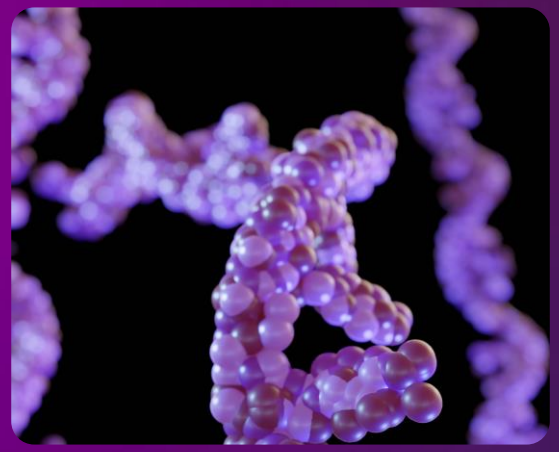
ReCode THERAPEUTICS

Corporate Overview

July 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

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

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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 by Bayer · Pfizer · Hunt Investment Group · Bioluminescence Ventures

MPM · TEKLA Capital Management LLC · Cystic Fibrosis Foundation · VIDA ventures · Osage University Partners · AMGEN · sanofi · Colle Ventures

ReCode Therapeutics

$370M Raised

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

	Candidate	Modality	Target	Delivery	Discovery	Preclinical	Phase 1/2
Respiratory Indications							
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			Intellia THERAPEUTICS
Other lung indications		Multiple	Undisclosed	Inhaled IV			
Other		mRNA	Undisclosed	Inhaled IV			
		Multiple	Undisclosed	Inhaled IV			
Liver Indications							
Various		Multiple	Undisclosed	IV		AskBio	
		Multiple	Undisclosed	IV			
CNS Indications							
Various		Multiple	Undisclosed	Intrathecal			

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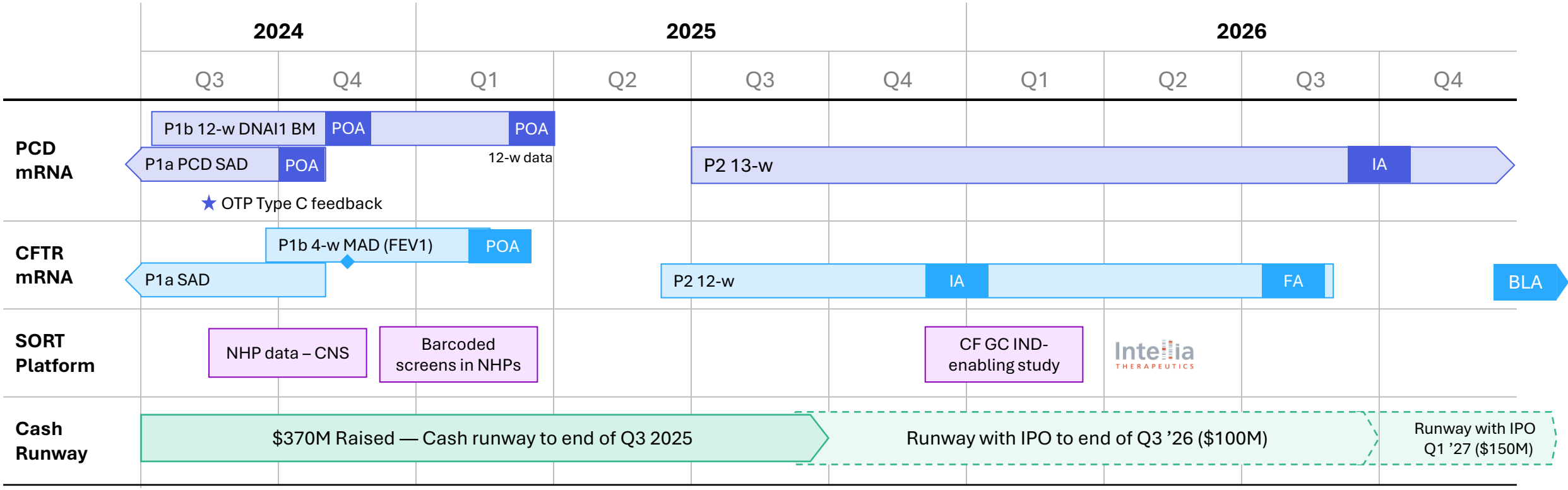
Significant opportunity with near-term milestones and cash through end of Q3 '25



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 to Date

CF and PCD Program updates

- Filed INDs and ex-US regulatory filings for CF and PCD
- Nearly 100 Healthy volunteers dosed across both studies
- PCD HV study completed, Ph1 SAD in patients initiated
- CF HV study nearing completion, dose range established for Ph1b MAD patient study

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 following IV SORT administration
- Announced 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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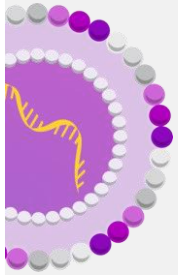
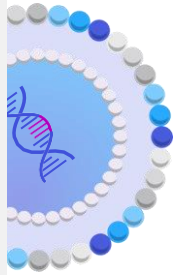
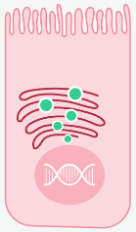
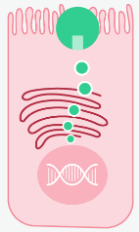
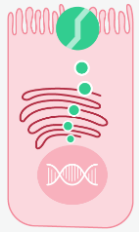
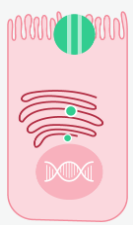
Two different treatment approaches to address CF patient needs

	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

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*

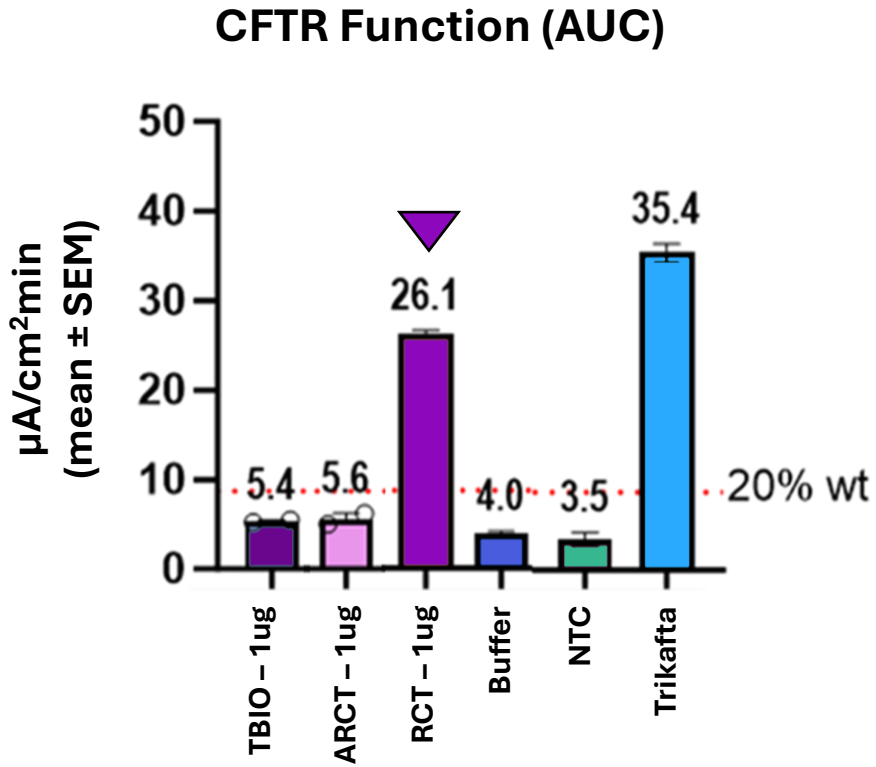
- **>13K patients not amenable to current therapies,** including patients not addressable by current therapies & poor responders to CFTR modulators.
- **>$1B commercial opportunity**

