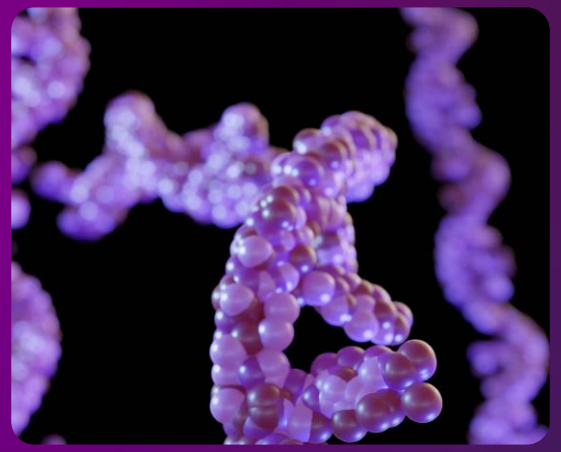
ReCode THERAPEUTICS

Corporate Overview

August 2024



Powering genetic medicines through tissue-specific delivery

Clinical Programs

- **First-in-class inhaled mRNA treatment** for primary ciliary dyskinesia (PCD)
- **Best-in-class inhaled mRNA treatment** for cystic fibrosis (CF)

Research

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

Partnering

- **Discovery research collaborations** across lung, liver, CNS
- **Tech synergy - delivering diverse genetic cargoes** to demonstrate tissue- and cell-selective genome engineering
- **Program deals** for PCD and CF

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Experienced team and strong investor syndicate

Team

Shehnaaz Suliman, MD, MBA, MPhil
CEO

alector · Roche · Genentech · GILEAD

David Lockhart, PhD
President and CSO

TranscriptTx · Amicus Therapeutics · ambit · Affymetrix

John Matthews, MD, PhD
CMO

23andMe · aimmune · Genentech · GSK

Marco Weinberg, PhD
SVP, Head of Research

AskBio · CSL · VERTEX

Jessica Couch, PhD, DABT
SVP, Early Development

genzyme · Genentech

Ariel Kantor, PhD
SVP, Business & Corporate Development

OXFORD SCIENCE ENTERPRISES · EVERCORE

Erica Jefferson
SVP, Corporate Affairs

FDA · alector · Genentech · pharmacyclics

Vladimir Kharitonov, PhD
SVP, CMC

PACIRA · Skyepharma

Select Board Members

Dean Mitchell
Board Chairman

Peter Thompson
OrbiMed

Alan Colowick
Matrix Capital

Oleg Nodelman
EcoR1

Helen Kim
Vida Ventures

Investors

OrbiMed · AyurMaya Capital Management · EcoR1 Capital · leaps · Pfizer · Hunt Investment Group · Bioluminescence Ventures

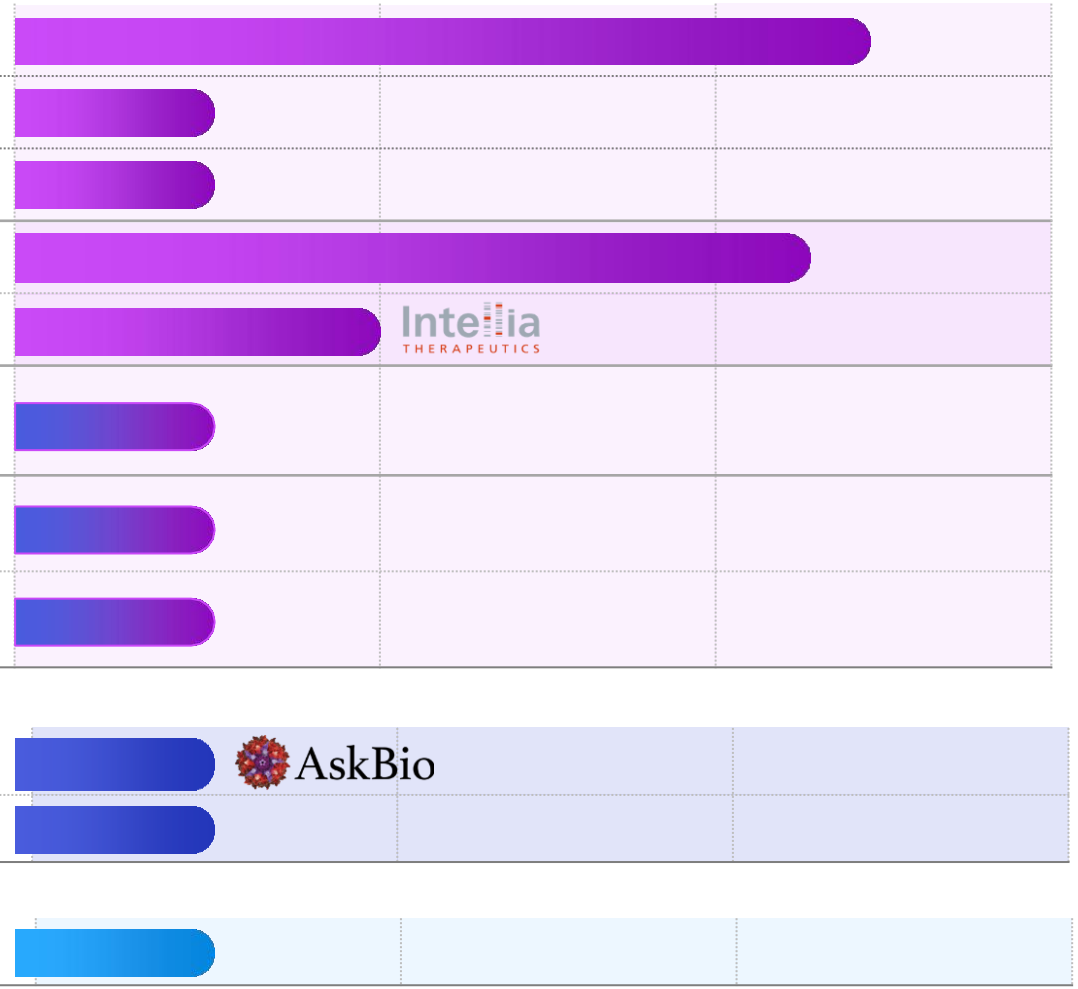
MPM · Tekla Capital Management LLC · Cystic Fibrosis Foundation · VIDA ventures · Osage University Partners · Amgen · sanofi · Colt Ventures

$370M Raised

ReCode Therapeutics

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

Respiratory Indications	Candidate	Modality	Target	Delivery
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
Other lung indications		Multiple	Undisclosed	Inhaled IV
Other		mRNA	Undisclosed	Inhaled IV
		Multiple	Undisclosed	Inhaled IV
Liver Indications				
Various		Multiple	Undisclosed	IV
		Multiple	Undisclosed	IV
CNS Indications				
Various		Multiple	Undisclosed	Intrathecal



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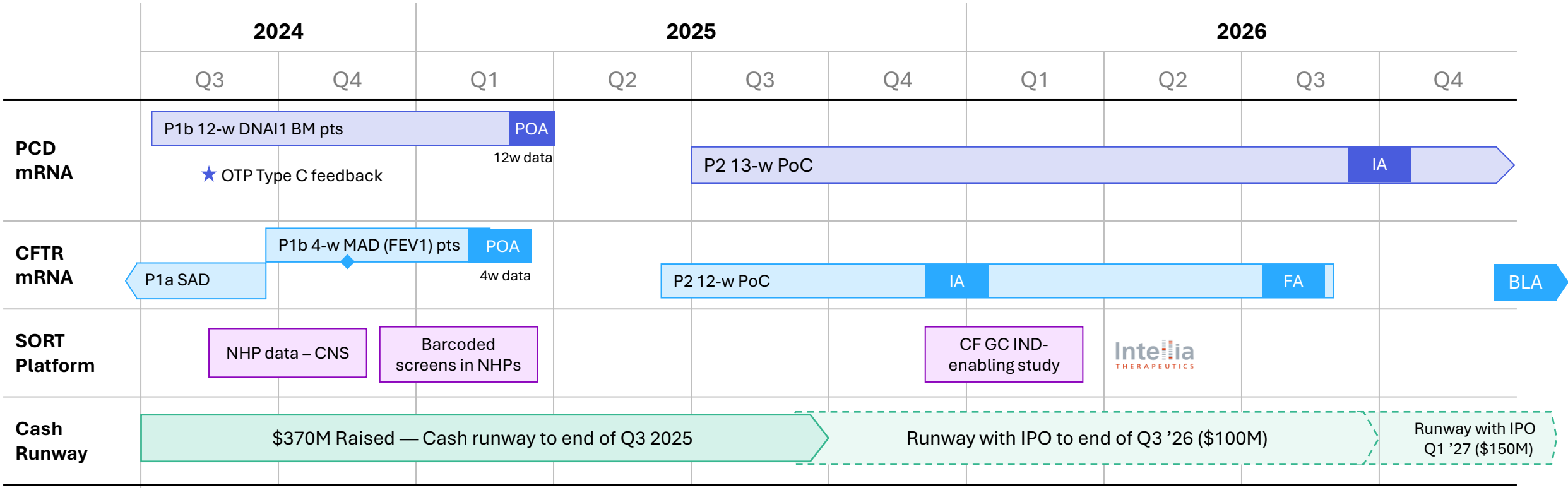
Significant opportunity with near-term milestones and cash through end of Q3 '25



Financing and key value-creating milestones

$50M series C/Crossover

- PCD and CF mRNA clinical POA
- Platform NHP data

$100-$150M IPO

- CF mRNA P2 IA
- CF mRNA P2 PoC
- PCD P2 IA

Abbreviations: BLA (application for accelerated marketing approval), DC (development candidate), IA (interim analysis to trigger start of confirmatory study for accelerated approval), FA (full analysis), GC (gene correction), MAD (multiple ascending dose), NHP (non-human primate), POA (proof of activity, e.g., convincing trend of clinically meaningful effect), POM (proof of mechanism, e.g., editing of human bronchial epithelial cells), SAD (single ascending dose)

2024 Progress

CF and PCD Program updates

- **Cleared INDs** and ex-US regulatory filings for CF and PCD
- **>100 Healthy volunteers dosed** across both indications
- **PCD Ph1 SAD in patients** initiated
- **Therapeutic dose ranges established for PCD biomarker and CF Ph1b patient studies**

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

Financing/Runway update

- Completed $75M Series B extension; **Cash runway through Q3 '25**

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Cystic Fibrosis (CF): RCT2100

