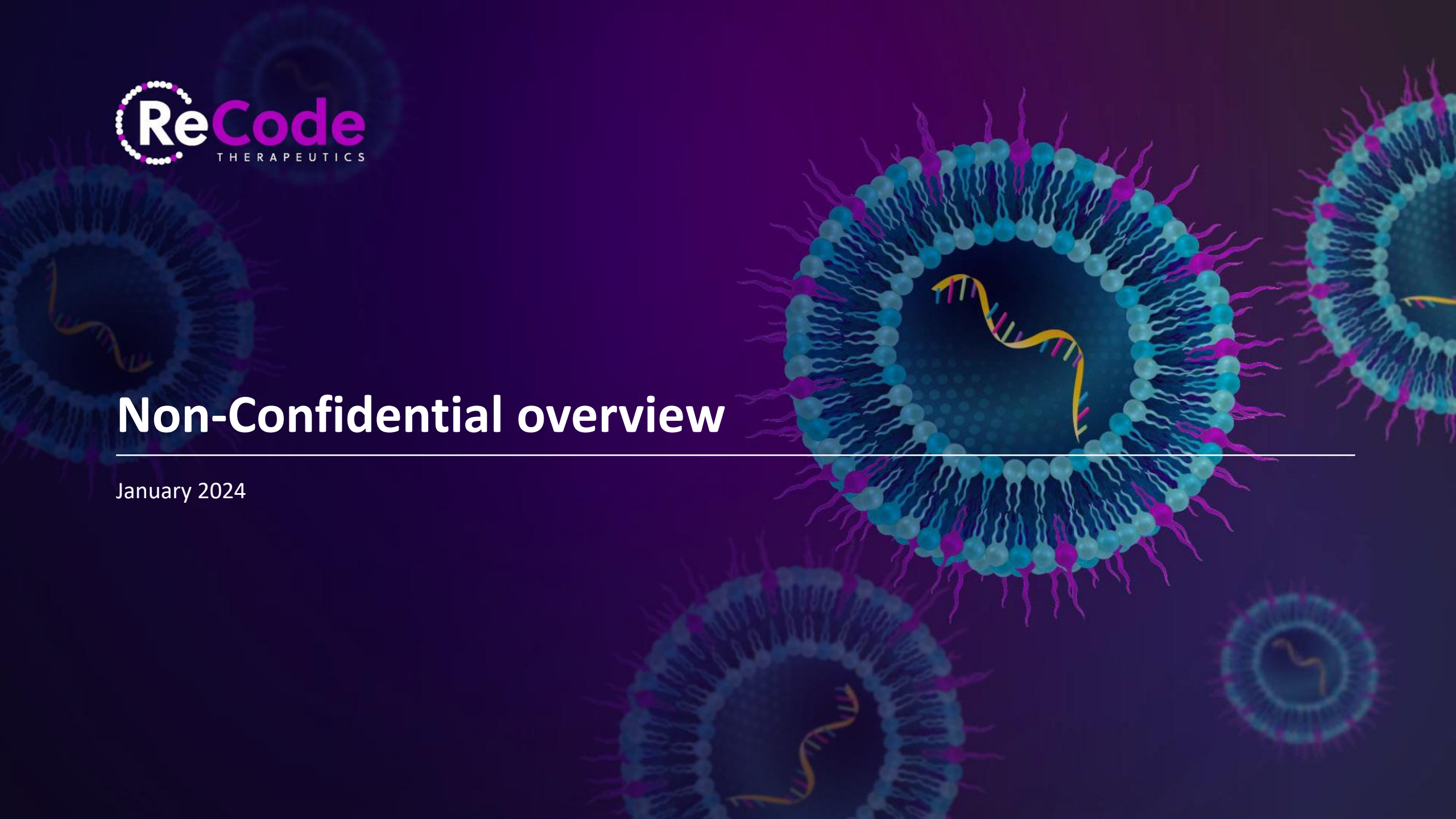




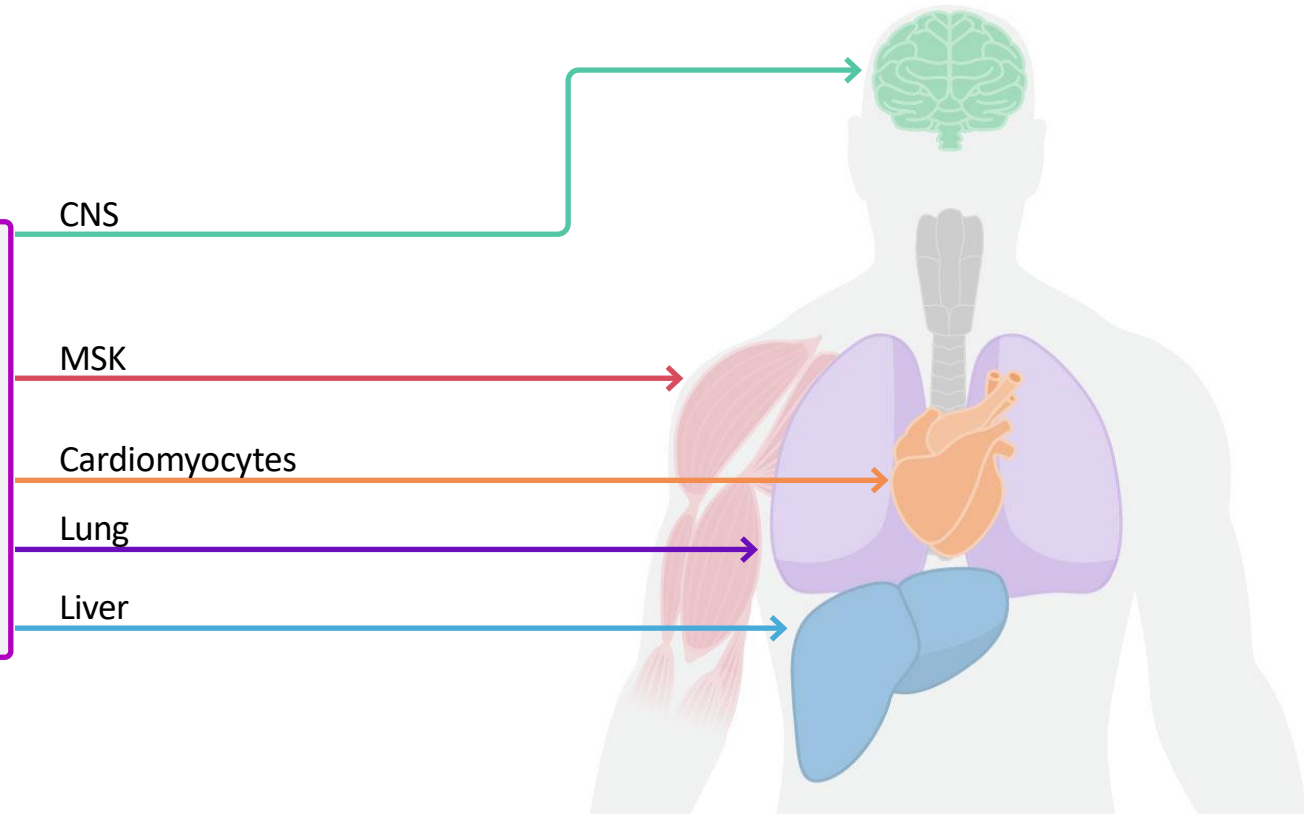
Non-Confidential overview

January 2024


















Our Mission

Powering the next wave of genetic medicines through tissue-specific delivery







Experienced team and strong investor syndicate

Team:

	<p>Shehnaaz Suliman, MD, MBA, MPhil CEO</p>	   
	<p>Jessica Couch, PhD, DABT SVP, Translational Sciences & Portfolio Strategy</p>	 
	<p>Marco Weinberg, PhD SVP, Research Innovation</p>	  
	<p>Ariel Kantor, PhD VP, Business Development and Platform Strategy</p>	 

	<p>David Lockhart, PhD President & CSO</p>	   
	<p>John Matthews, MD, PhD SVP, Clinical Development</p>	   
	<p>Erica Jefferson SVP, Corporate Affairs</p>	   

Select Board Members:

	<p>Peter Thompson OrbiMed</p>
	<p>Alan Colowick Matrix Capital</p>
	<p>Helen Kim Vida Ventures</p>
	<p>Ed Hurwitz MPM Capital</p>

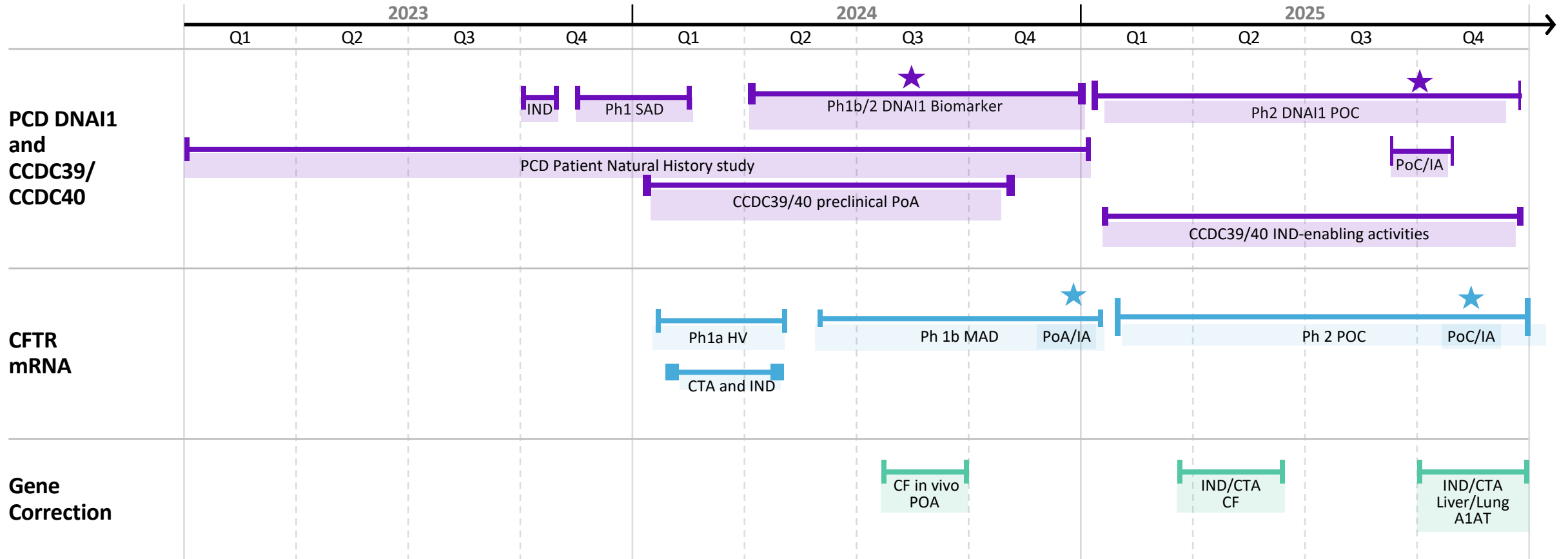
Investors:

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

Indication		Modality	Target	Delivery	Discovery	Preclinical	Phase 1/2
Lung	Primary Ciliary Dyskinesia (PCD)	RCT1100 mRNA	DNAI1	Inhaled	████████████████████	████████████████████	████████████████████
		mRNA	CCDC39 /40	Inhaled	██████████████████		
		mRNA	PCD gene 3	Inhaled	██████████████████		
	Cystic Fibrosis (CF)	RCT2100 mRNA	CFTR	Inhaled	████████████████████	████████████████████	██████████████████
		Gene correction	CFTR	Inhaled	████████████████████		
		Gene Correction	CFTR	Inhaled IV	██████████████████		
	Other Lung Indications	mRNA	Undisclosed	Inhaled IV	██████████████████		
Gene correction		Undisclosed	Inhaled IV	██████████████████			
CNS	Various	Multiple	Undisclosed	Intrathecal	██████████████████		

Cash runway to Q3 '25 supports biomarker, PoC data in PCD and PoA data in CF



\$340M Raised -- Cash runway to Q3 2025



POM = proof of mechanism, e.g., protein translation in nasal epithelial cells;
POA = proof of activity, e.g., convincing trend of clinically meaningful effect;
POC = proof of clinically meaningful effect, e.g., statistical significance on key endpoint(s);

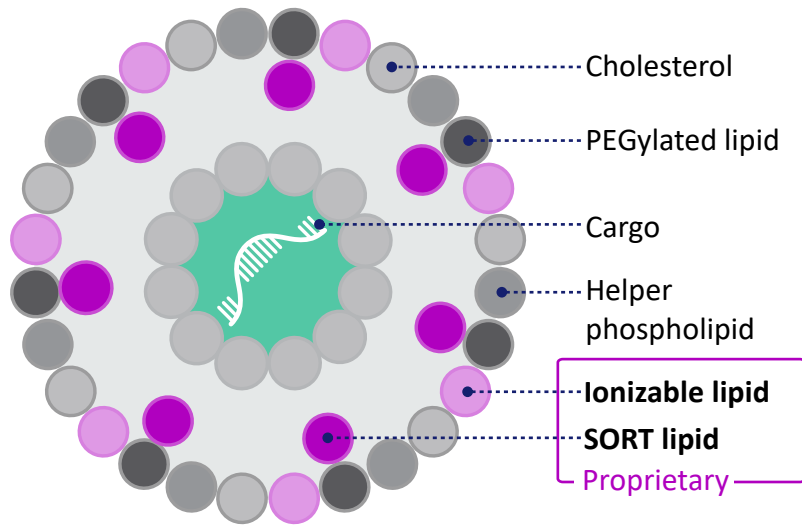
Boxes represent milestones and not actual project timelines;
IA = Interim analysis to trigger start of confirmatory study for accelerated approval;
IT = Intrathecal delivery.

SORT platform

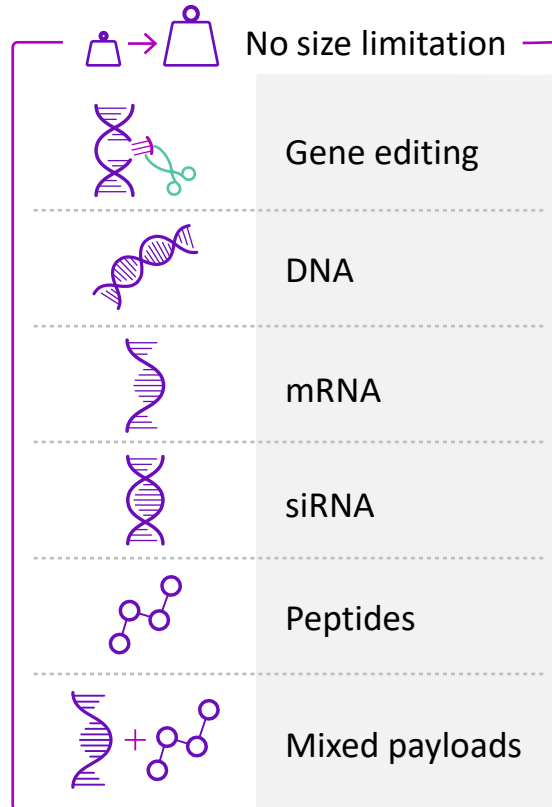


Selective organ targeting lipid nanoparticles (SORT LNP) deliver diverse genetic payloads beyond the liver