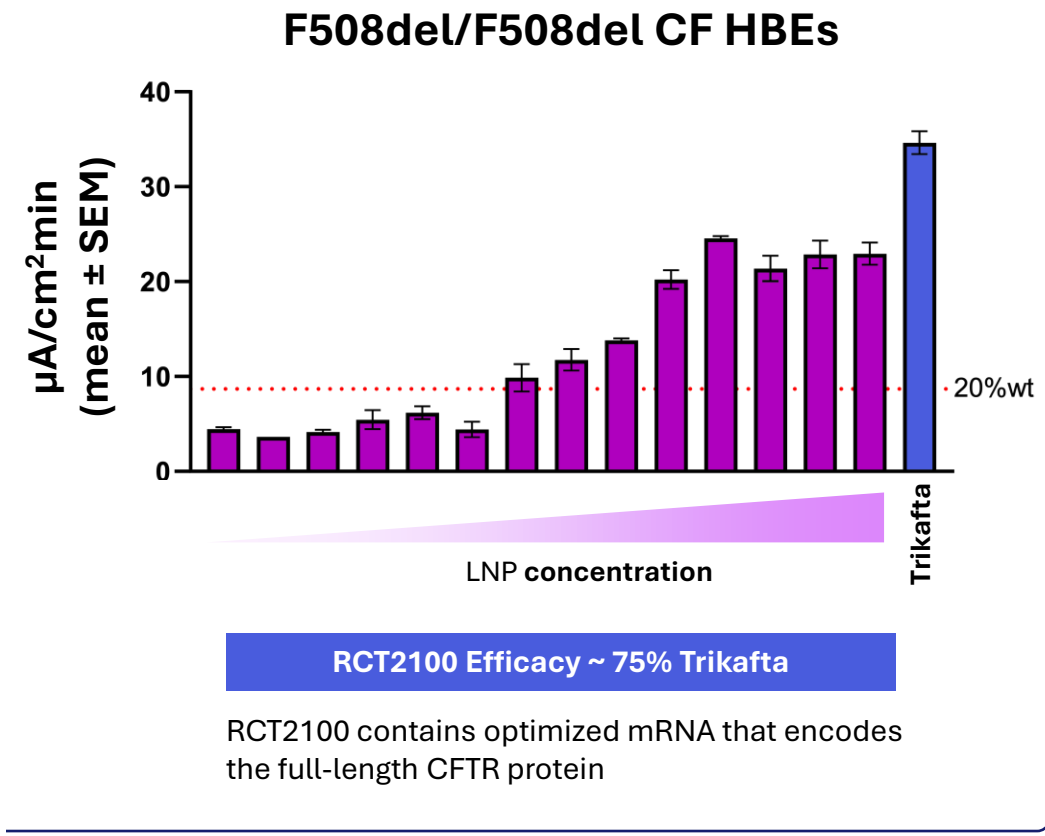
***31 years** life expectancy

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 exceeds potency F508del/F508del CF HBEs





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

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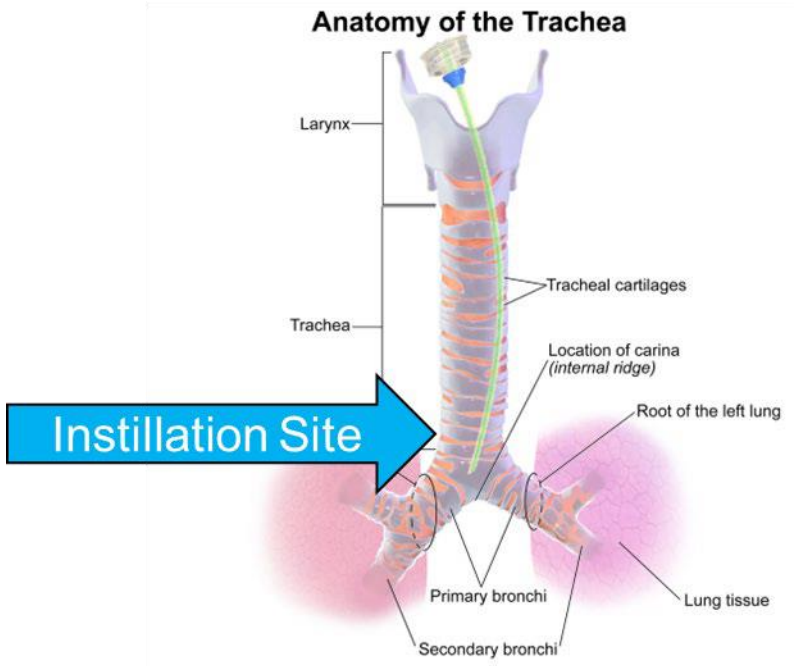
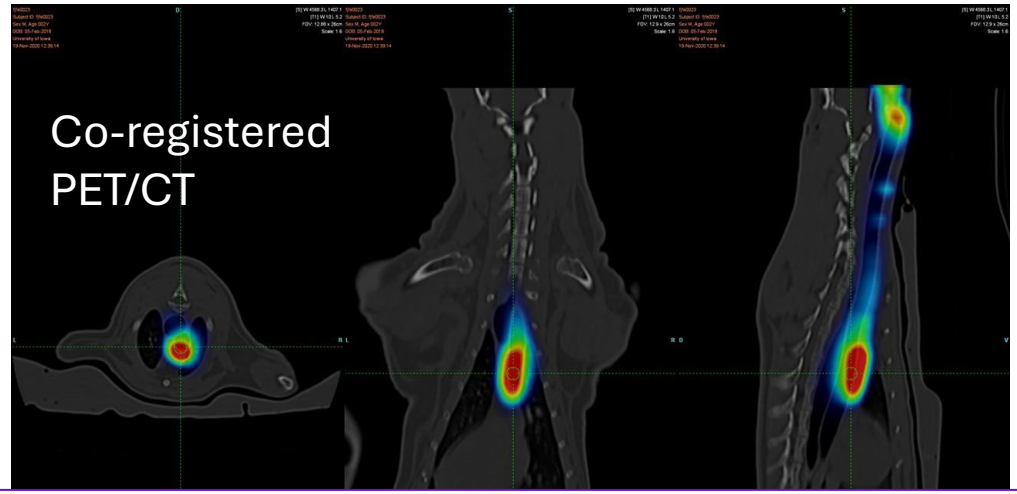
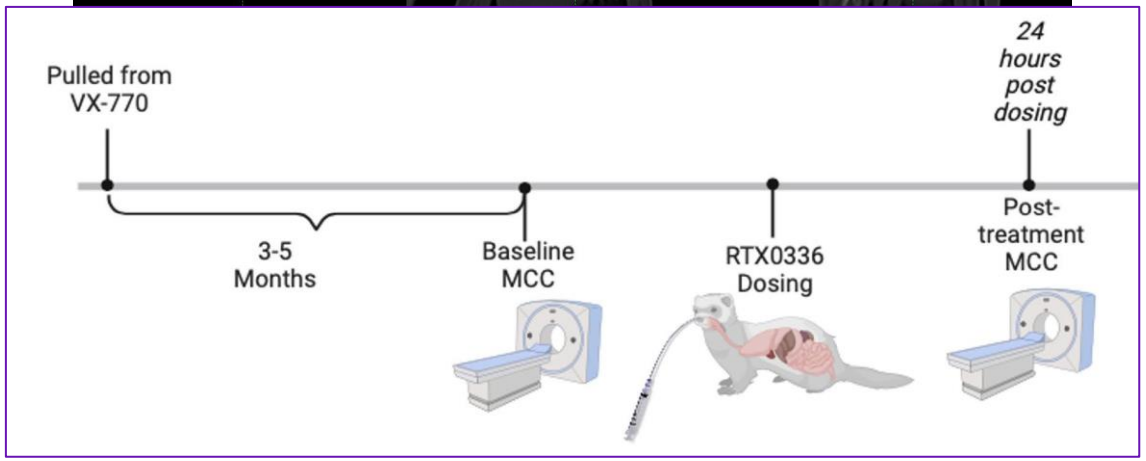
PET/CT CF Ferret Tracheal Mucociliary Clearance Assay

- Instill 50 μL of Ga^{68} macroaggregated albumin at carina
- Image movement for 15 minutes