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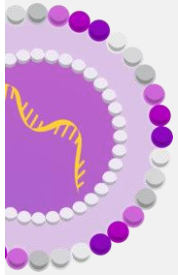
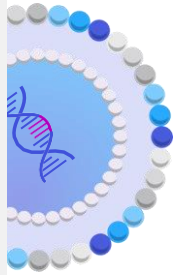
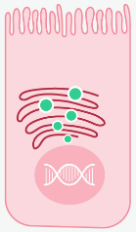
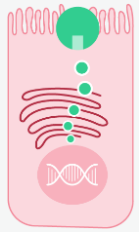
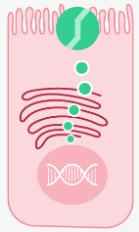
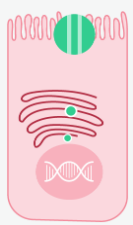
Two different treatment approaches to address CF patient needs

	CFTR mRNA replacement	CFTR gene correction
Cargo	 mRNA optimized for stability, translation efficiency and reduced immune activation	 All-in-one HDR-independent gene correction machinery
Administration	Inhaled SORT LNP	Inhaled SORT LNP
Target	Airway epithelial cells (secretory and ionocytes)	Airway basal (stem) cells
Population	**~13K** patients not eligible for or unable to tolerate CFTR modulators	**~100K** All adults with CF

Immediate focus on the 10%+ of CF patients with no treatment

For ~130,000 patients worldwide, the following classes of mutations are eligible for CFTR modulators:

Class 2	Class 3	Class 4	Class 5
			
Protein processing mutations	Gating Mutations	Conduction mutations	Insufficient protein mutations
ΔF508, N1303K, G85E*	G551D, V520F, S549R*	R117H, R334W, S1235R*	A455E, 2657+5G>A*

53 years life expectancy

For the ~13K patients with nonsense mutations:

Class1

Lack of protein production

G542X, R553X, W1282X*

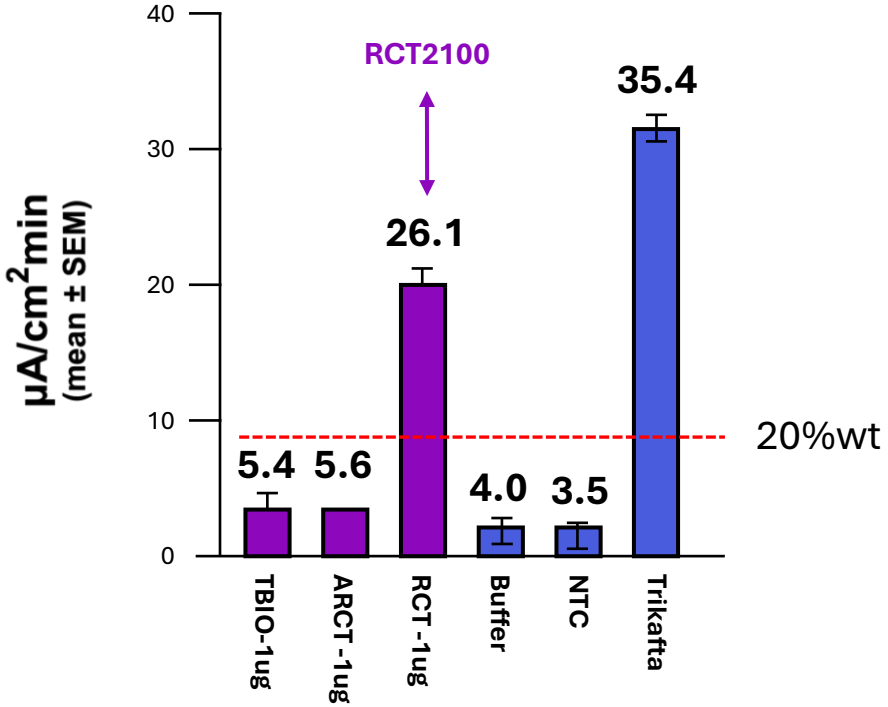
- **>13K patients not amenable to current therapies,** including patients not addressable by current therapies & poor responders to CFTR modulators.
- **>$1B commercial opportunity**

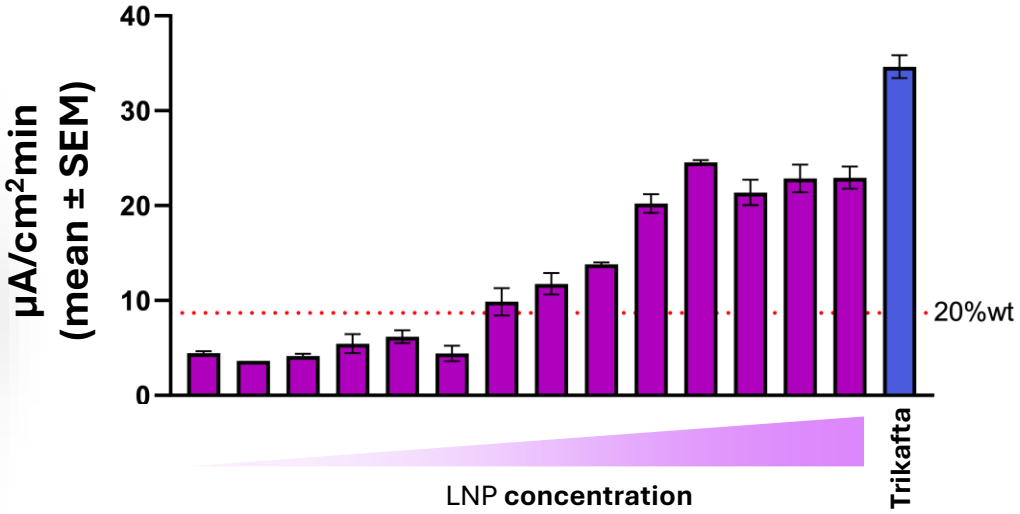
***31 years** life expectancy

1. Cystic Fibrosis Foundation

*Examples of class I – V mutations
*2022 CFF Patient Registry Annual Report, Hill et. al. Journal of Cystic Fibrosis 21 (2022)

RCT2100 restores CFTR function in F508del/F508del hBEs with higher potency compared to competitor formulations





RCT2100 Efficacy ~ 75% Trikafta

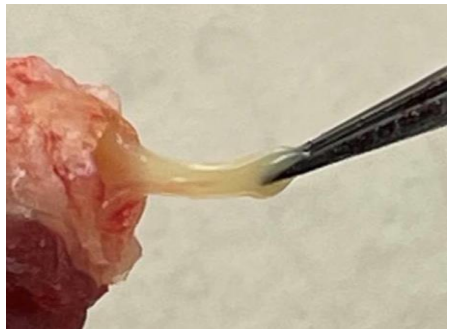
RCT2100 contains optimized mRNA that encodes the full-length CFTR protein

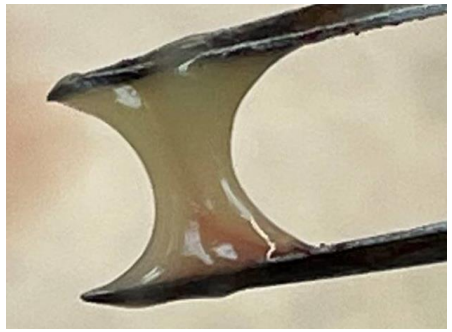
RCT2100 shows significant potency and efficacy in patient-derived fully differentiated CF hBEs in the presence of mucus via apical delivery

RCT2100 efficiently delivers to tracheal epithelium of CF Ferrets and cuts through mucus

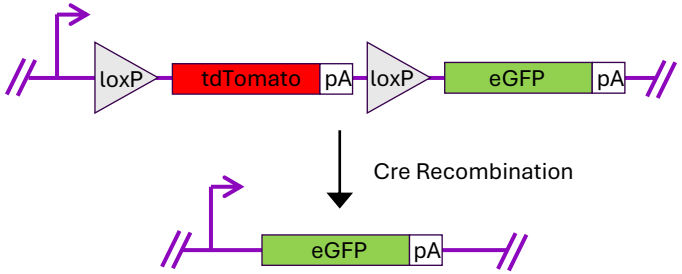
Grade 1 disease severity

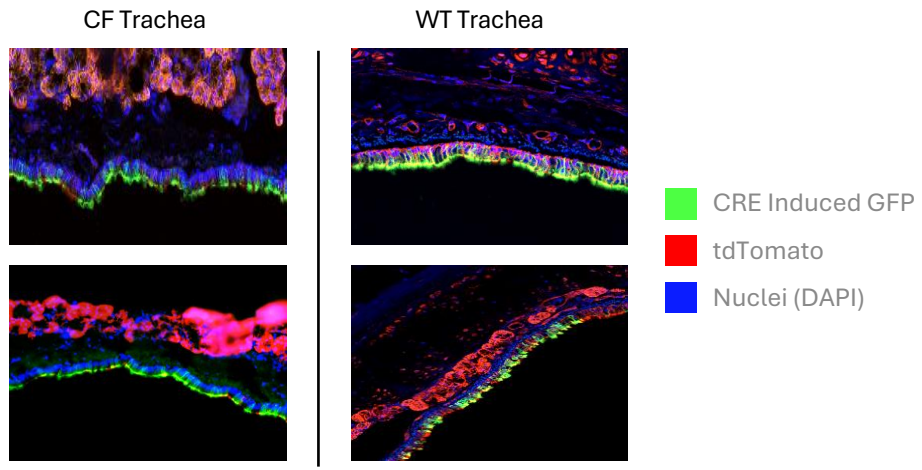
- Dehydrated mucus
- MCC defect
- No mucus plugs or sig. lung infections