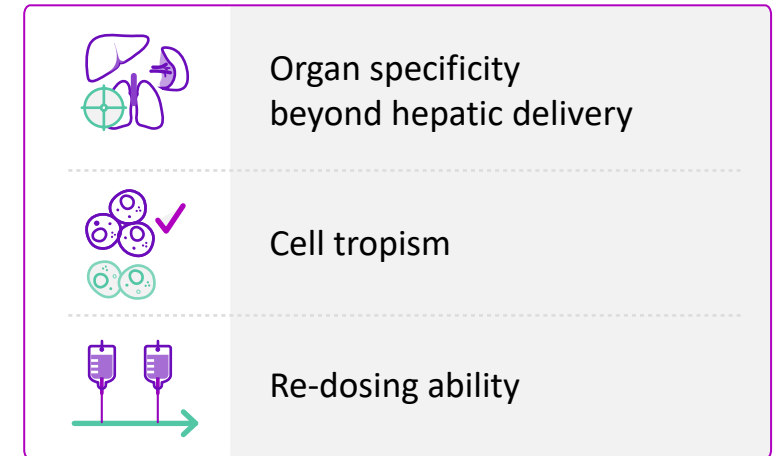
Sort LNP architecture



Possible payloads



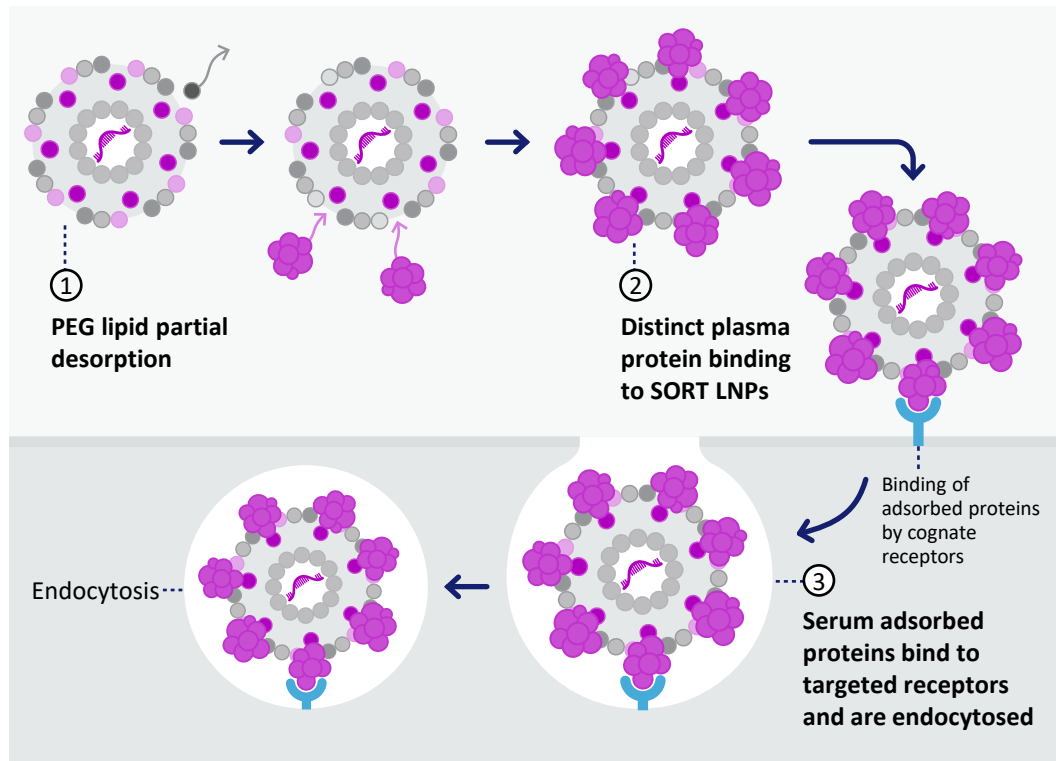
SORT LNPs advantages



Administration methods:



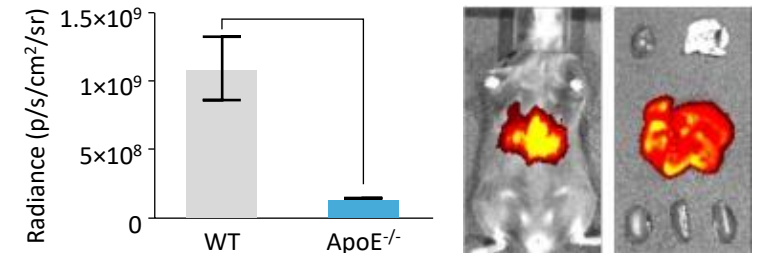
SORT LNPs use an endogenous targeting mechanism of action through adsorption of specific plasma proteins



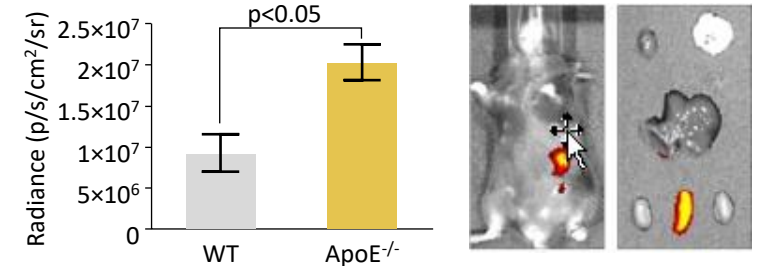
Extra-hepatic delivery of SORT LNPs occurs via an ApoE-independent mechanism