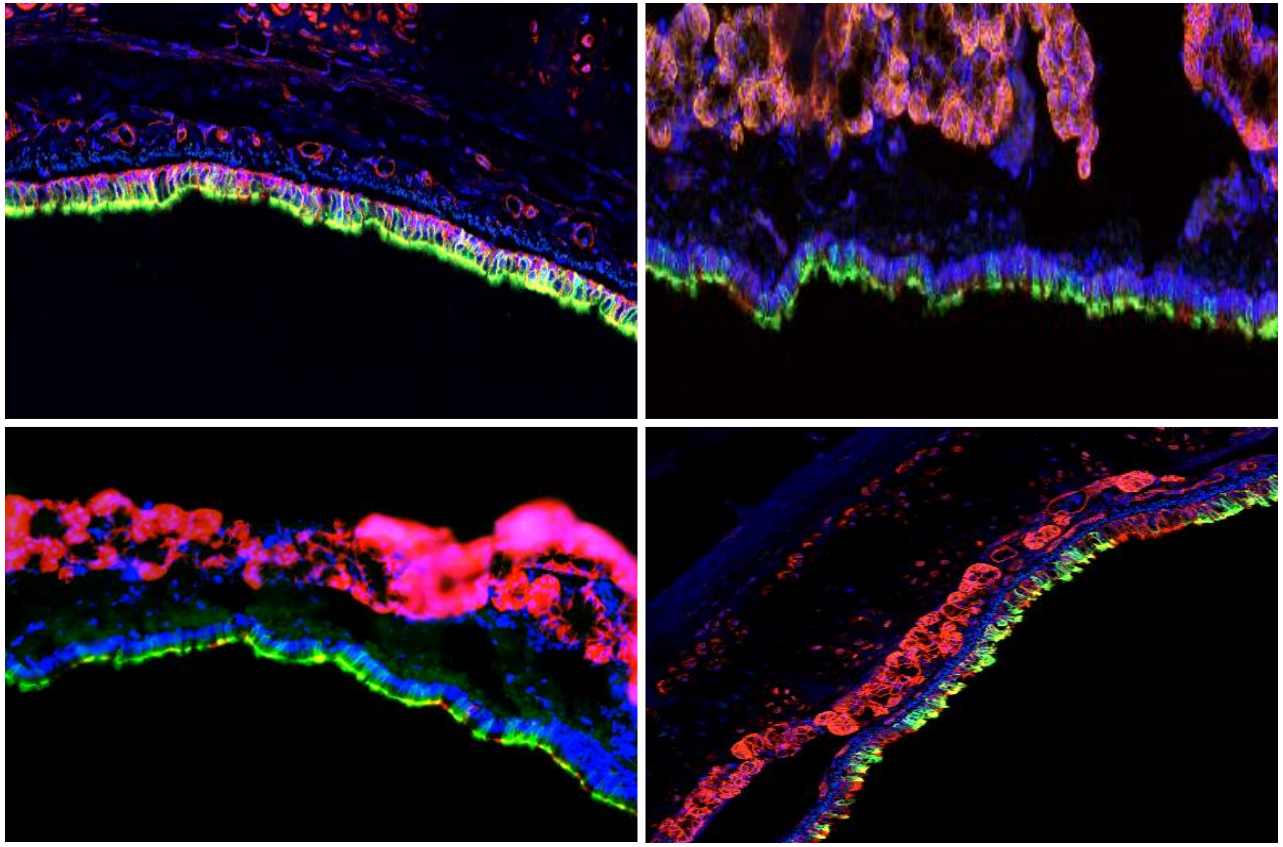


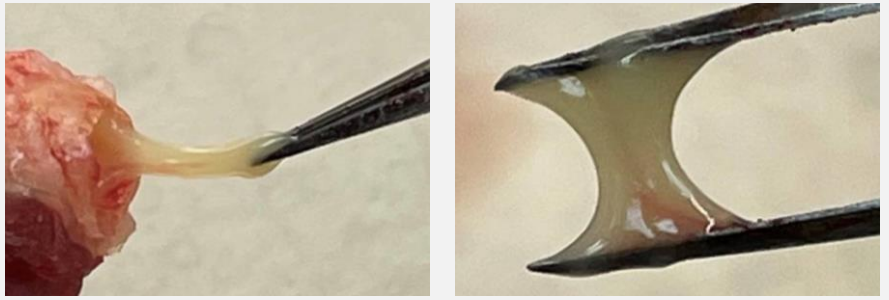




Data generated at U Iowa Engelhardt lab

RCT2100 LNP Efficiently Delivers to Tracheal Epithelium of CF Ferrets in the Presence of Mucus (Single Intratracheal Administration)





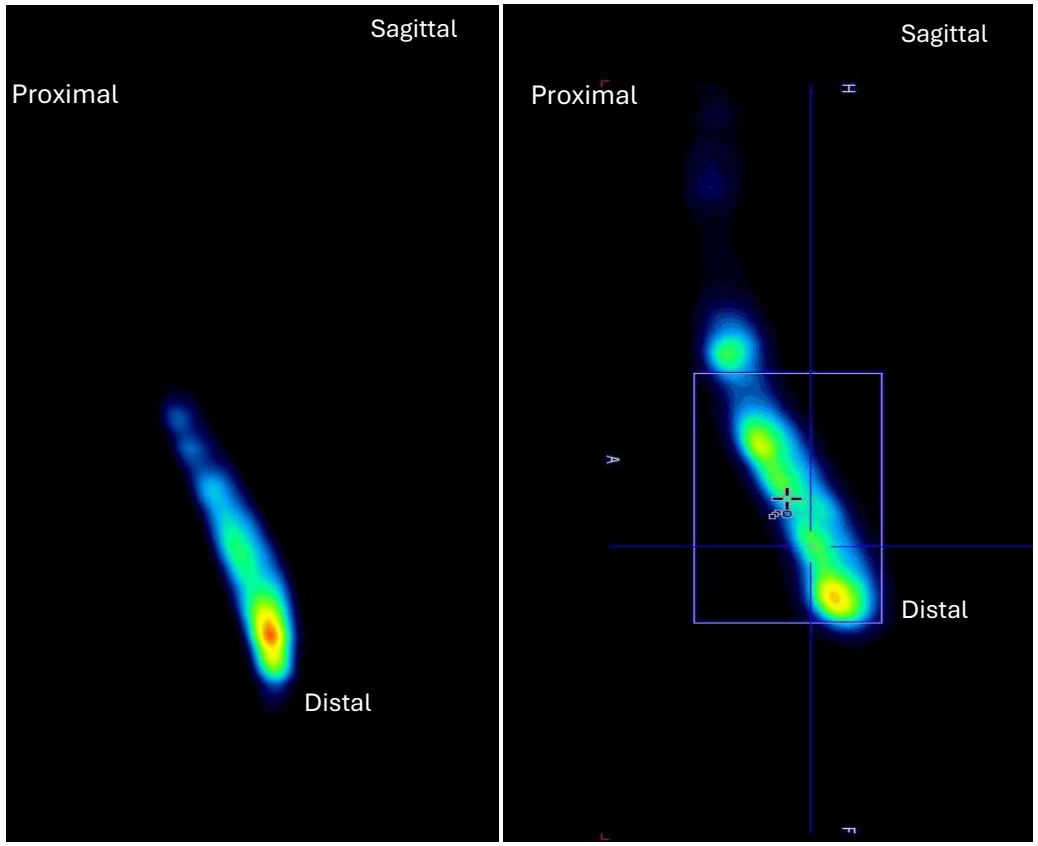
Grade 1 disease severity

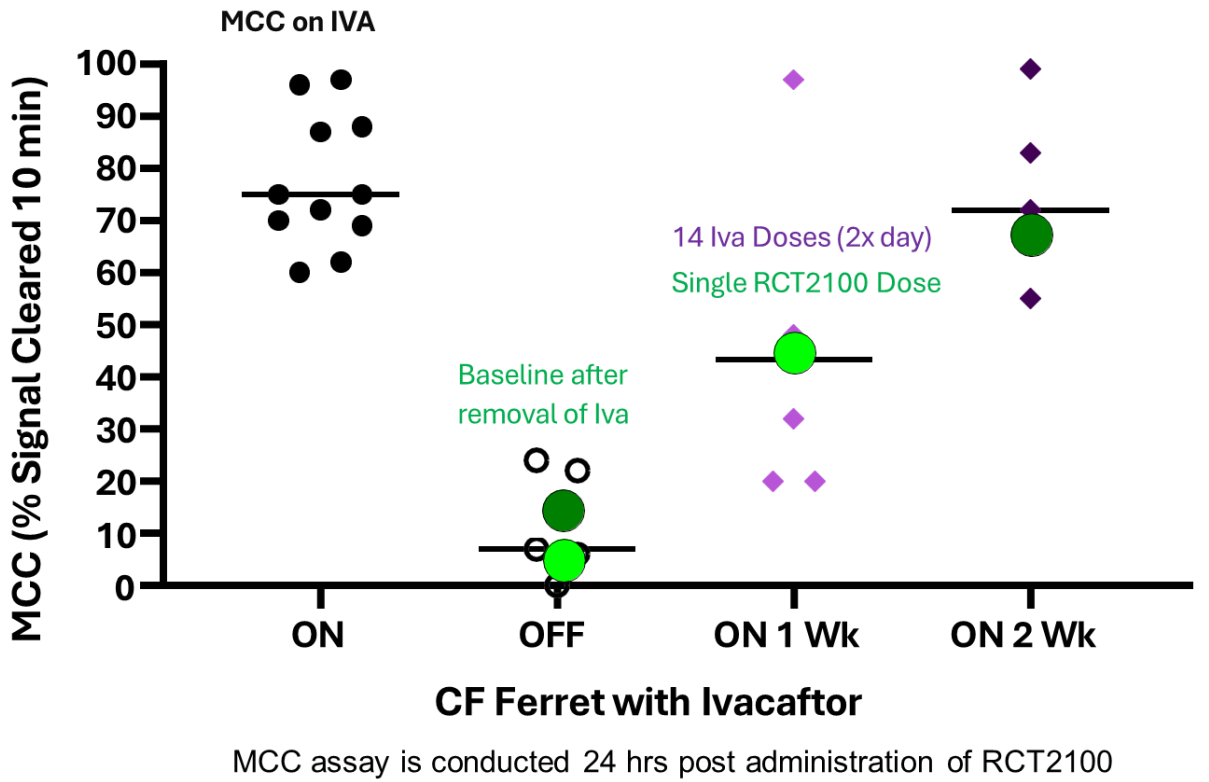
- Dehydrated mucus
- MCC defect
- No mucus plugs or sig. lung infections