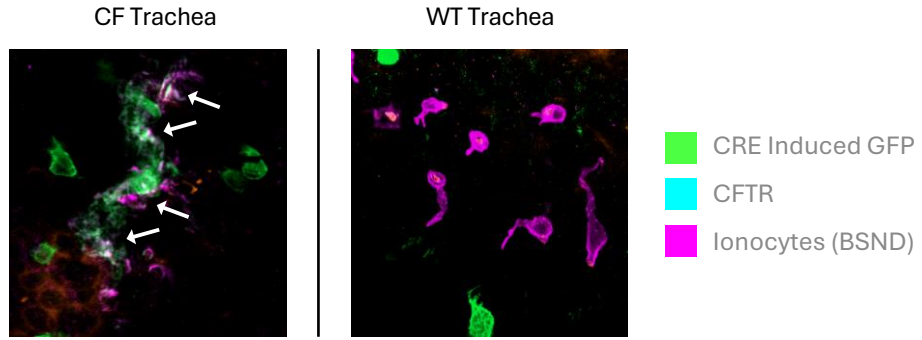




RCT21000 LNPs
Encapsulating Cre mRNA



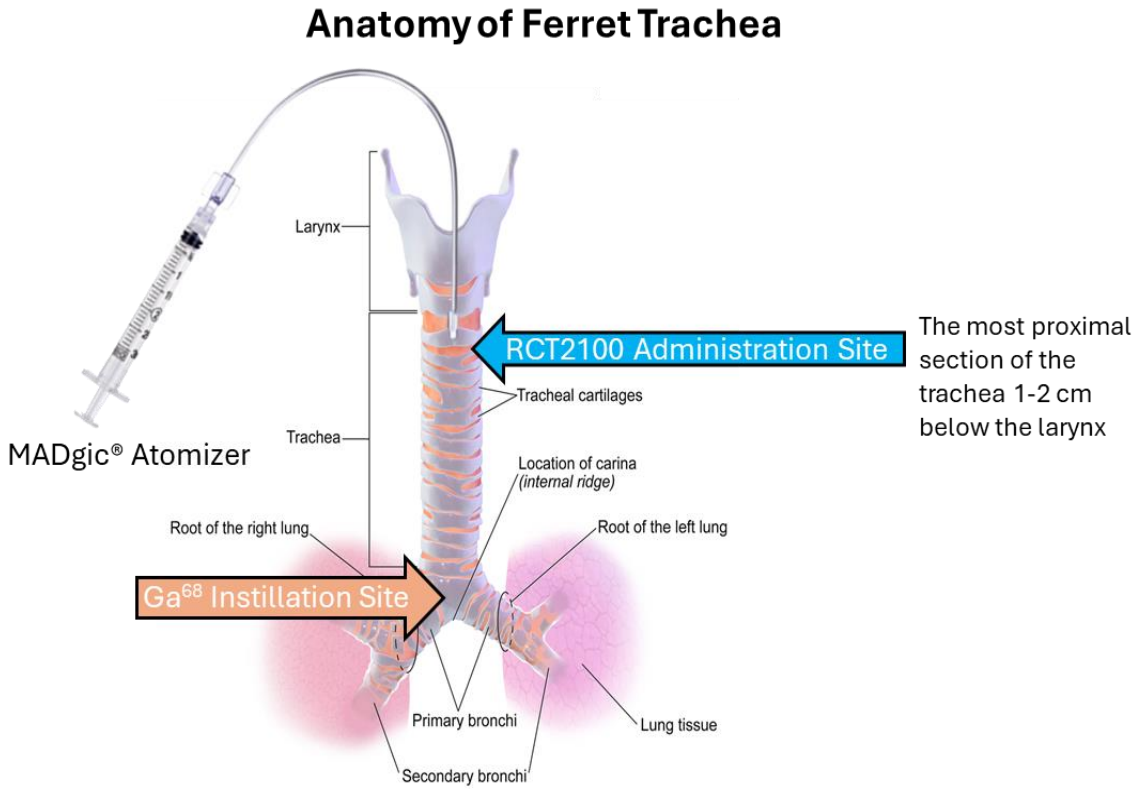




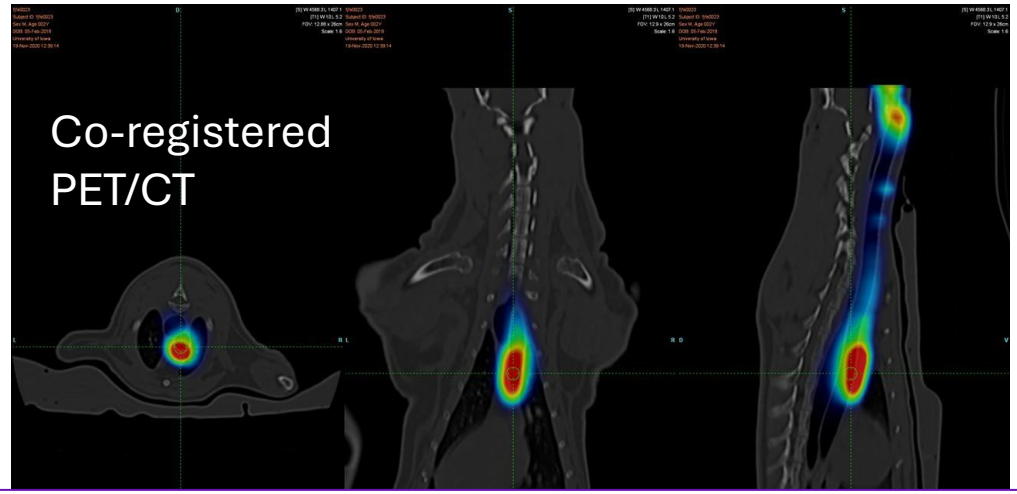
Data generated at U Iowa Engelhardt lab

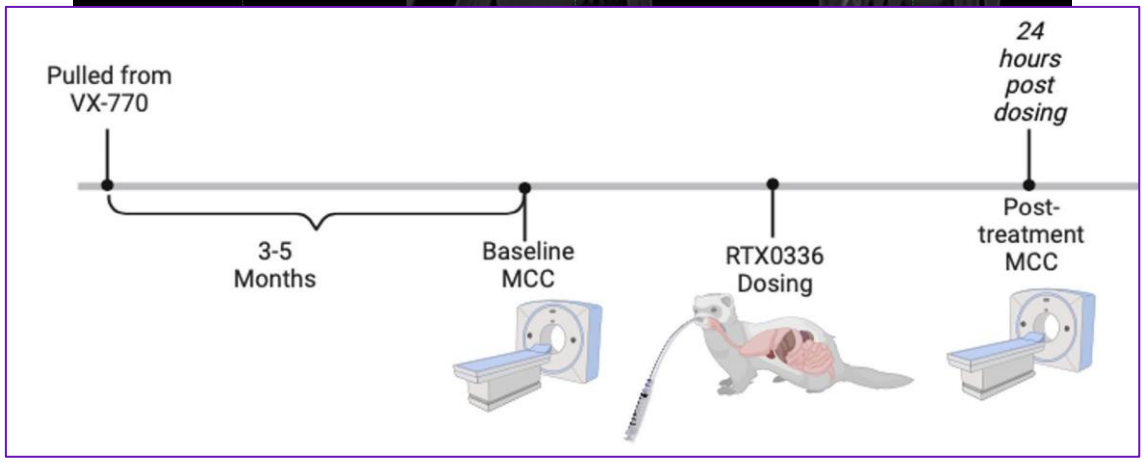
CF Ferret Tracheal Mucociliary Clearance Assay is gold standard in vivo model

- Administer RCT2100 via MADgic Atomizer
- After 24 hrs, instill Ga^{68} macroaggregated albumin at carina
- Image movement of tracer for 15 minutes



The most proximal section of the trachea 1-2 cm below the larynx

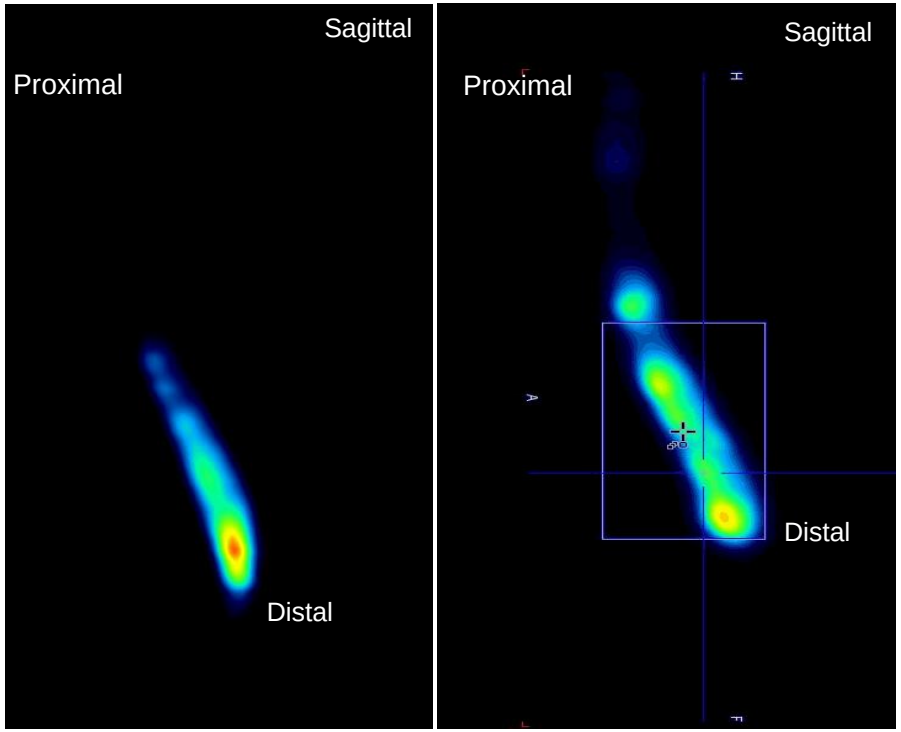




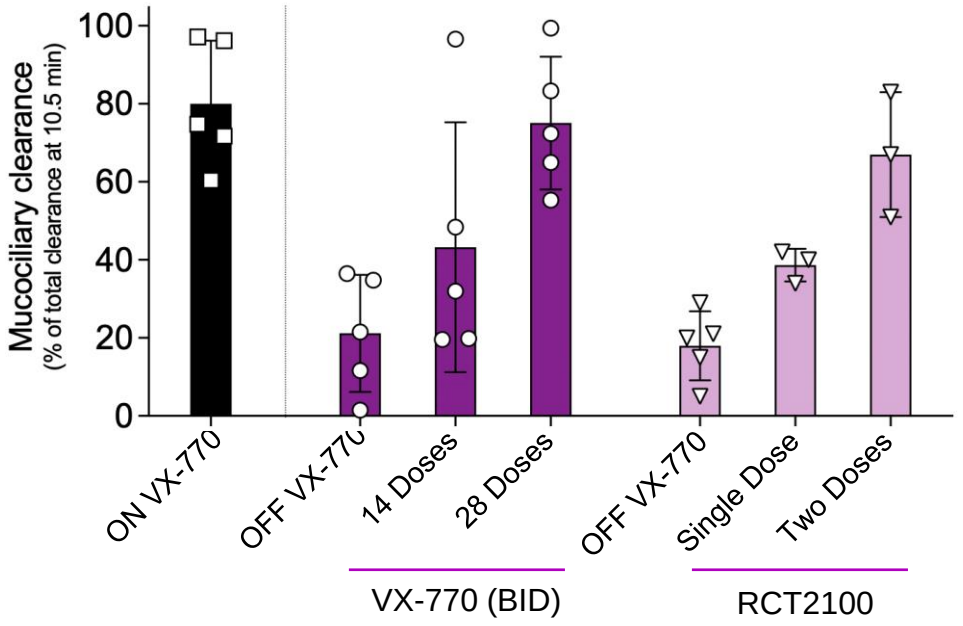
Data generated at U Iowa Engelhardt lab

High levels of CFTR-dependent MCC recovery observed within 24 hours after administration