Binding of plasma proteins targets SORT LNPs to specific organs

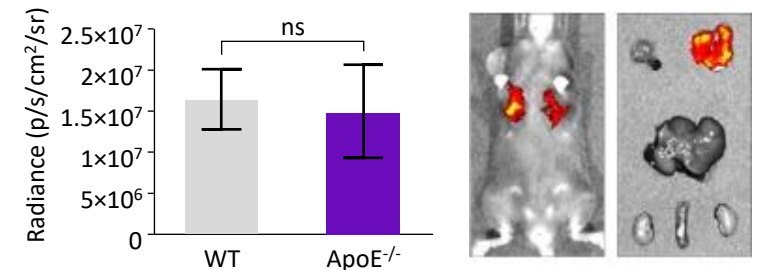
ApoE for Liver



B2 Glycoprotein I for Spleen

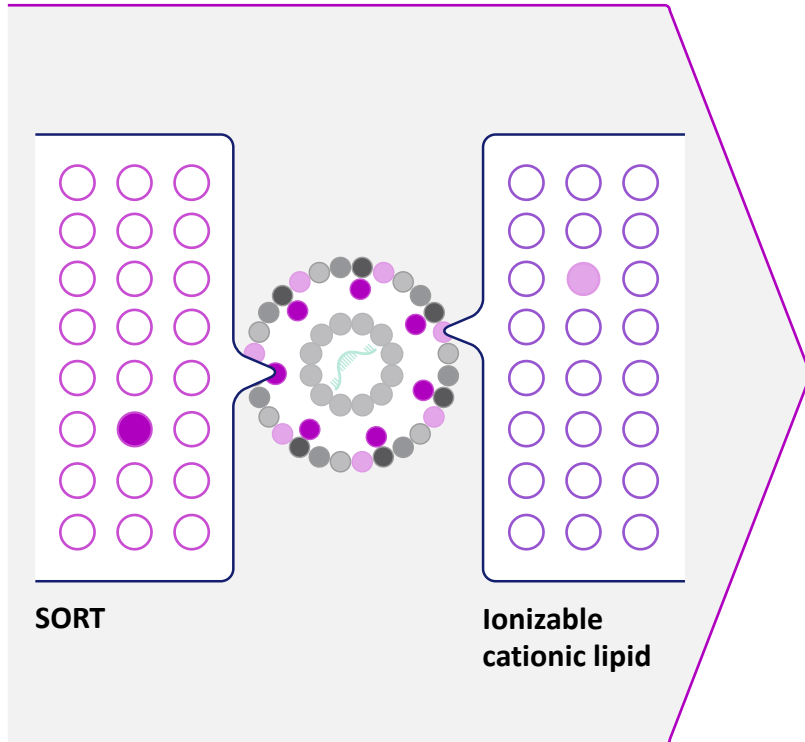


Vitronectin for Lung



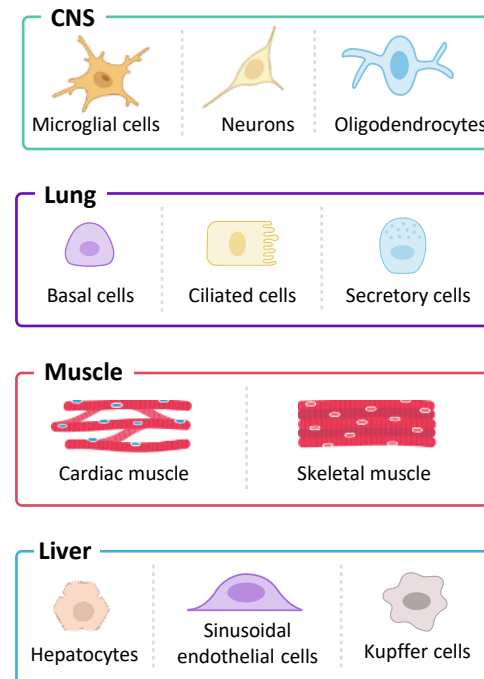
SORT platform

Library of > 5,000 SORT LNPs



Our LNPs are designed by tweaking the ionizable + SORT lipids and their relative molar ratios.

Selective organ targeting beyond the liver



Our endogenous targeting mechanism allows SORT LNPs to reach multiple organs, specific tissues and cells.

Patents

New lipids, SORT LNPs, Therapeutics

150+ applications

40+ issued patents

30+ patent families

2000+ novel 1st gen dendrimers/ionizable lipids

WW Coverage

Distinct LNPs in a crowded and litigious space

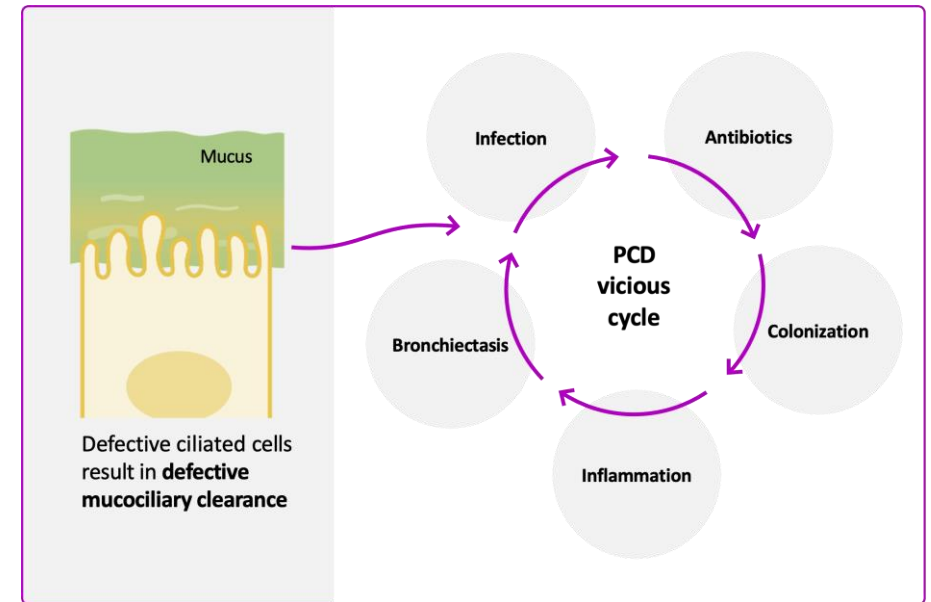
WW and exclusive IP rights

Primary Ciliary Dyskinesia



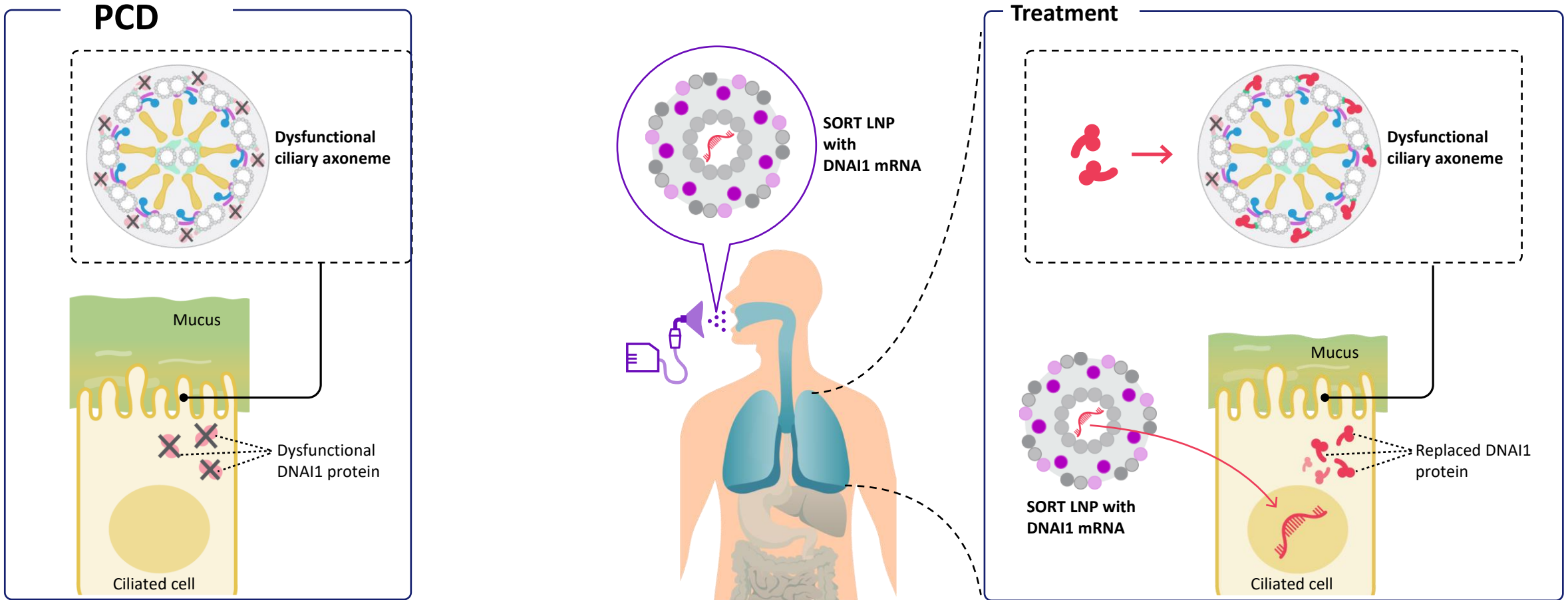
Primary Ciliary Dyskinesia (PCD) is orphan respiratory disease with no treatment