CRE Induced GFP
Td-Tomato
Nuclei (DAPI)

Data generated at U Iowa Engelhardt lab

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

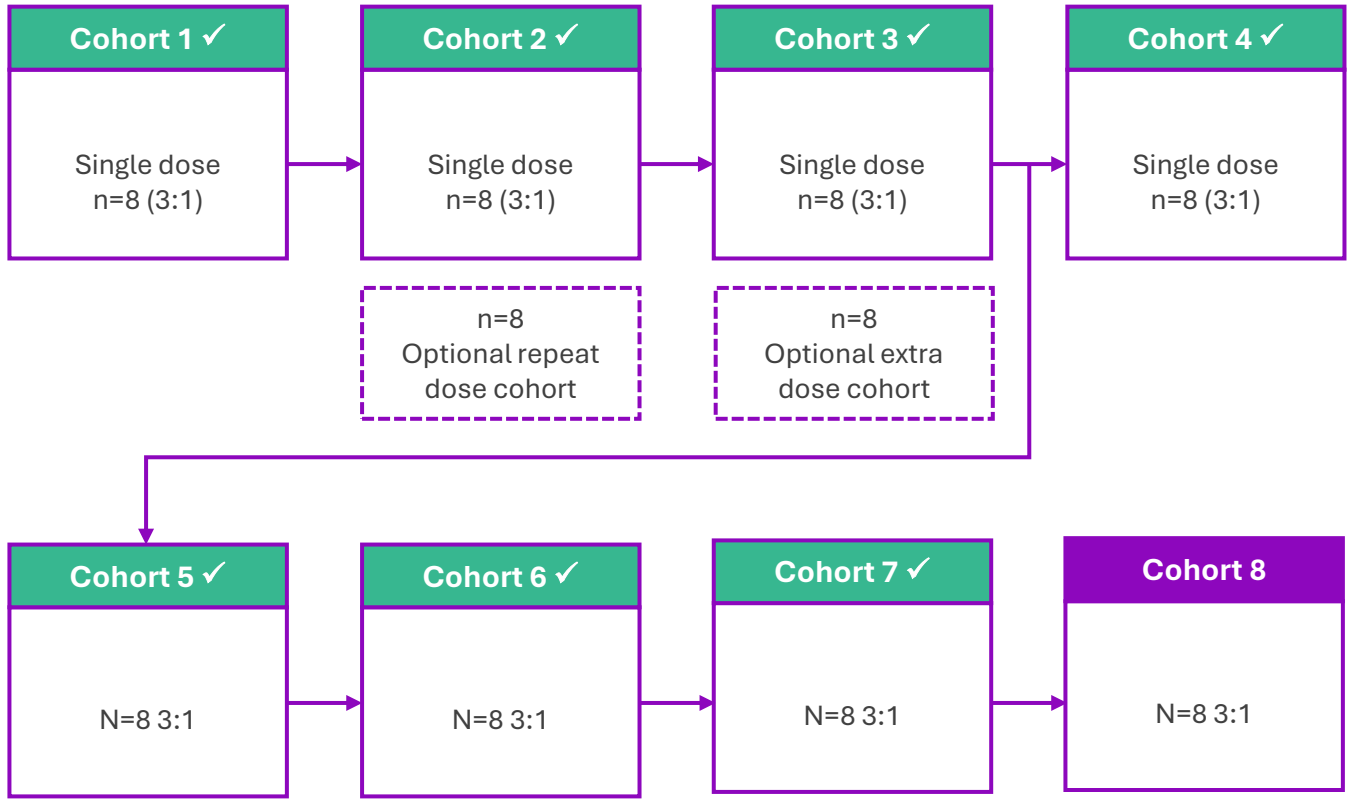




MCC assay is conducted 24 hrs post administration of RCT2100

CF Phase 1 SAD Healthy Volunteer Study (Ongoing)

HV: SINGLE-ASCENDING DOSE



CF Phase 1 MAD Patient Study will test three doses

CF: MULTIPLE-ASCENDING DOSE

Cohort 1

1mg x 4 weeks
n=3 - 6

Cohort 2

Dose TBD x 4 weeks
n=3 - 6

Cohort 3

Dose TBD x 4 weeks
n=3 - 6

optional

Expansion cohort

Dose TBD x 12 weeks
n=6

Safety follow up visits:
4, 12 and 24 weeks after last dose

Primary Ciliary Dyskinesia (PCD)

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PCD is an orphan respiratory disease with no approved treatment

PCD is a rare disease caused by mutations in genes resulting in dysfunctional cilia, leading to deficient mucociliary clearance (MCC), chronic respiratory infections and loss of lung function

>100,000

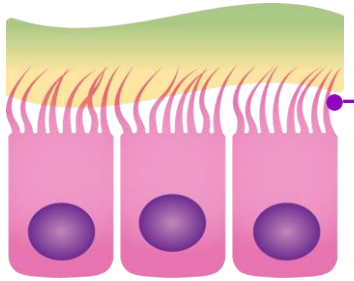
estimated prevalence across mutations in US, UK and EU5[1]

0

approved disease-modifying treatments

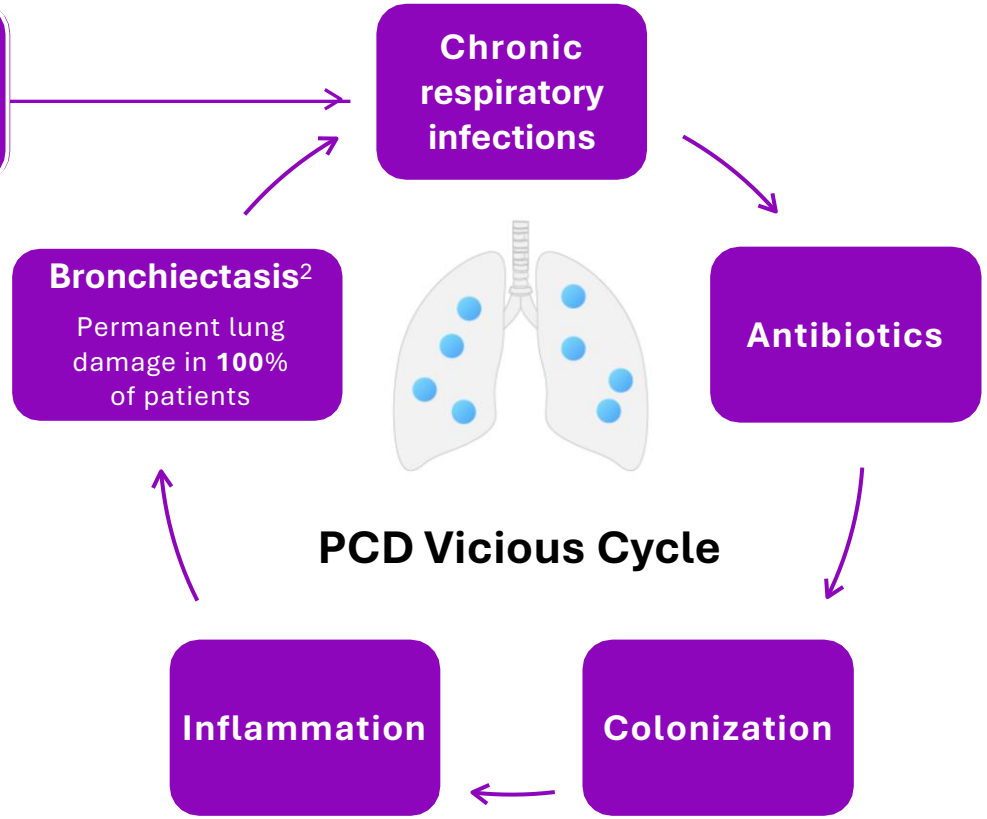
$1B

Market potential for most prevalent genes (DNA1, DNAH5)