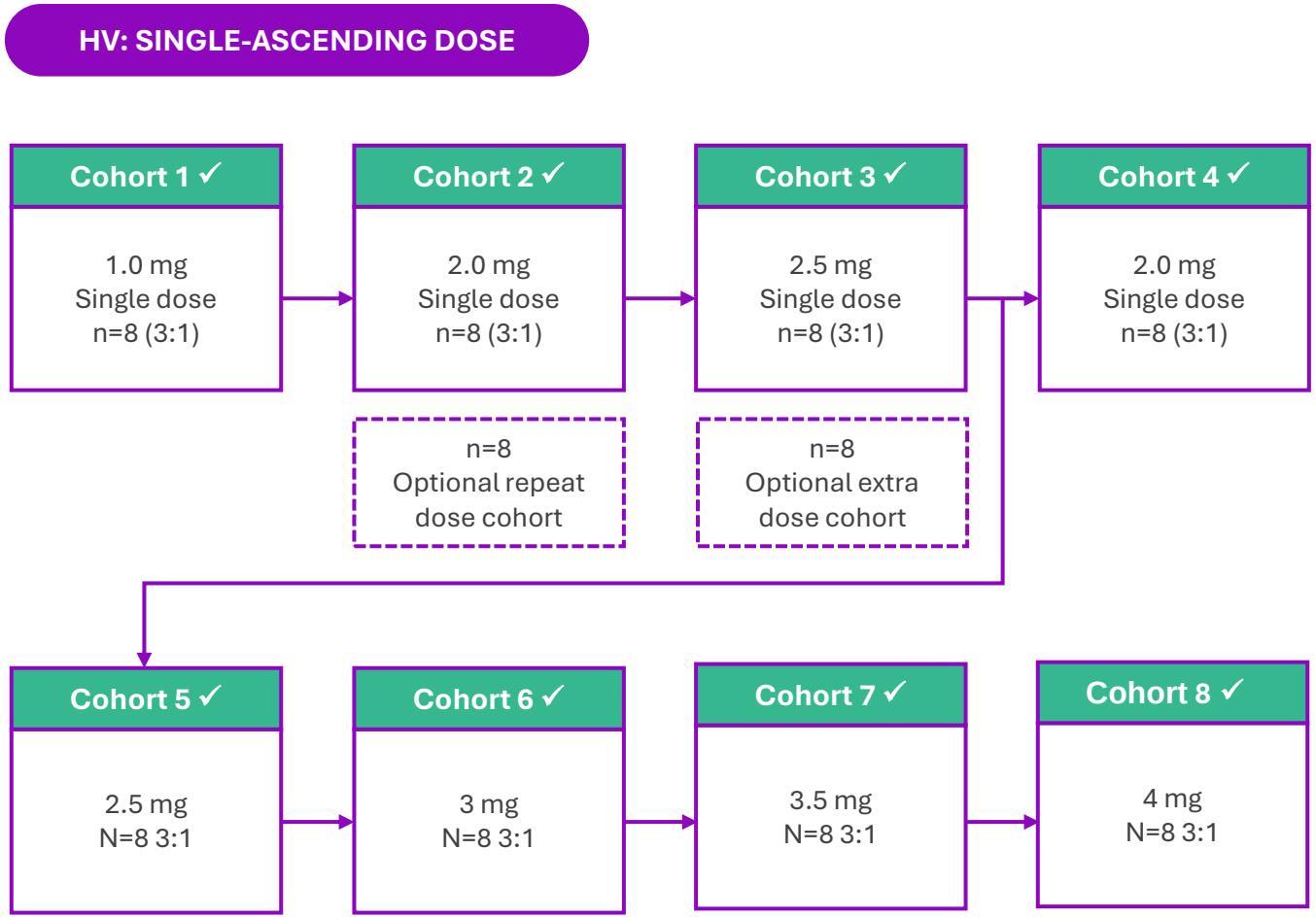
Baseline **24 hrs. post dose**



RCT2100 Demonstrates Rescue of MCC Comparable to VX-770



CF Phase 1 SAD Healthy Volunteer Study well tolerated (Ongoing)



- **Overall, well tolerated and supports progressing to MAD patient study.**
- Adverse events, were as expected - most prevalent AEs were mild fevers manageable with ibuprofen and paracetamol.
- No bronchospasm or requirement for bronchodilators.
- **Dosing in expected therapeutic dose range (3mg +).**

Primary Ciliary Dyskinesia (PCD)

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PCD is an orphan respiratory disease with no approved treatment

PCD caused by mutations in genes **resulting in dysfunctional cilia**, resulting in **deficient mucociliary clearance (MCC)**, chronic respiratory infections and loss of lung function

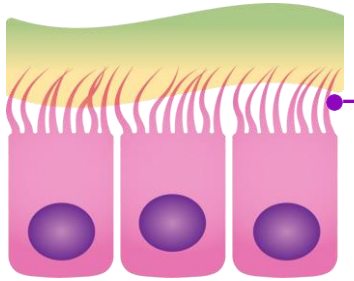
>100,000 patients

estimated prevalence across mutations in US, UK and EU5[1]

No approved treatments

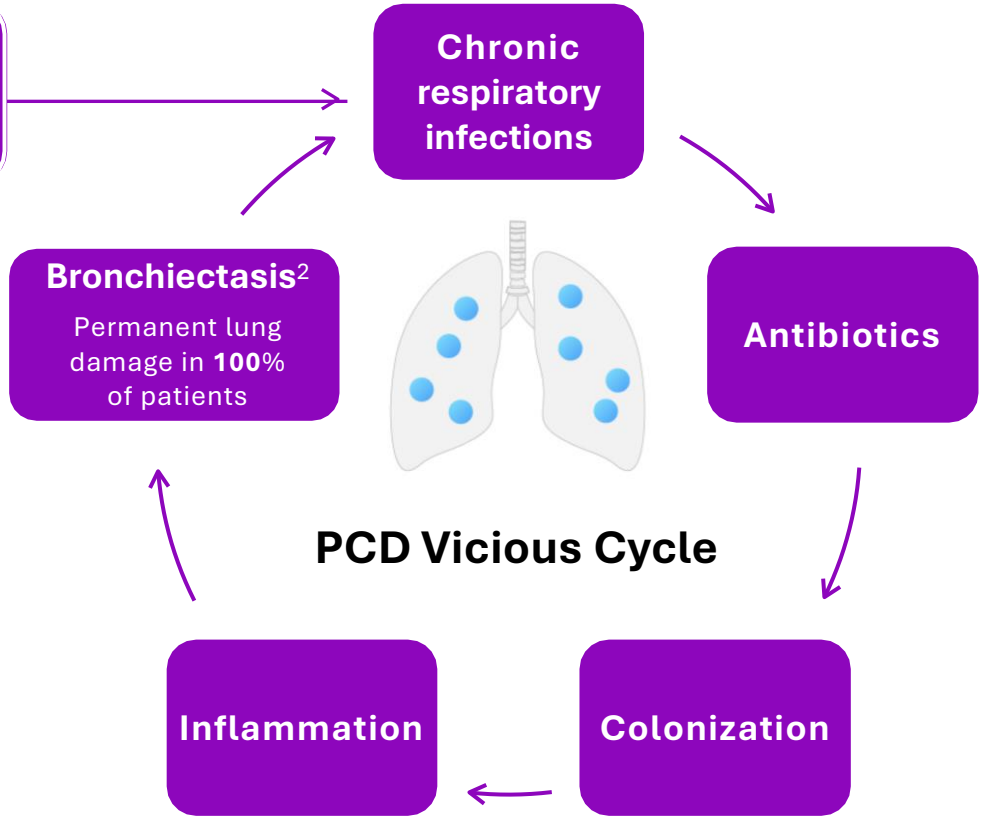
$1B market

for most prevalent genes (DNA1, DNAH5)



Mutations in genes cause dysfunctional cilia*

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



PCD is a life altering, life shortening, disease with high morbidity and progressive lung function decline

"People with PCD experience a diminished quality of life."

Pediatric Pulmonologist at PCD Clinic

- If left untreated, children with PCD can have lung damage early in life.
- Adults may go undiagnosed while their disease gets progressively worse.

Strong physician and patient enthusiasm for RCT1100

First disease modifying treatment for PCD Patients

> “There’s nothing out there that offers a therapy that addresses the mutation and gets to disease modification. I think [RCT1100] would galvanize the community to increase awareness and promote early diagnosis as well.”
> —*Pulmonologist, Stanford University*

Favorable Dosing and Administration

Less than 10 mins to administer with PARI eflow nebulizer

> “Patients would be very excited to see those administration times. Many patients are on over an hour of treatment regimens per day and would happily trade that for 30-minutes a week for treatment that increases lung function. It’s a no-brainer for them.”
> —*Pediatric Pulmonologist, Naval Medical Center of San Diego*

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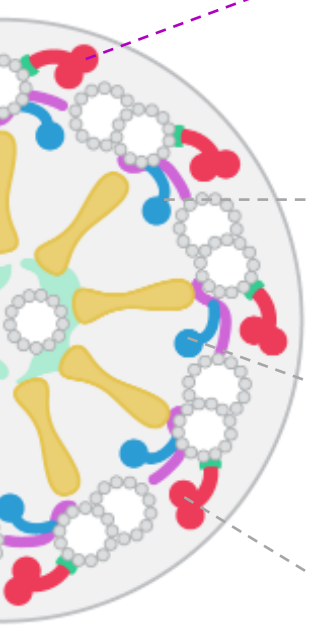
PCD is >$1B franchise opportunity with no competition



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

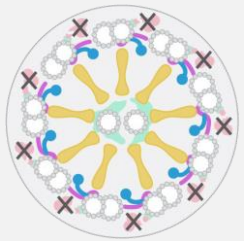
31-45K patients
with mutations
in the four most
prevalent PCD genes