- PCD is an orphan respiratory disease caused by defective mucociliary clearance resulting in chronic recurrent respiratory infections and lung function decline
- Estimated prevalence across mutations is >100,000 in US, EU5¹
- Mutations in genes result in dysfunctional cilia (hair-like structures that line the upper and lower airways)
- Chronic respiratory infections results in permanent lung damage (bronchiectasis) and diminished lung function
- No approved treatments

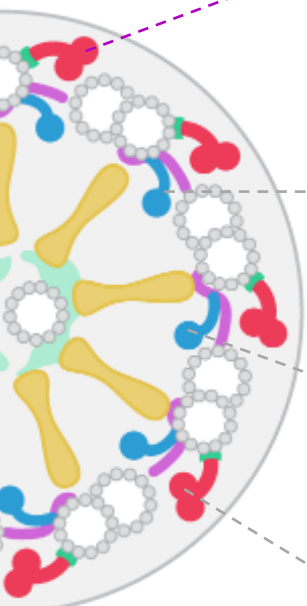


RCT1100 restores ciliary activity and repairs defective mucociliary clearance

RCT1100



PCD franchise is substantial with no competition



	Patients, US & EU5	Estimated sales
<p>RCT1100</p> <p>~7% Outer dynein arm defects DNAI1</p>	~10K	~\$470M
<p>~7% Inner dynein/MTD defects CCDC39</p>	~7K	~\$330M
<p>~3-4% Inner dynein/MTD defects CCDC40</p>	~3-4K	~\$200M
<p>~20% Outer dynein arm defects DNAH5</p>	~20K	~\$900M

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

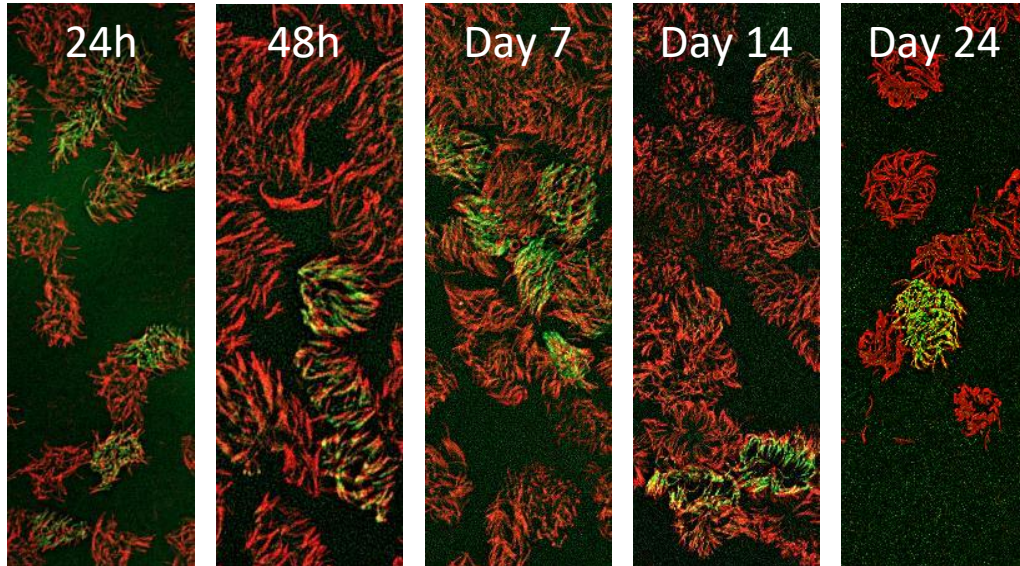
>100,000
US, UK and EU5 prevalence

\$1B+
market potential for most
prevalent genes

In vitro data demonstrate restoration of ciliary function in human bronchial epithelia cell assay

RCT1100

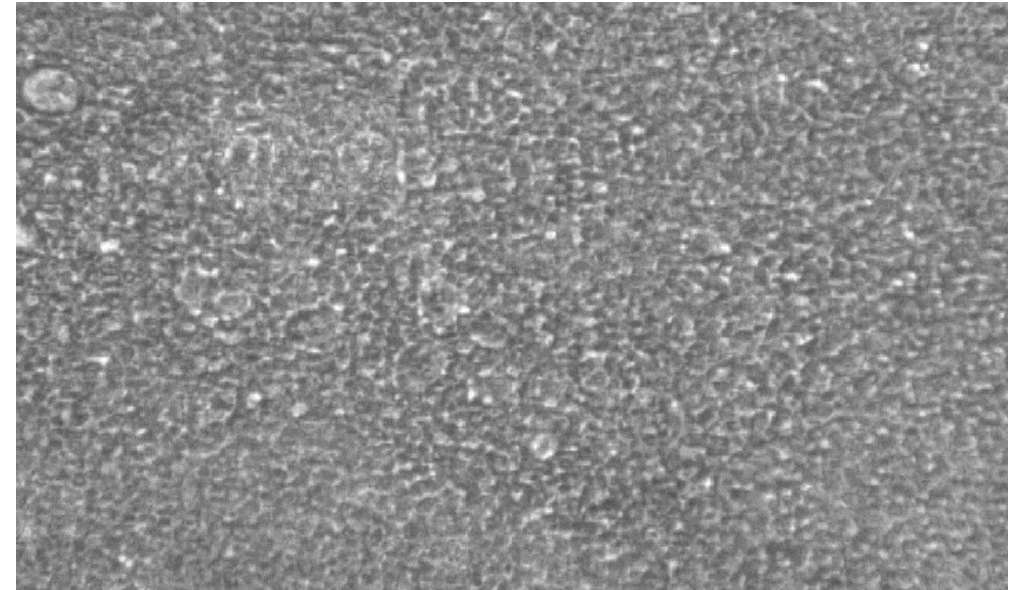
Structural incorporation



Legend: Acetylated α -tubulin (Cilia), DNAI1-HA, DNAI1-HA Colocalization with Cilia

Integration of DNAI1-HA protein into ciliary axonemes seen within 24 h post-dose with durable expression up to 24 days after a single administration

Functional rescue

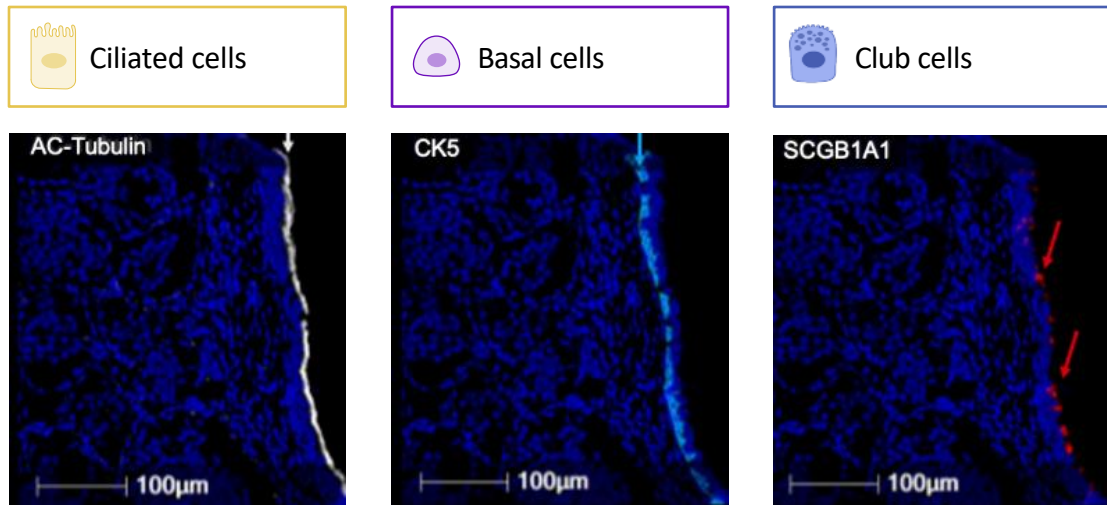


Video showing ciliary rescue - note the rescue across the whole field (appears as shimmering) , the swirl in the top left is from coordinated movement of a patch of dried mucous