Mutations in genes cause dysfunctional cilia*

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



PCD has a high burden disease for patients

“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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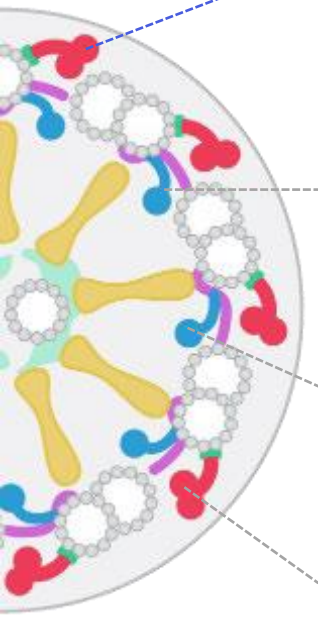
PCD is >$1B franchise opportunity with no competition



		Patients, US & EU5	Estimated sales
RCT1100	**~7%** Outer dynein arm defects **DNAI1**	**~7K**	**~$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

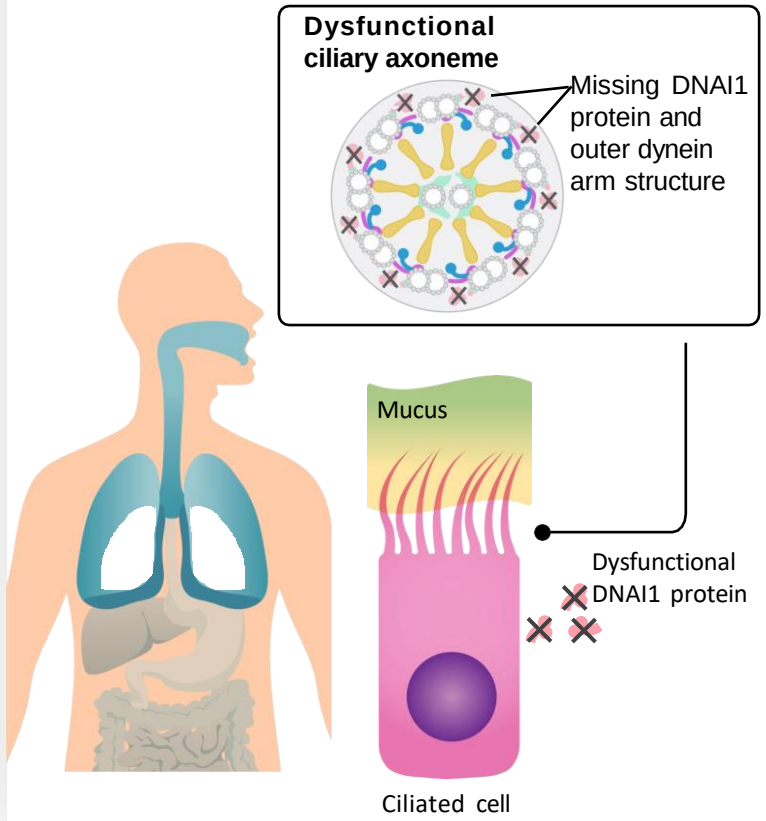
>100,000
US, UK and EU5 prevalence

$1B+
market potential for most prevalent genes

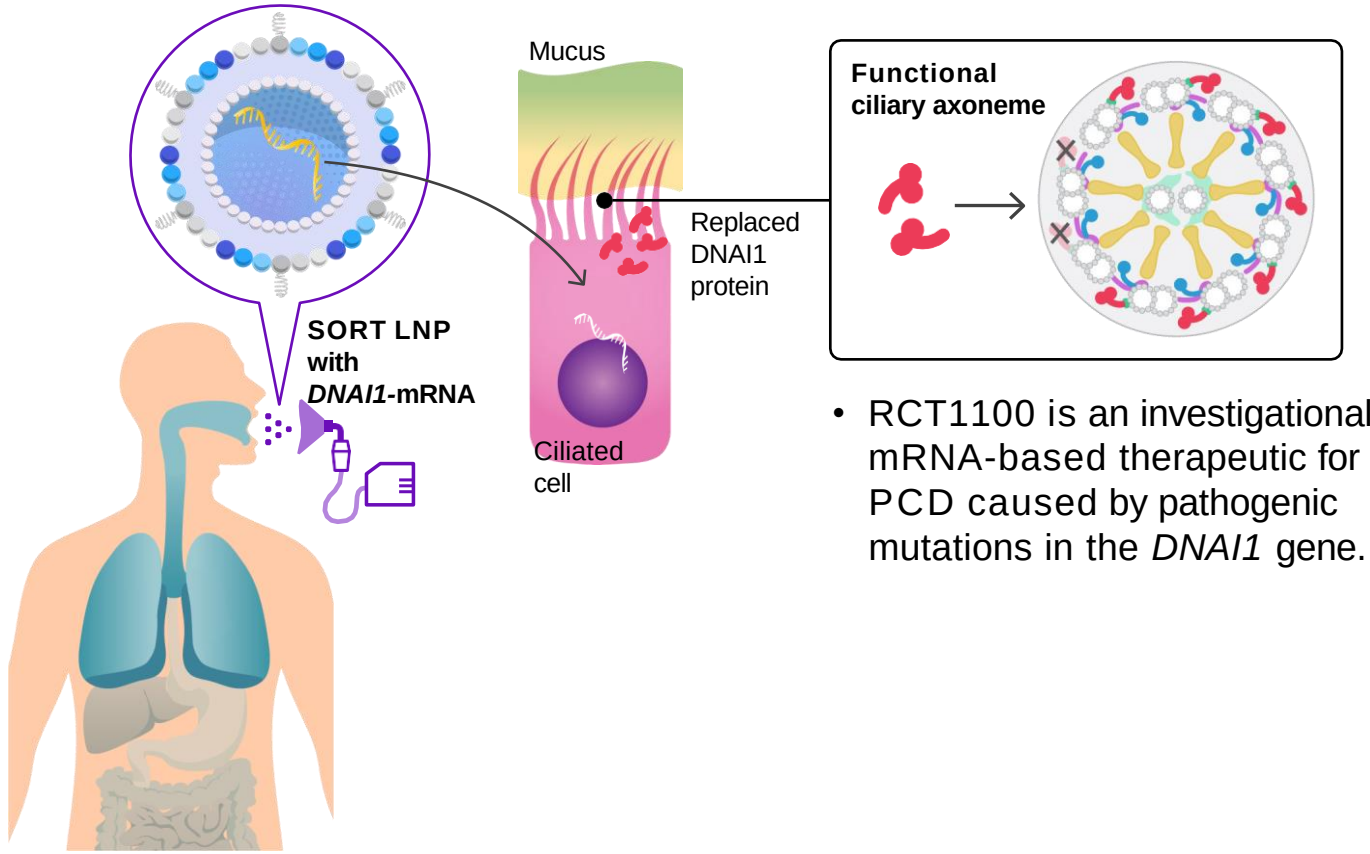
RCT1100 is an inhaled mRNA therapeutic targeting DNAI1 mutation