RCT1100 is an inhaled mRNA therapeutic targeting DNAI1 mutations

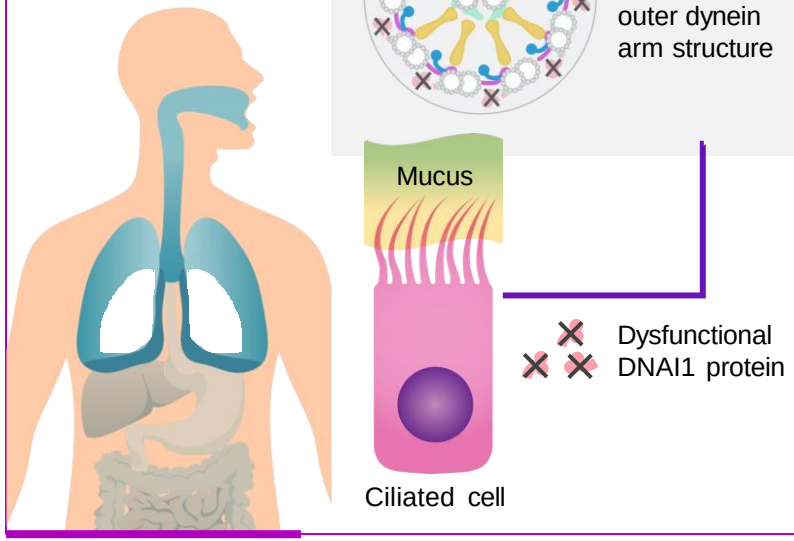
PCD

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

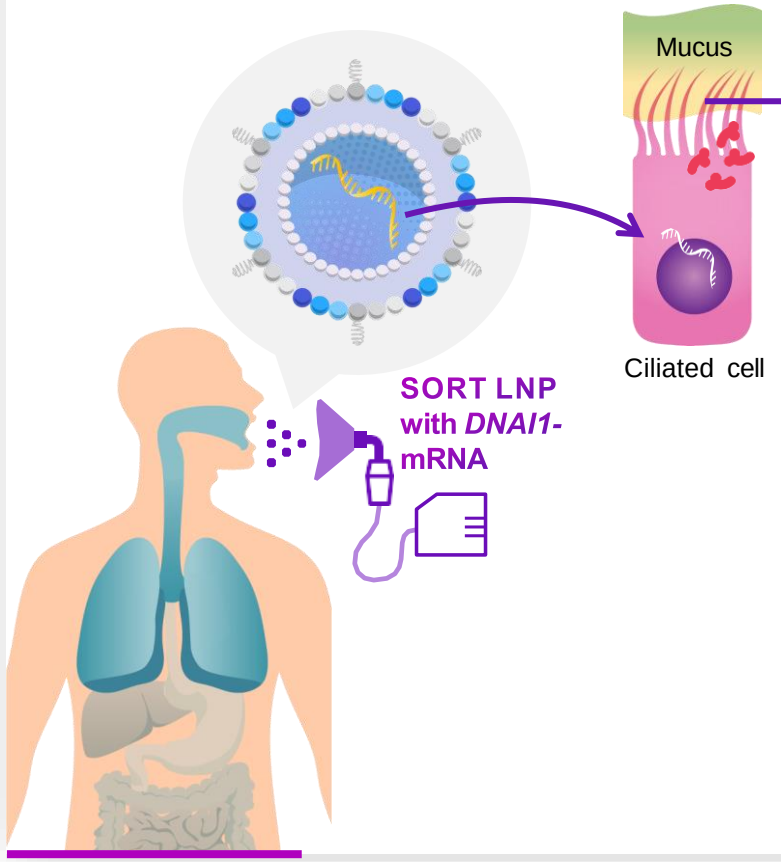
Dysfunctional ciliary axoneme



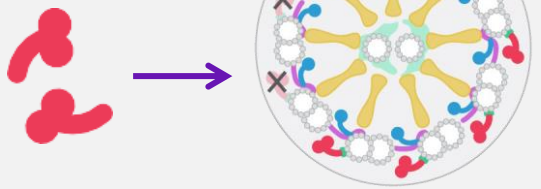
Missing DNAI1 protein and outer dynein arm structure



Treatment



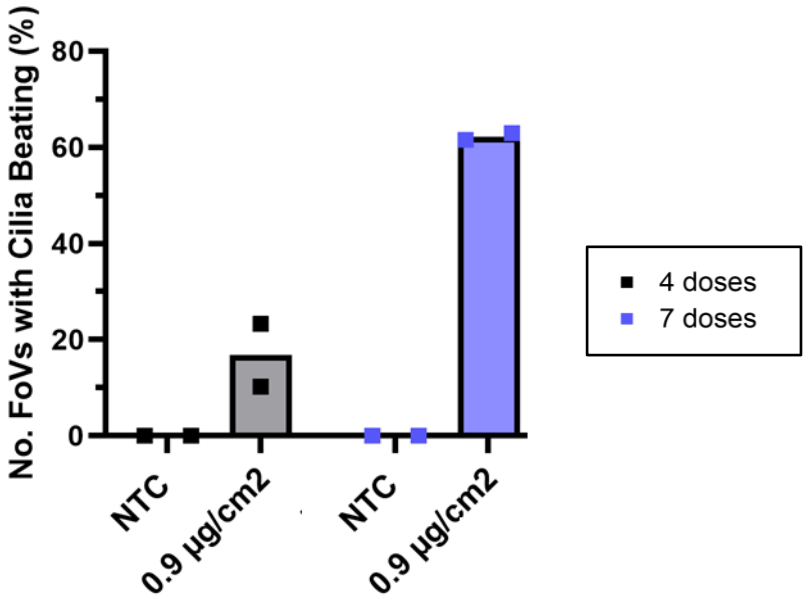
Functional ciliary axoneme



RCT1100 is an investigational mRNA-based therapeutic for PCD caused by pathogenic mutations in the *DNAI1* gene.

Restoration of DNAI1 protein and ciliary activity demonstrated in patient nasal epithelial cells (hNEs)

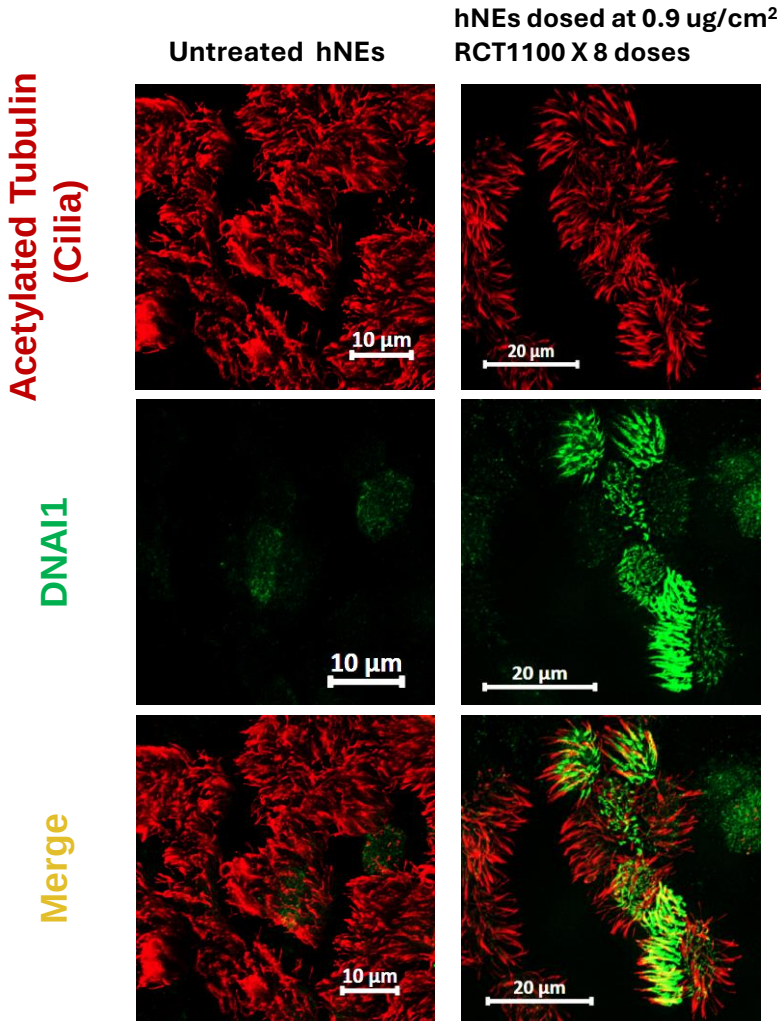
Increased ciliary activity achieved with repeated nebulized administrations



NTC – Non-Treated Control

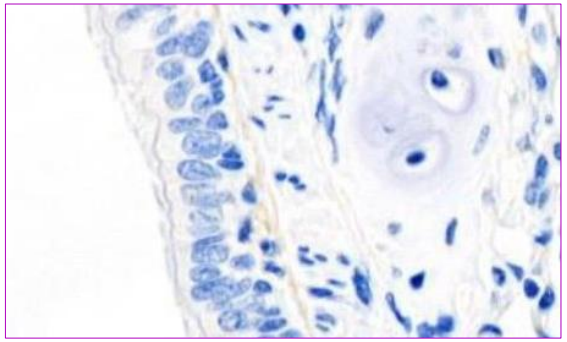
- Up to 60% of fields of view show ciliary beating
- 0.9 ug/cm^2 corresponds to 3 mg nebulized dose

DNA1 protein expression demonstrated in cilia with repeated nebulized administrations

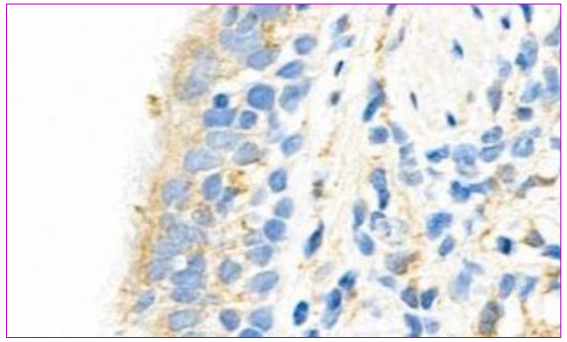


NHP data demonstrate increased expression of DNAI1 protein in target cells with repeated dosing