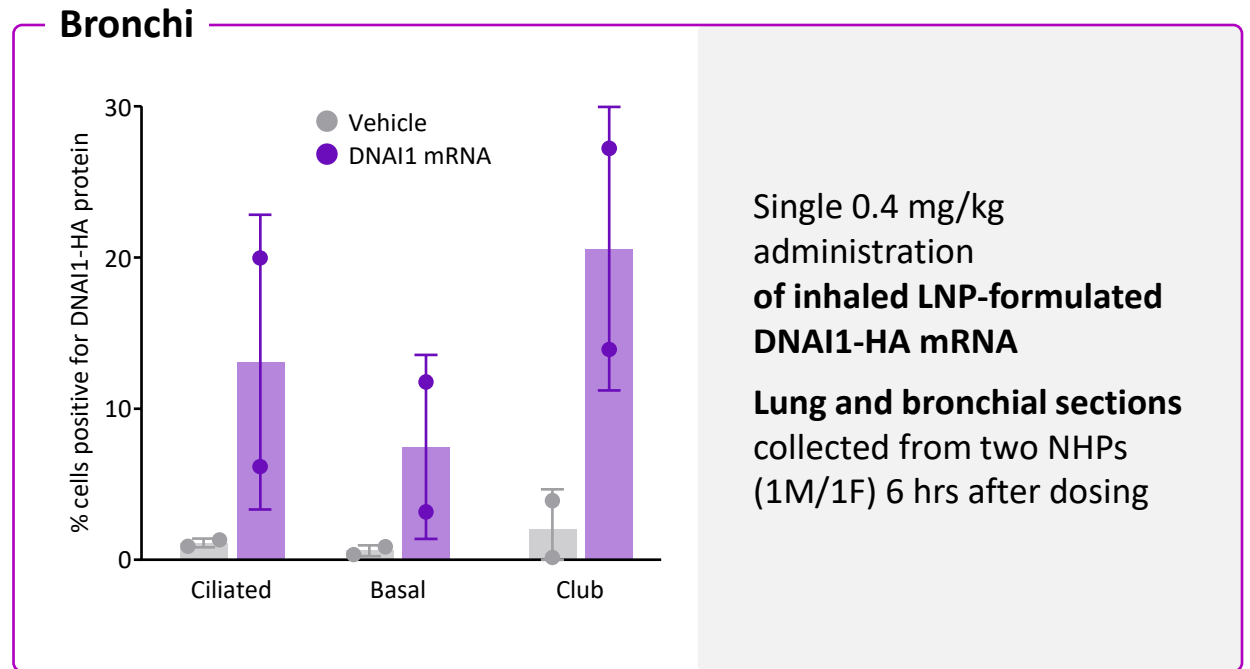
Aerosolized delivery of *DNAI1*-encapsulated SORT LNPs demonstrates ciliary function rescue in human bronchial epithelial cells [video]

In vivo data demonstrate expression of DNAI1 protein in target cells in NHPs

RCT1100

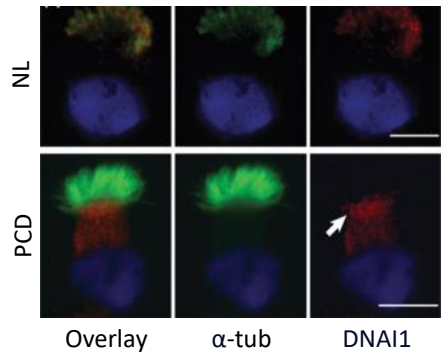


Multiplex immunofluorescence panel of **cell-type specific markers** for detection of newly-made protein in NHP target airway cells



PCD clinical biomarkers have read-through to proof-of-concept

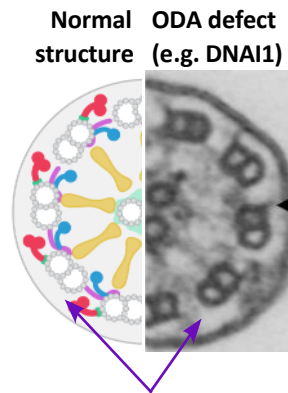
Phase 1c PCD patient functional biomarker study



Immunofluorescence (IF)

showing protein expression in disease-relevant cells

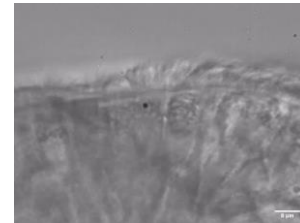
PLoS One 8 (2013) e59436



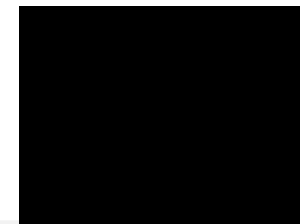
Transmission electron microscopy (TEM)

showing rescue of the ciliary axoneme structure

Clin Chest Med 43 (2022) 127–140



Healthy Normal; Cilia beat at approximately 10 Hz

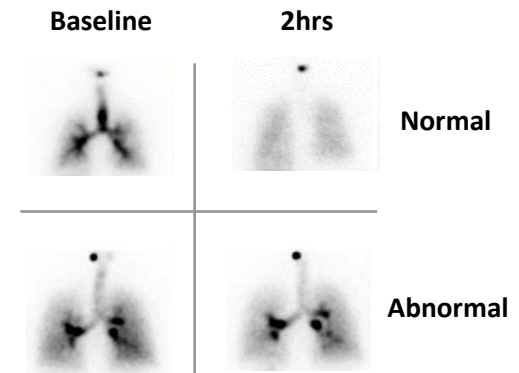


DNAI1; (This is a video, the cilia are not moving)

High-speed video microscopy

showing rescue of ciliary beat frequency and beat pattern

Clin Chest Med 43 (2022) 127–140



Mucociliary clearance (MCC)

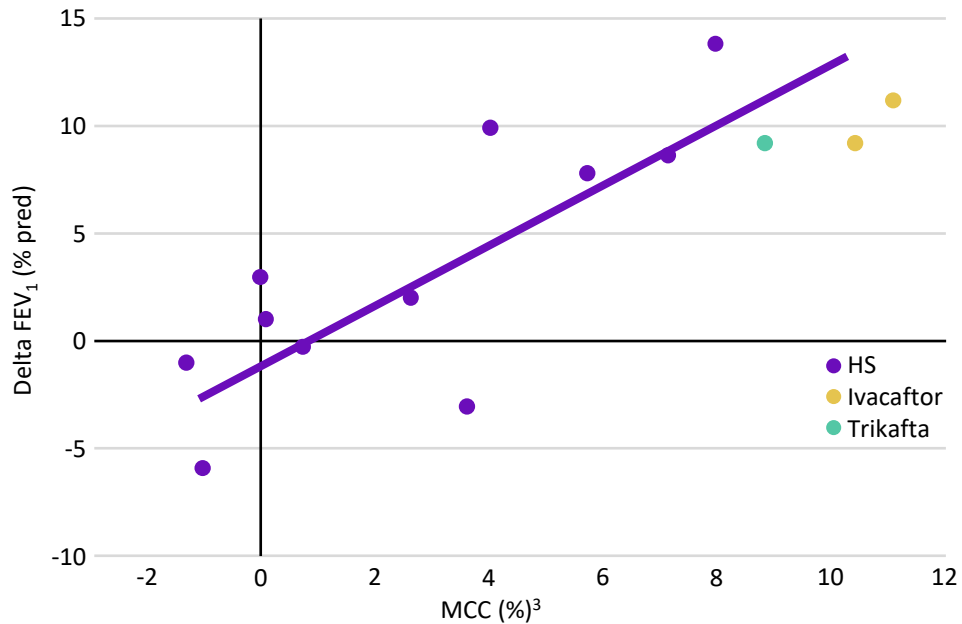
Inhaled radio-aerosol showing whole lung mucociliary clearance