PCD

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

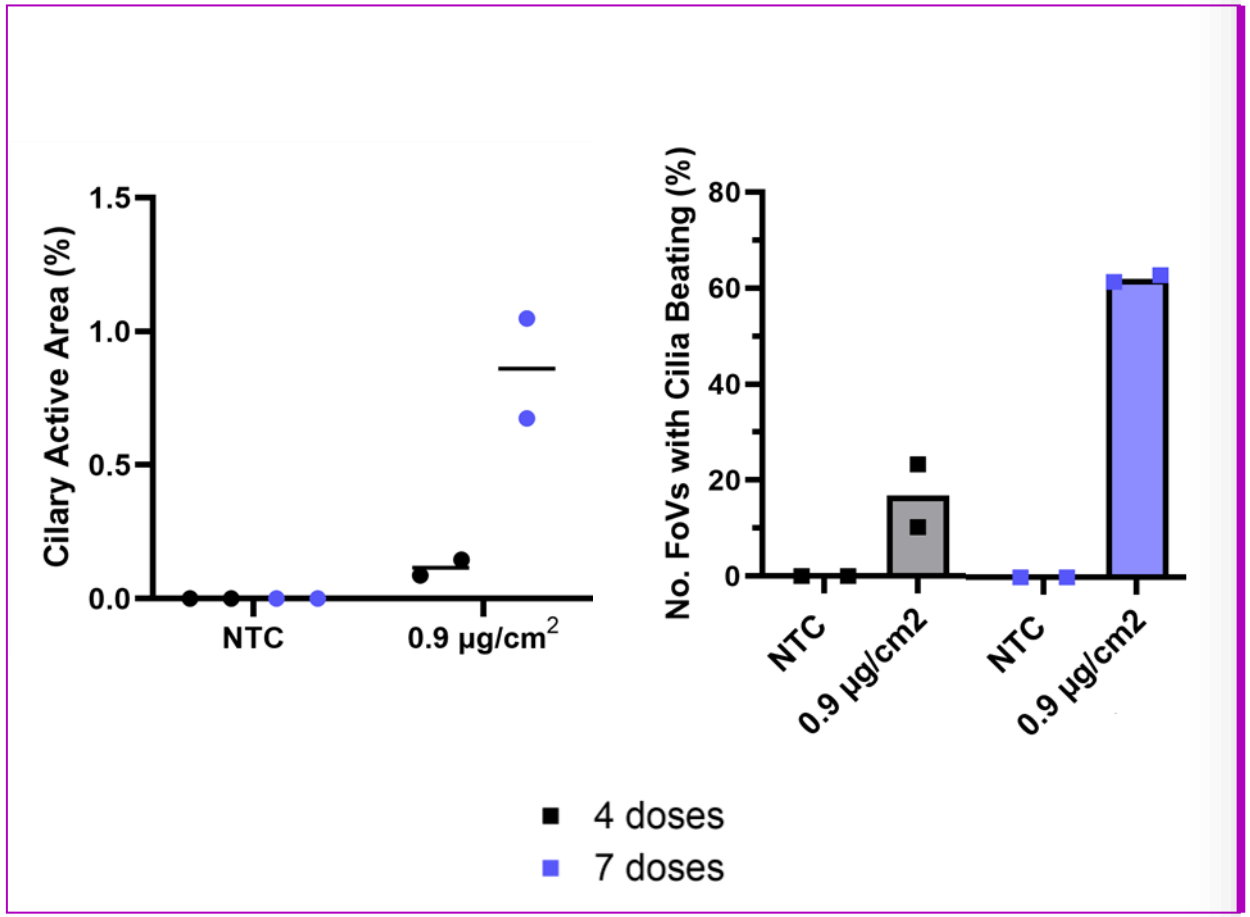


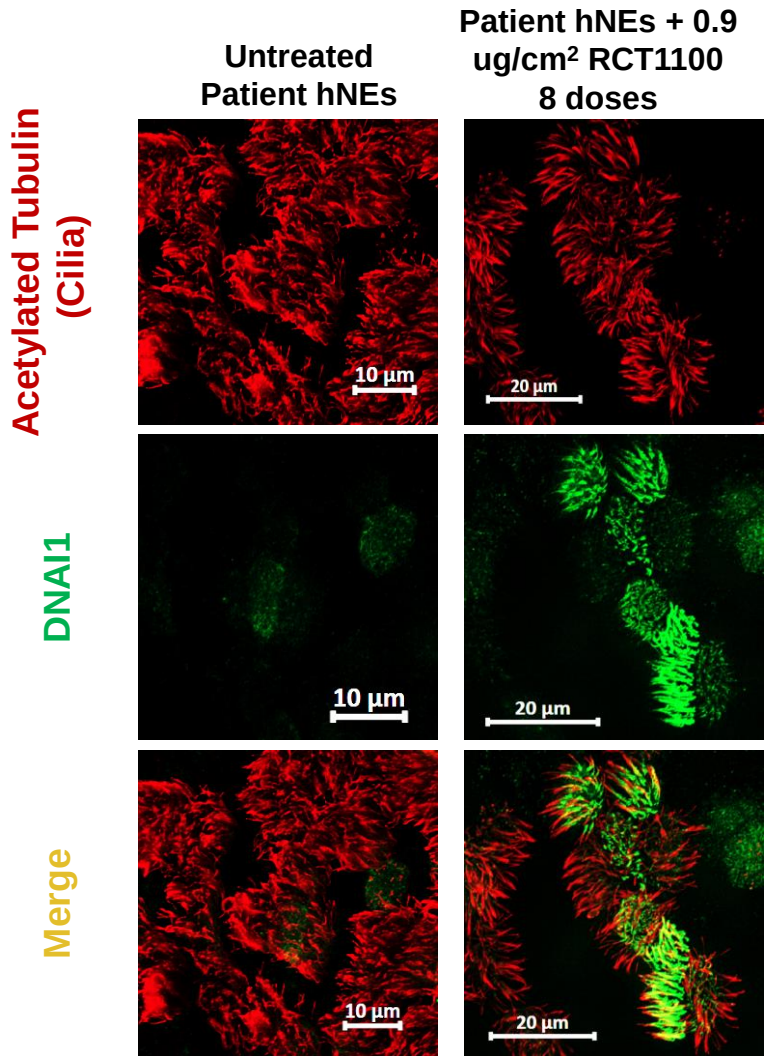
Treatment



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

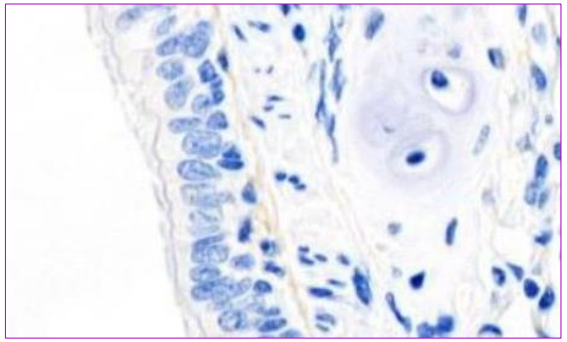
Restoration of DNAI1 protein and ciliary activity at 0.9 ug/cm2 (predicted ~3 mg nebulized dose) following repeated dosing with nebulized RCT1100 in patient hNEs



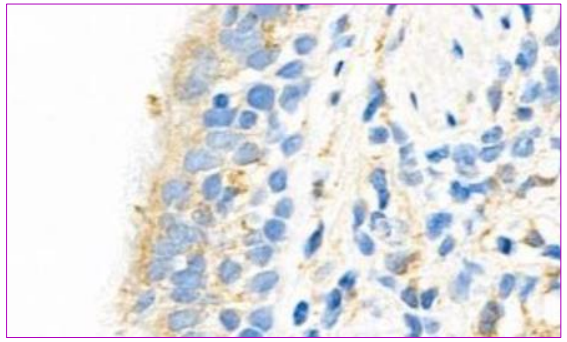


NHP data demonstrate dose-dependent increase in expression of DNAI1 protein in target cells and rapid clearance

Protein level derived from mRNA delivered via nebulization is dose-dependent



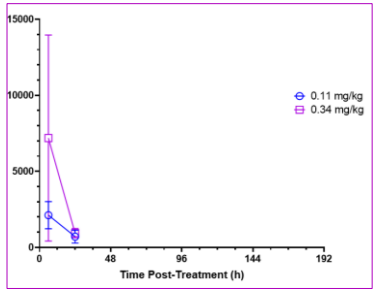
Vehicle Control



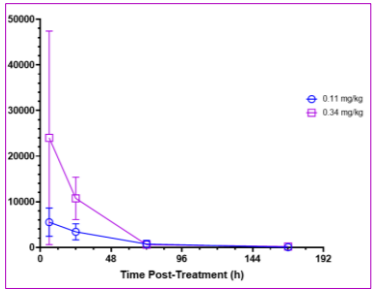
Low dose (3x/week)

Clear signal accumulation and high levels of protein expression are detected in the airway epithelial cells and cilia of NHPs after 6-week repeat-dose studies even at a low-dose (0.14 mg/kg; images at 24 hours post-dose)

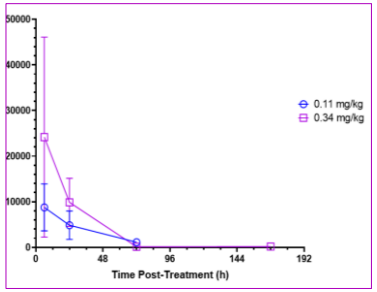
SORT LNP lipids are cleared rapidly from the NHP lung



Ionizable lipid



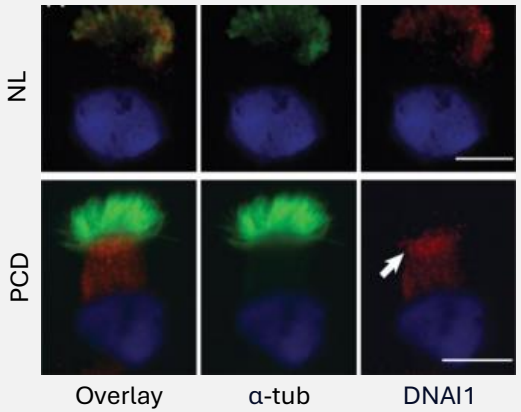
DMG-PEG



SORT Lipid

Ionizable lipid, DMG-PEG, and SORT lipid levels at or below the limit of quantification at 48-hours following single-dose inhalation administration at low dose (0.11 mg/kg) or high dose (0.34 mg/kg)