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



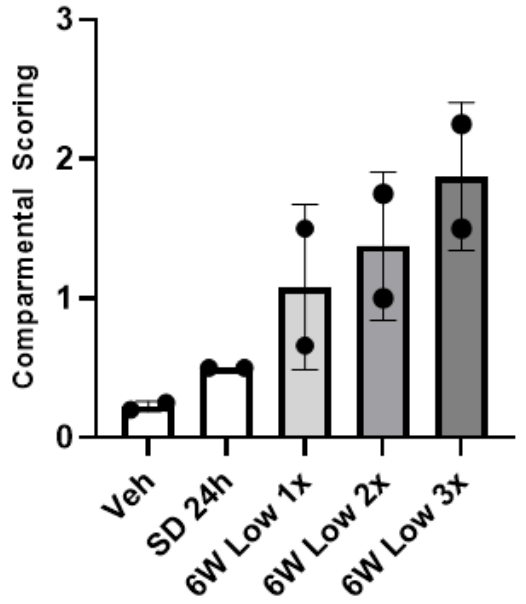
Vehicle Control



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

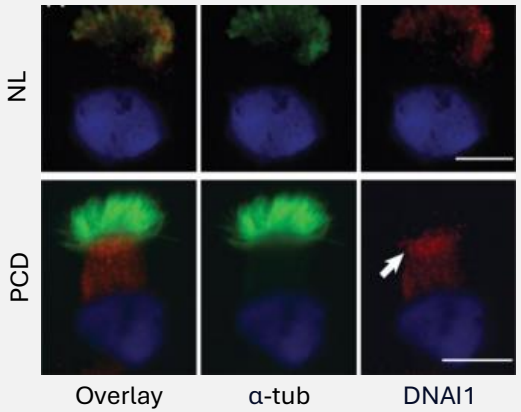
2 = 50% of airways indicate epithelial-specific signal

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

RCT1100 Phase 1b biomarker study provides evidence of restoration of mucociliary function

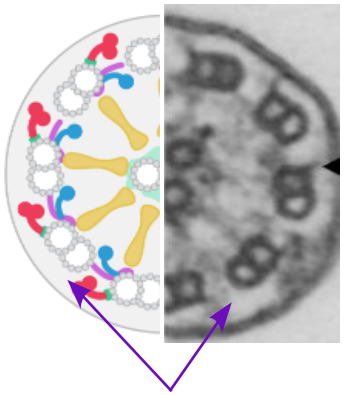


Immunofluorescence (IF)

showing protein expression in disease-relevant cells

PLoS One 8 (2013) e59436

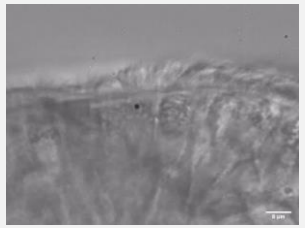
Normal vs defective ODA structure (e.g. DNAI1)



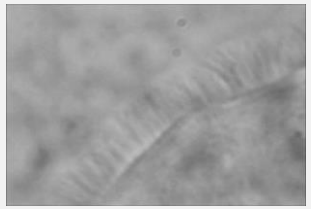
Transmission electron microscopy (TEM)

showing rescue of the ciliary axoneme structure

Clin Chest Med 43 (2022) 127–140



Healthy Normal; Cilia beat at approximately 10 Hz

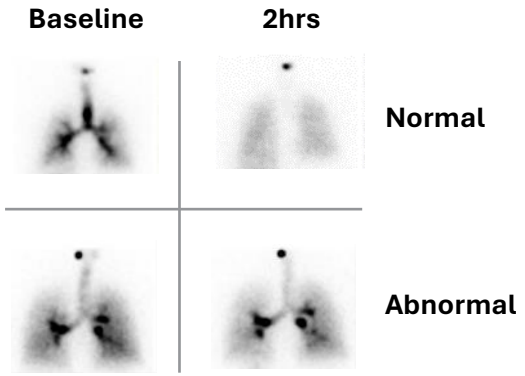


DNAI1; (This is a video, the cilia are not moving)

High-speed video microscopy

showing rescue of ciliary beat frequency and beat pattern

Clin Chest Med 43 (2022) 127–140



Mucociliary clearance (MCC)

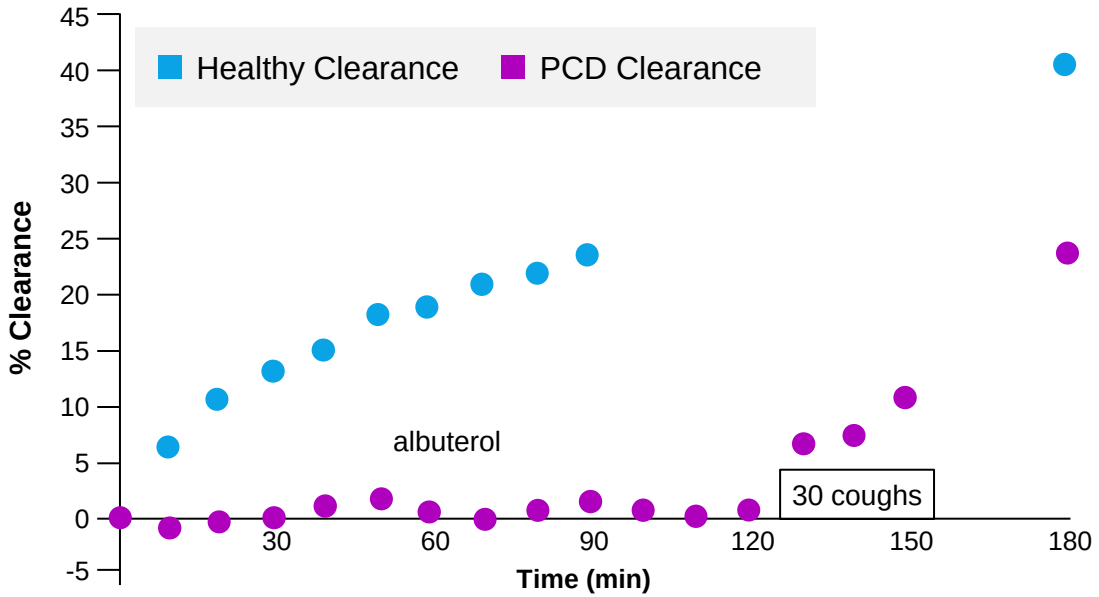
Inhaled radio-aerosol showing whole lung mucociliary clearance

Marthin et al. 2023

Patient data anticipated Q4 ’24

Mucociliary clearance restoration is a sensitive measure and has strong predictive clinical value

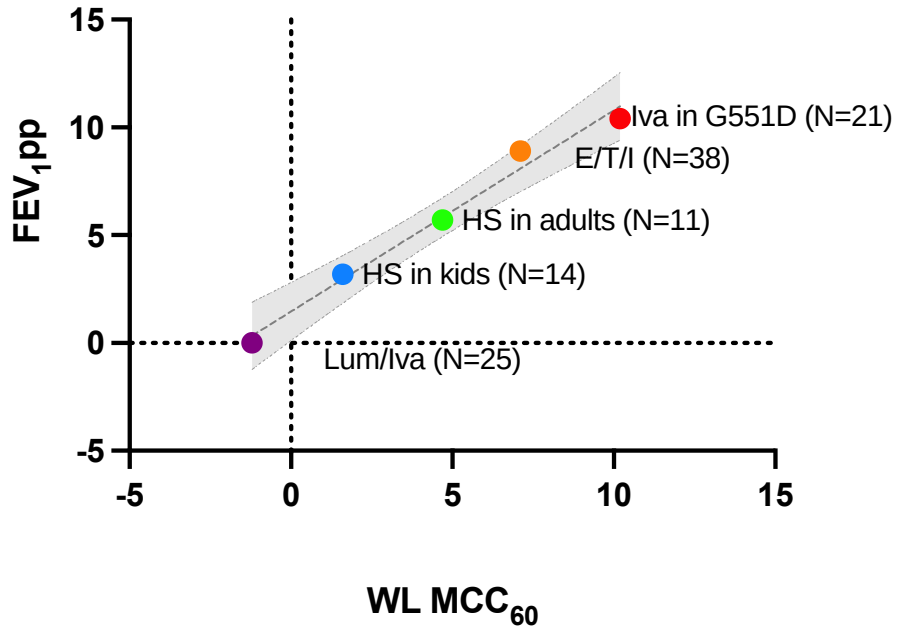
Comparison of MCC in PCD patients vs. Healthy Controls



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. FEV1 in CF[1]

Absolute change in Whole Lung MCC vs. FEV1 in CF



1. Unpublished data from Scott Donaldson, UNC

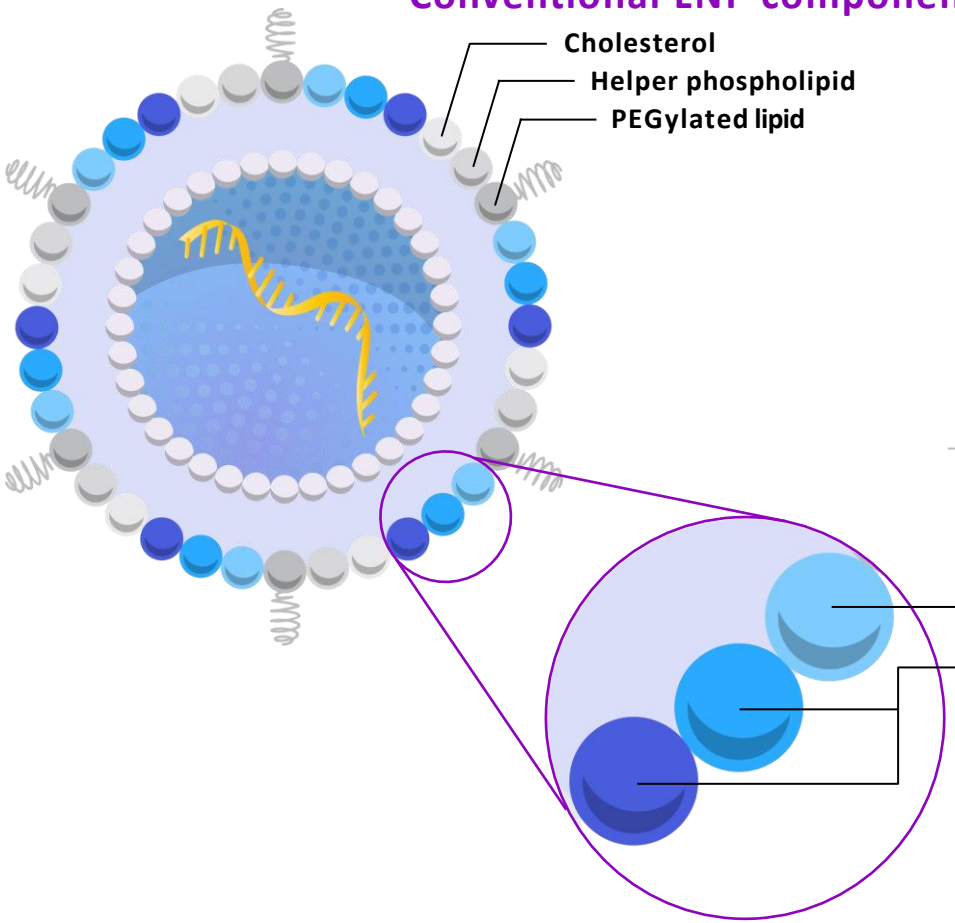
Novel Selective Organ Targeting (SORT) Lipid Nanoparticle (LNP) Platform