Marthin et al. 2023

Patient biomarker data anticipated Q3 '24

The correlation between MCC and FEV₁ has been independently validated

Relationship between MCC and FEV₁ in patients after HS treatment^{1,2}, Ivacaftor⁴, or Trikafta⁵

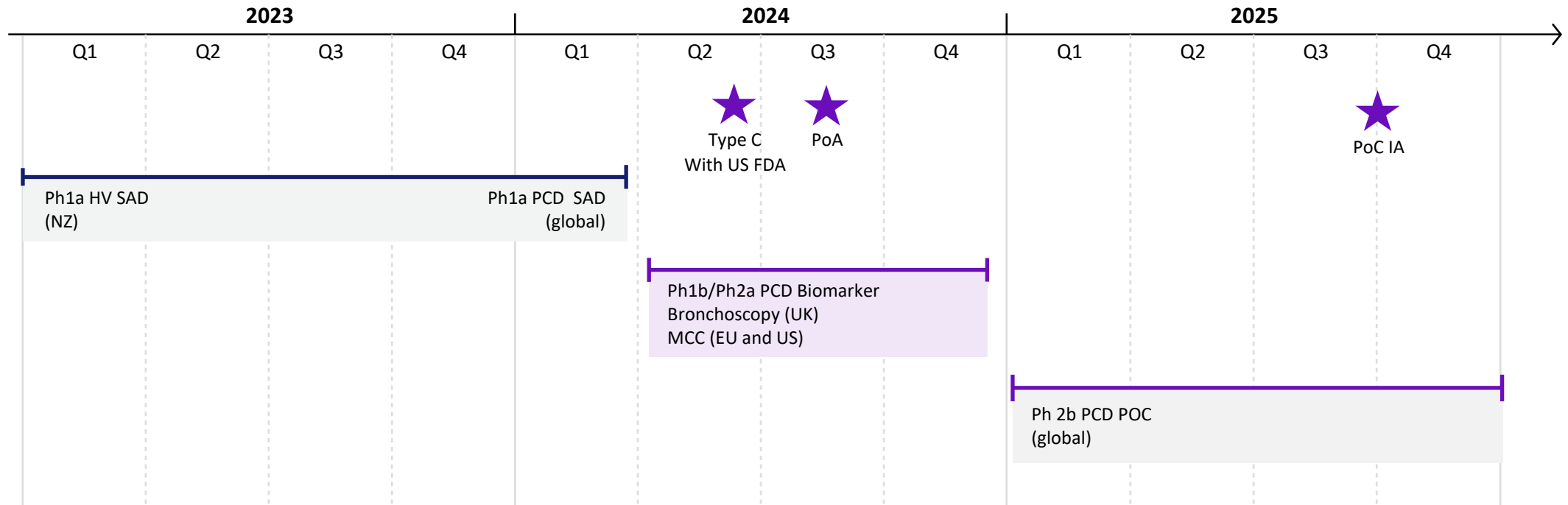


...the correlation between changes in AveClr90 [MCC] and FEV₁ revealed a highly significant relationship in subjects who were randomized to HS (R²=0.67, p = 0.002), suggesting that sustained improvement in MCC might predict improvements in lung function¹

...a significant (P < 0.005) relationship between the FEV₁ and MCC changes was observed... the change in whole lung and central lung MCC was significantly related to the observed change in FEV₁⁴

PCD programs have path to potential accelerated approval

RCT1100
DNAI1




Cystic Fibrosis



Cystic Fibrosis lead program targets nonsense mutation carriers

No available treatment

Class 1 **10%**



Lack of protein production

G542X, R553X, W1282X*

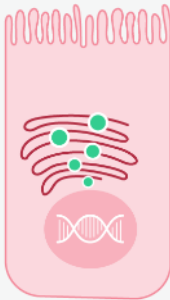
>13K **31**

patients not amenable to current therapies¹ years life expectancy

¹Includes patients not addressable by current therapies & poor responders to CFTR modulators

Eligible for CFTR modulator therapies


Class 2



Protein processing mutations

ΔF508, N1303K, G85E*


Class 3



Gating mutations

G551D, V520F, S549R*

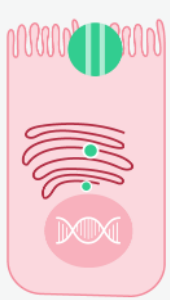
Class 4



Conduction mutations

R117H, R334W, S1235R*

Class 5



Insufficient protein mutations

A455E, 2657+5G>A*

~130,000 **53 years**

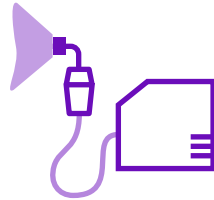
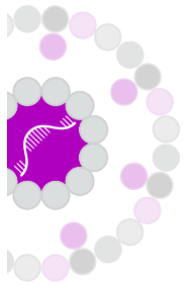
patients worldwide life expectancy

* Examples of class I – V mutations

SORT LNP technology addresses CF patients through mRNA and gene correction

RCT2100

CFTR mRNA replacement



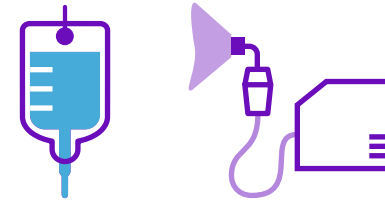
Cargo:
mRNA optimized
for stability, efficiency
and reduced
immune activation

Formulation:
Inhaled Lung SORT

8K – 13K
Patients not amenable
to current therapies

~1K
CF patients unable to tolerate
CFTR modulators


CFTR gene correction



Cargo:
All-in-one
HDR-independent
gene correction
machinery

Formulation:
IV and inhaled
Lung SORT

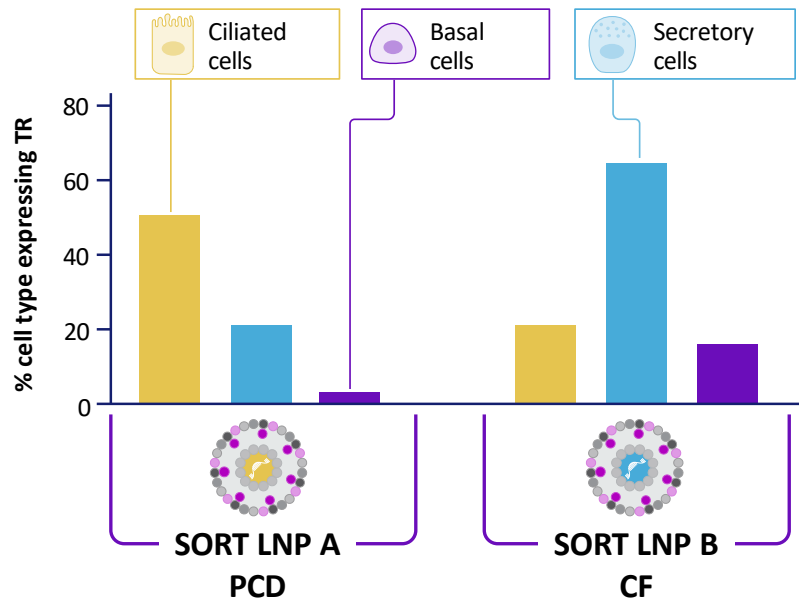
~100K
All adults with CF

 Delivery to airway
basal cells in NHPs (IV)