RCT1100: Phase 1b clinical functional biomarker study to confirm proof-of-activity

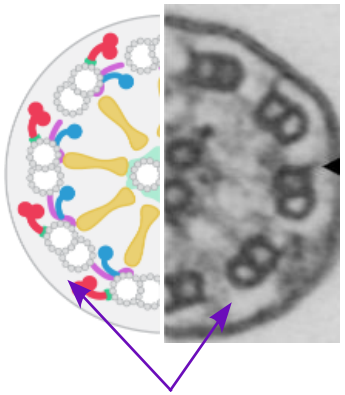


Immunofluorescence (IF)

showing protein expression in disease-relevant cells

PLoS One 8 (2013) e59436

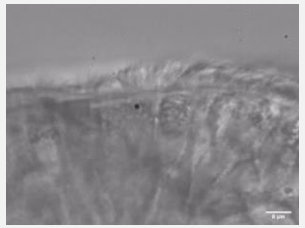
Normal ODA defect structure (e.g. DNAI1)



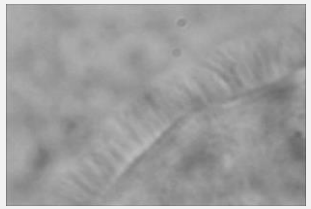
Transmission electron microscopy (TEM)

showing rescue of the ciliary axoneme structure

Clin Chest Med 43 (2022) 127–140



Healthy Normal; Cilia beat at approximately 10 Hz

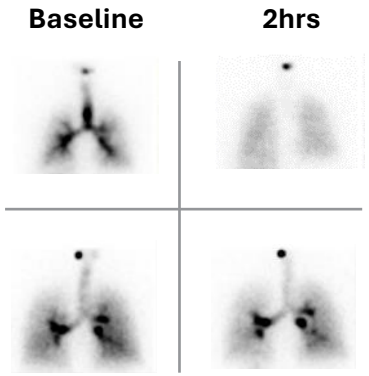


DNAI1; (This is a video, the cilia are not moving)

High-speed video microscopy

showing rescue of ciliary beat frequency and beat pattern

Clin Chest Med 43 (2022) 127–140



Mucociliary clearance (MCC)

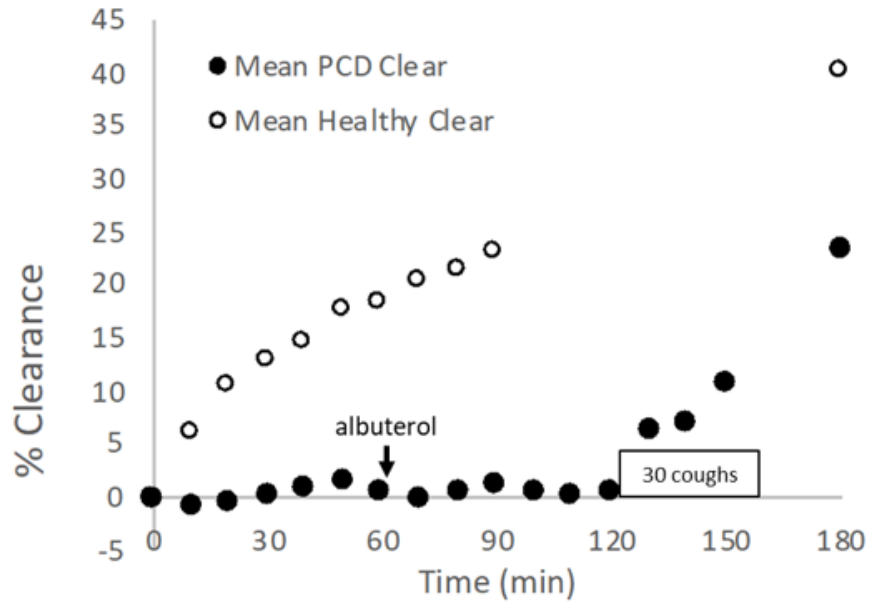
Inhaled radio-aerosol showing whole lung mucociliary clearance

Marthin et al. 2023

Patient data anticipated Q4 ’24

Pulmonary Radioaerosol Mucociliary Clearance is a sensitive assay that is likely to predict clinical benefit

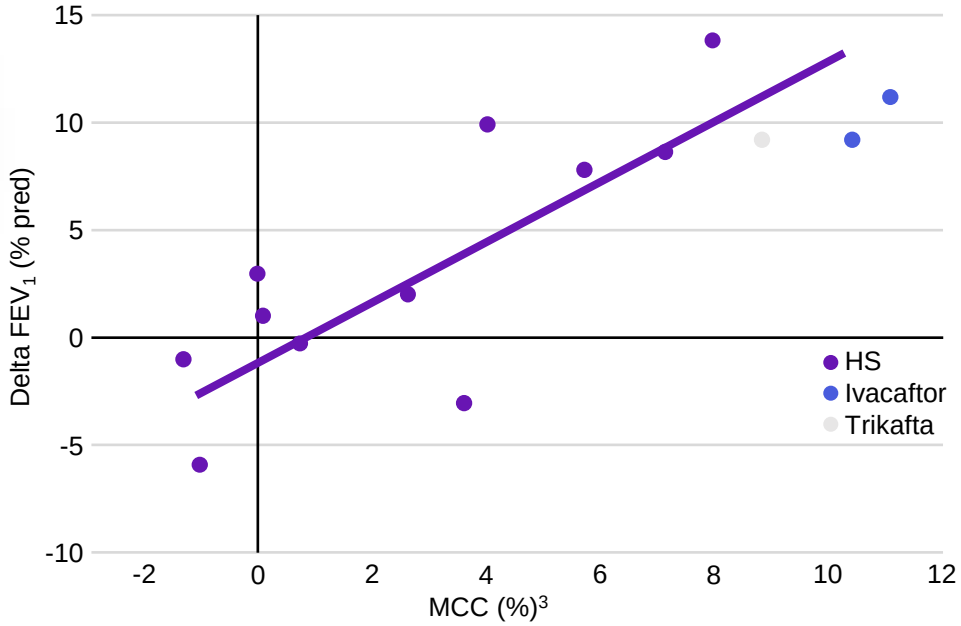
Comparison in MCC in PCD patients vs. Healthy Controls



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 60min and performed 30 voluntary coughs between 120-150 minutes

Absolute change in Whole Lung MCC vs. FEV1 in CF

Relationship between MCC and FEV_1 in patients after HS treatment[1,2], Ivacaftor[4], or Trikafta[5]



1 Donaldson et al., 2020, 2 Correlation between change in MCC (AveClr90) and FEV_1% predicted after 4 weeks of HS treatment. Pearson R^2- 0.67; p = 0.002,
3 Delta AveClr90, 4 Donaldson et al., 2018, data at 1 month and 3 months from baseline, 5 Donaldson et al., 2023, 1 month from baseline