ReCode THERAPEUTICS

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

Sort LNP architecture

Conventional LNP components



+ Proprietary lipids

Novel ionizable lipid

SORT lipids

Additional 5th and 6th SORT lipid directs LNP to specific tissues and cells

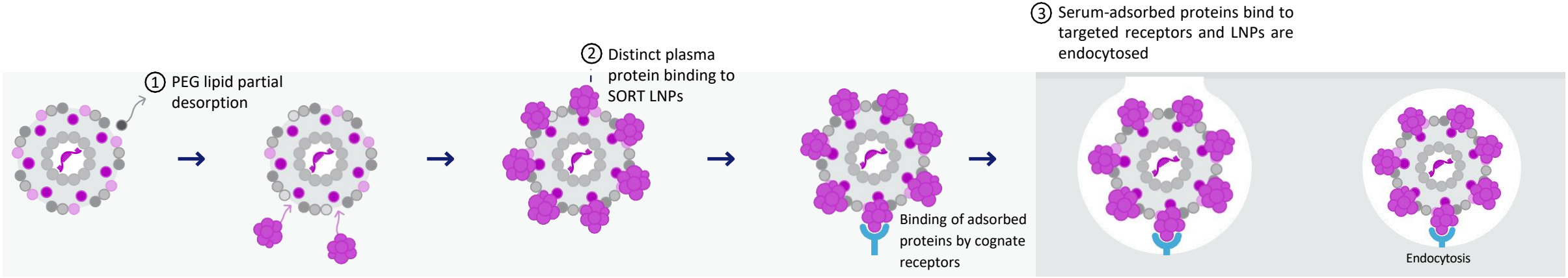
Possible payloads

- Gene editing
- DNA
- mRNA
- siRNA
- Peptides
- Mixed payloads

Administration methods

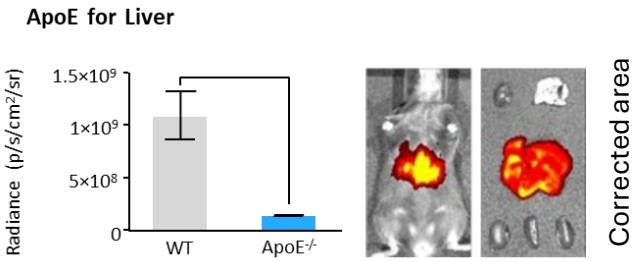
- Nebulizer (local)
- IV (systemic)
- Intrathecal

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

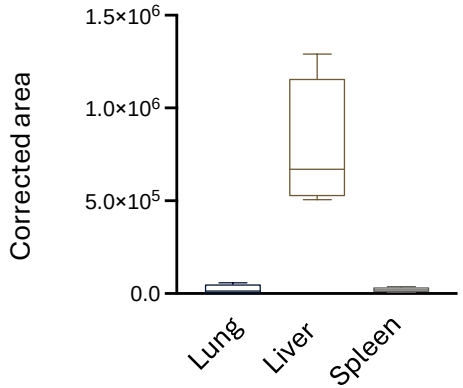


Extra-hepatic delivery of SORT LNPs occurs via an ApoE-independent mechanism

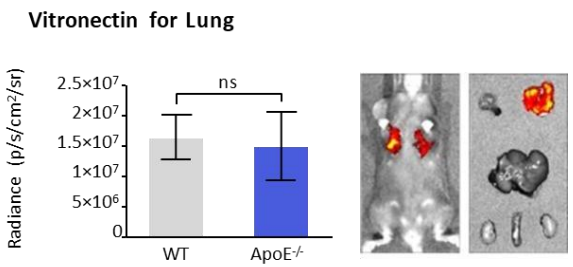
Liver SORT LNP



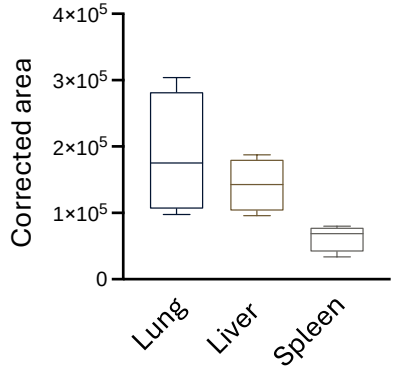
Tissue-specific expression of hits



Lung SORT LNP

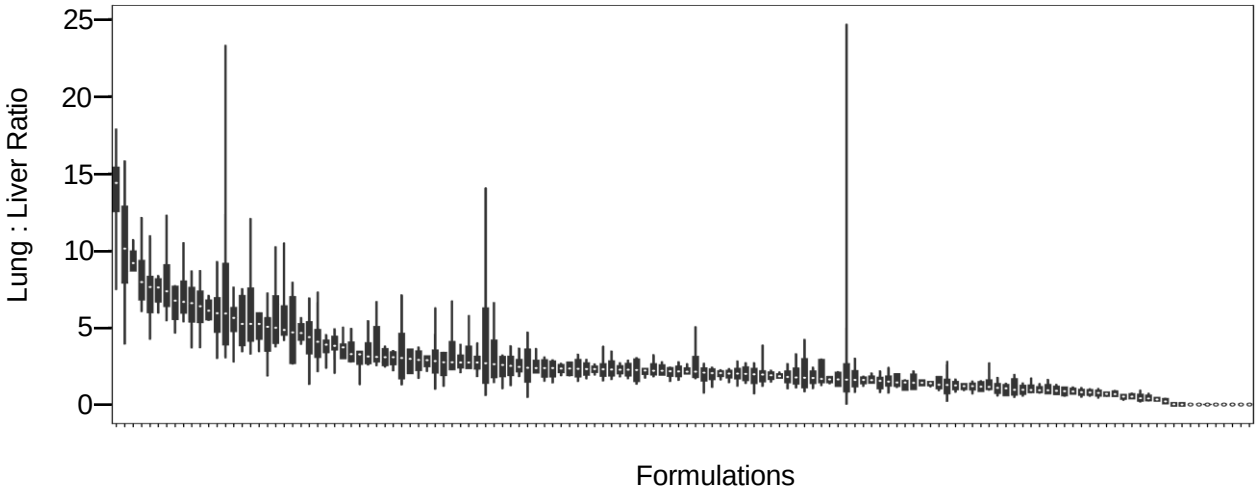


Tissue-specific expression of hits

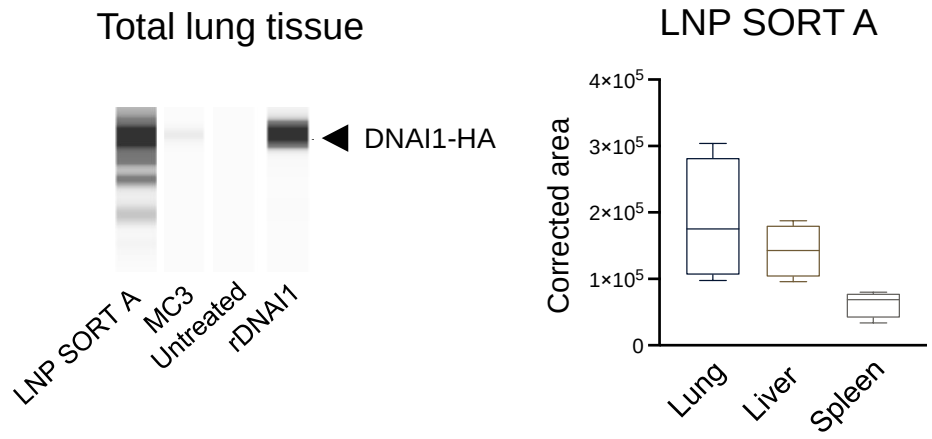


IV SORT LNPs are optimized for extrahepatic selectivity

Distribution of Lung : Liver Ratios for LNPs



Tissue-specific expression of hits in IV dosed rats



- Screened ~200 unique LNP formulations in rats via IV administration
- LNPs identified with high lung expression relative to established benchmark LNPs
- Validated hits in rats via intracellular expression of an orthogonal protein product (DNAI1-HA)

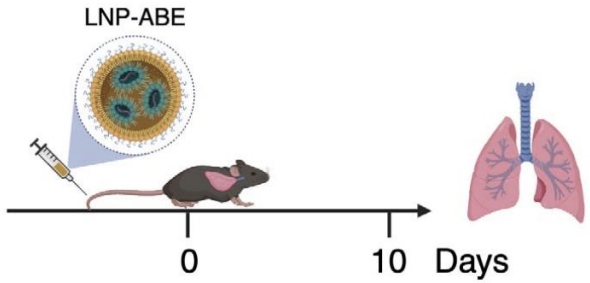
Direct and persistent *in vivo* gene editing of mouse lung epithelial cells demonstrated