Rational LNP design and optimization resulted in best-in-class SORT LNP CF development candidate RCT2100

Tuned cell tropism

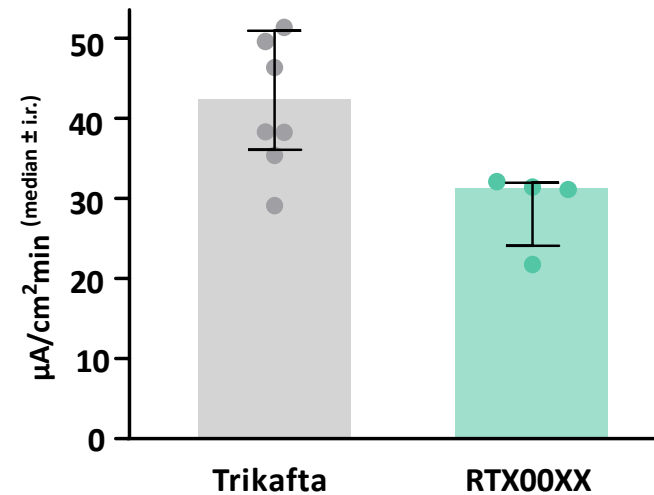
human bronchial epithelial cells



SORT LNPs from PCD program were optimized for delivery to ionocytes (not shown) and secretory cells.

Next generation formulation optimized device performance, manufacturability & potency

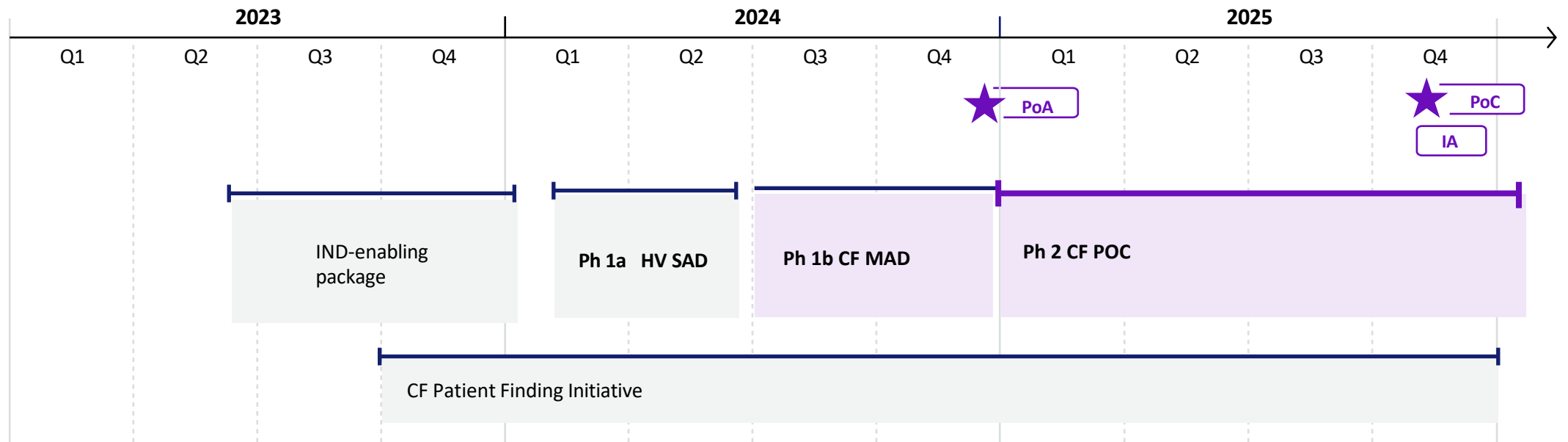
CF F508del/F508del hBEs



Development of a new class of SORT LNPs significantly improved potency and LNP stability.

RCT2100 has path to potential accelerated approval

RCT2100



SORT LNPs are compatible with diverse gene editors

Enabling the establishment of a genome engineering tool kit

Identify Indications Based on Technical Feasibility and Partner Interest



- Cystic fibrosis
- Alpha-1 antitrypsin deficiency



- Neurodegenerative diseases
- Neurodevelopmental diseases



- Neuromuscular diseases
- Cardiomyopathies

Choose Optimal Gene Editor

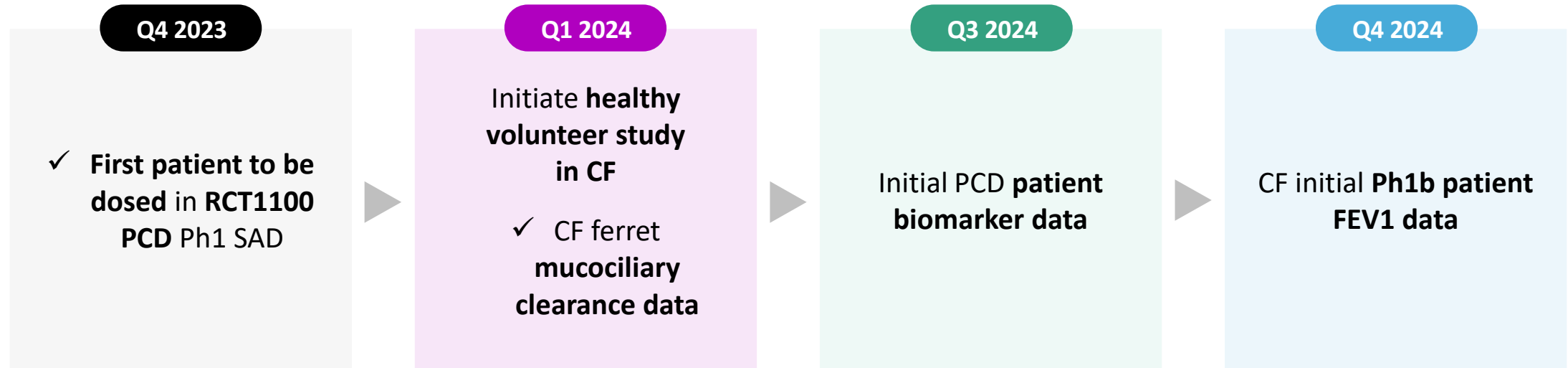
Target effector profile

- Effector needed (e.g., excision, replacement, knockdown)
- Effector characteristics (e.g., PAM, # of gRNAs, etc.)
- Length of DNA / RNA impact
- Target tissue / cell type (i.e., dividing, nondividing)
- Nucleic acid format

Potential ReCode Genome Engineering Tool Kit

- DNA nucleases
- RNA nucleases
- DNA base editors
- RNA editors
- RT editors
- CRISPR transposases / retrotransposases
- CRISPR epigenome editing modifiers

Upcoming Portfolio Milestones



Highlights



Leading tissue-specific LNP delivery platform



Near-term PoA in PCD and CF



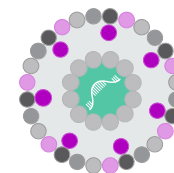
Well capitalized with runway to Q3 '25



Experienced leadership team



Deal upside and platform expansion



- CNS
- Skeletal muscle
- Cardiomyocytes



Non-Confidential overview

January 2024