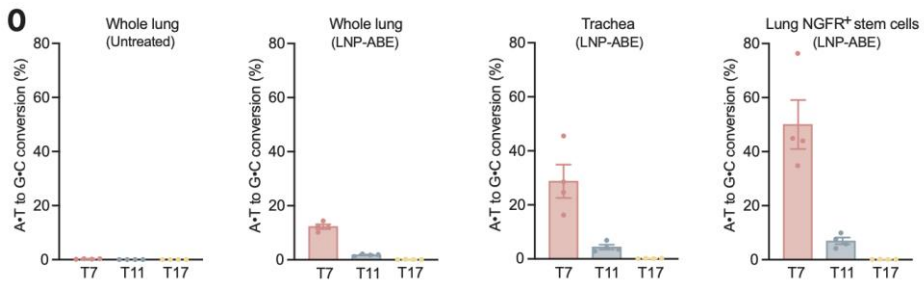
Science

GENE EDITING

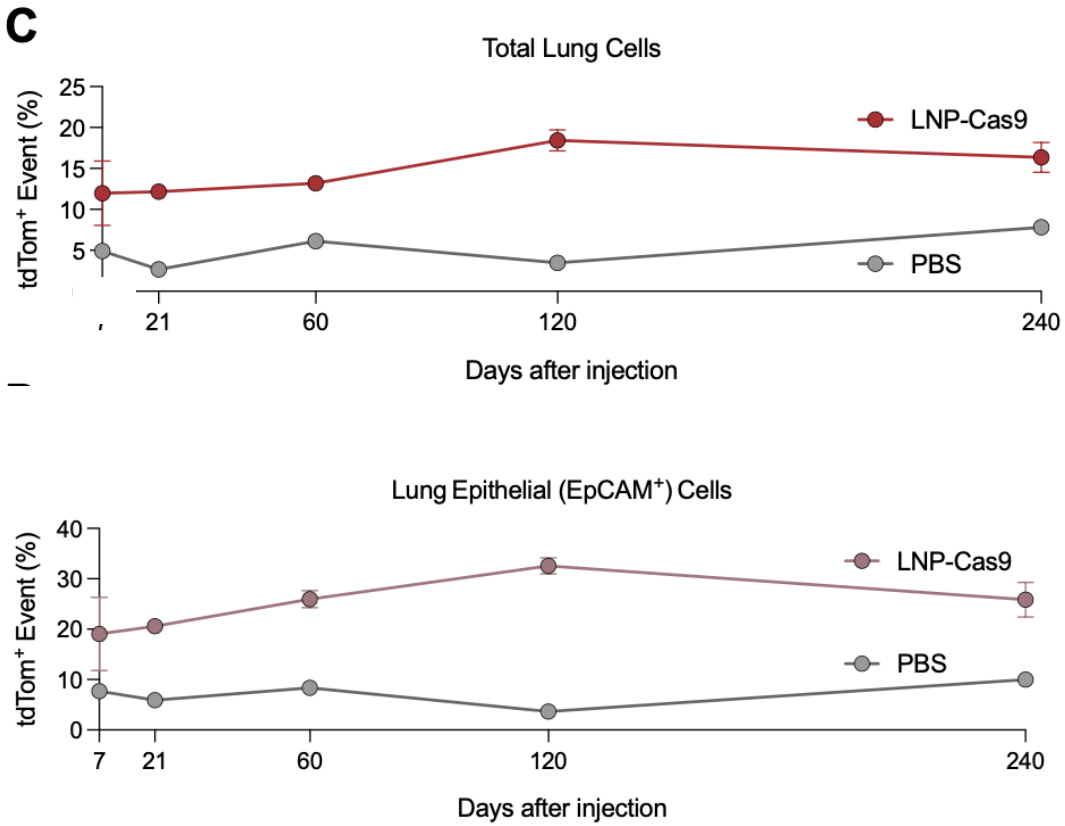
In vivo editing of lung stem cells for durable gene correction in mice

ABE gene correction of CFTR hR553X mouse lung basal cells after a single administration*



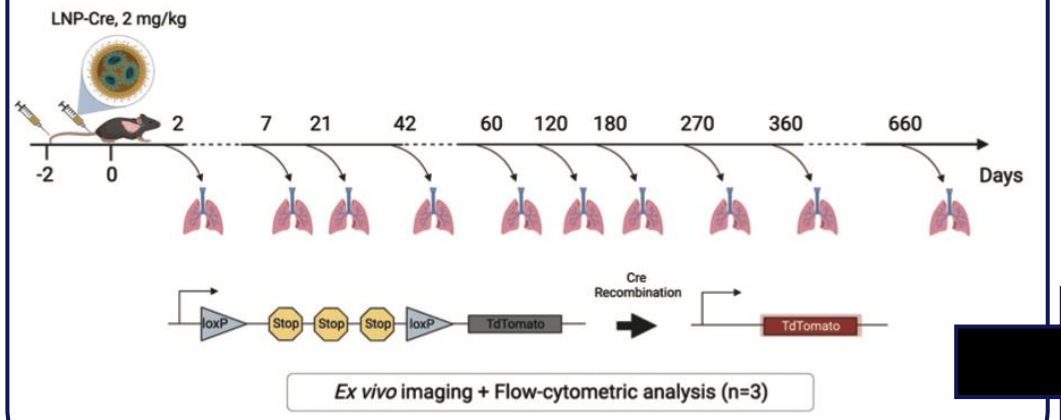


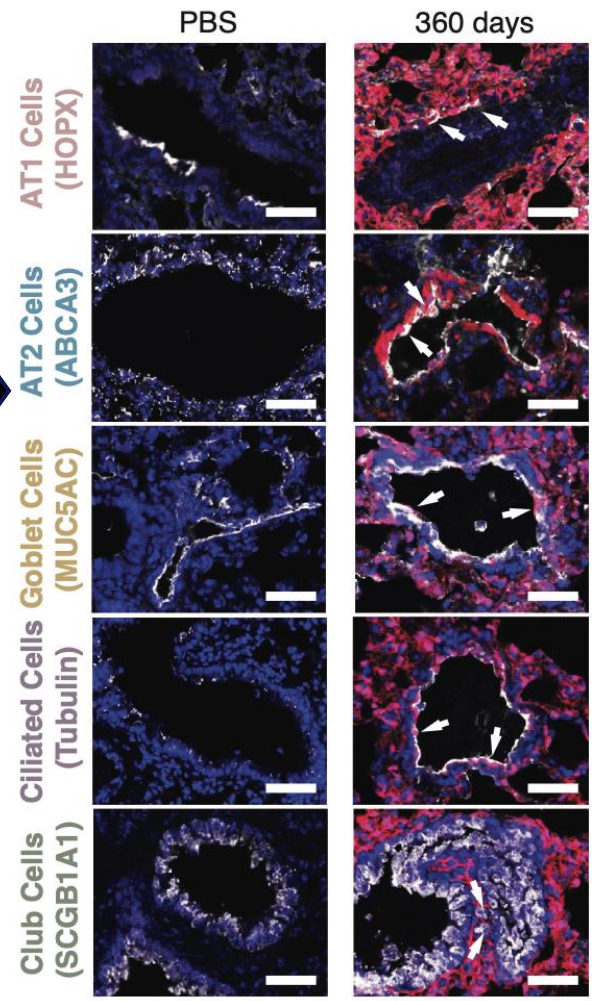
Durable in vivo gene editing in Ai14 mouse lung with LNP-Cas9*

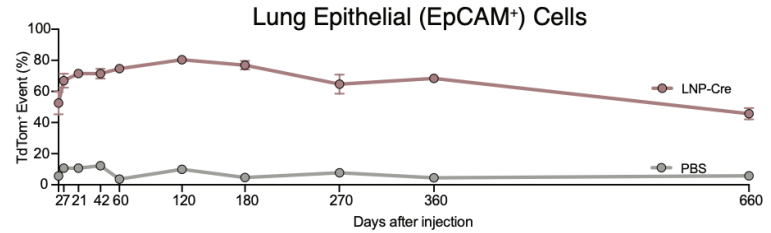


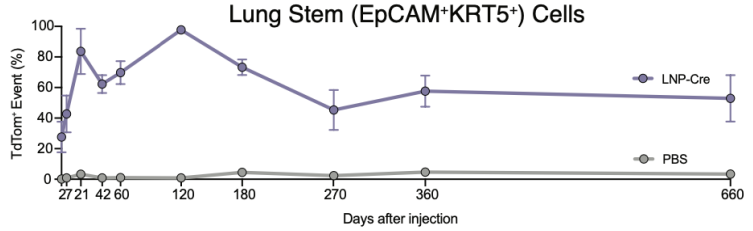
* Data from Science (2024)

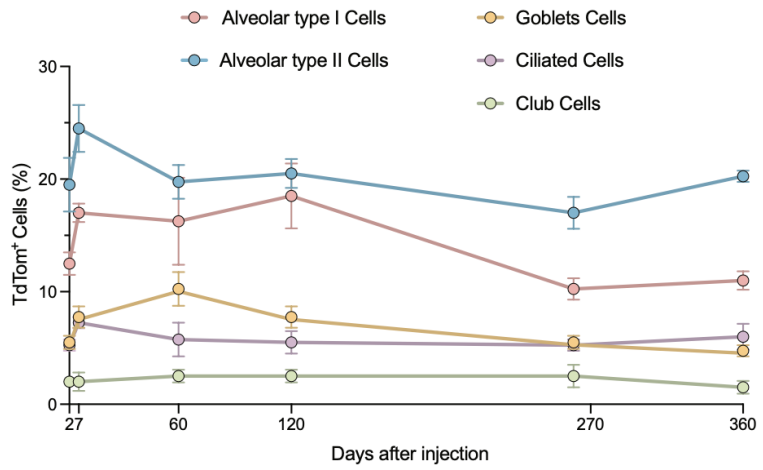
Durable *in vivo* gene editing of mouse lung epithelial cells >1 year











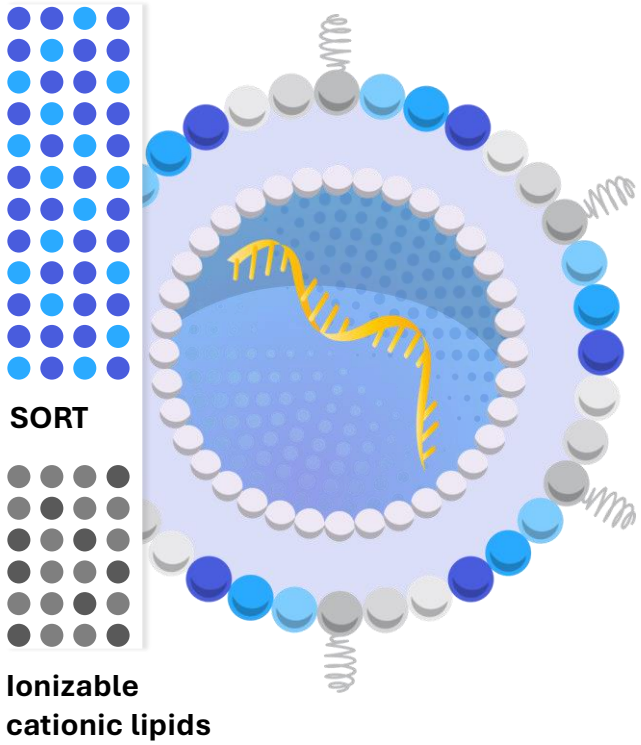
Why this is important

- 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.

Only LNP platform with FTO from large chemically diverse LNP library without requirement for stacked licenses

Library

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



Patents

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

150+ applications

40+ issued patents

30+ patent families

300+ class novel 1st & 2nd gen ionizable, SORT, and PEG lipids

WW Coverage

Distinct LNPs in a crowded and litigious space

WW and exclusive IP rights

One license

Know-How

Therapeutic-grade LNP manufacturing

MOAs & optimization

Composition identification & optimization

ReCode THERAPEUTICS

ReCode THERAPEUTICS

Corporate Overview

August 2024