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

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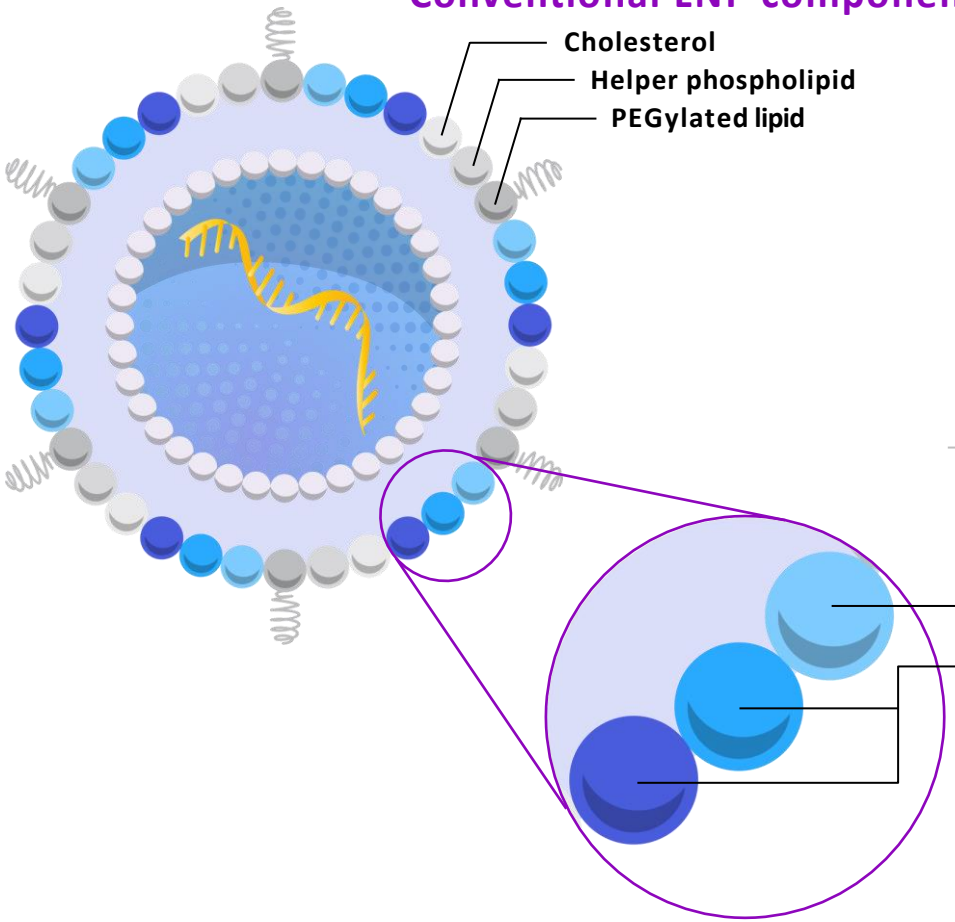
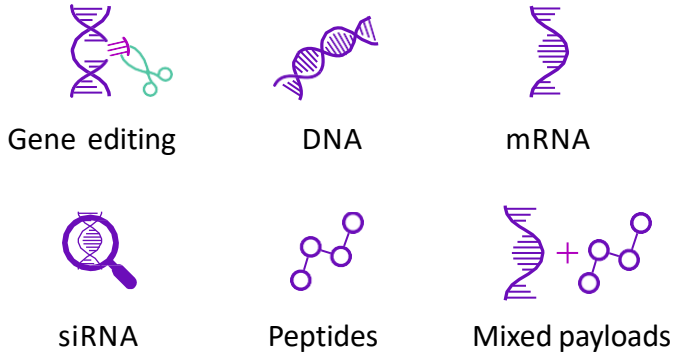
Selective organ targeting lipid nanoparticles **(SORT LNPs)** deliver **diverse genetic payloads** beyond the liver

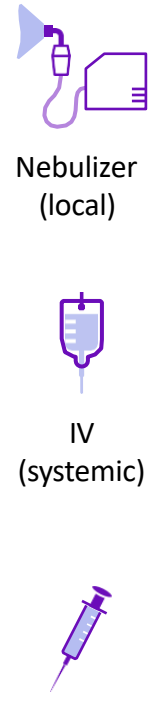
Sort LNP architecture



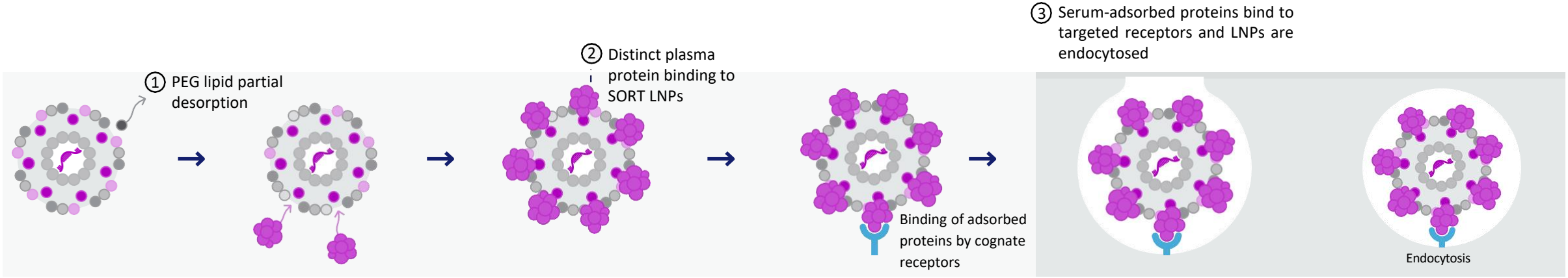
Possible payloads



Administration methods

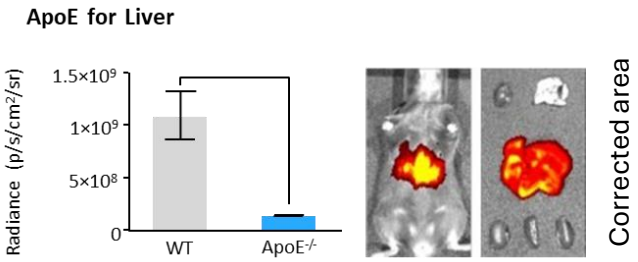


SORT LNPs use an **endogenous targeting mechanism of action** through adsorption of specific plasma proteins

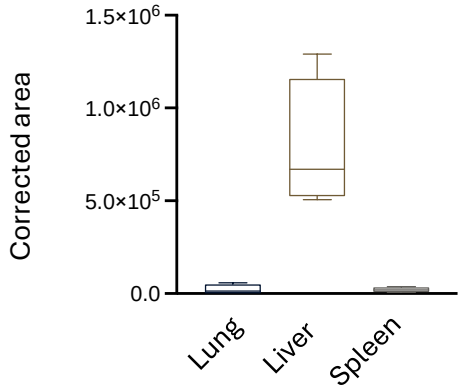


Extra-hepatic delivery of SORT LNPs occurs via an ApoE-independent mechanism

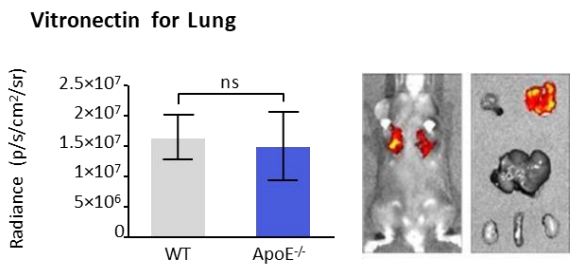
Liver SORT LNP



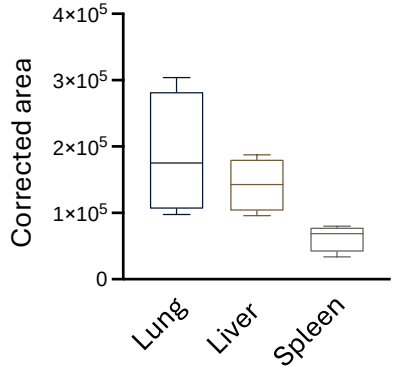
Tissue-specific expression of hits



Lung SORT LNP

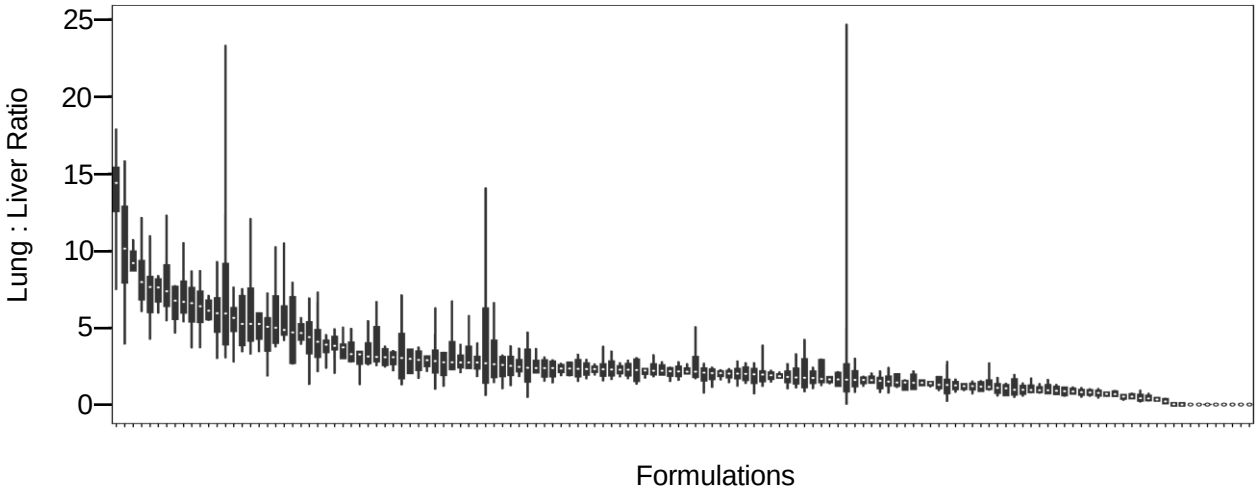


Tissue-specific expression of hits

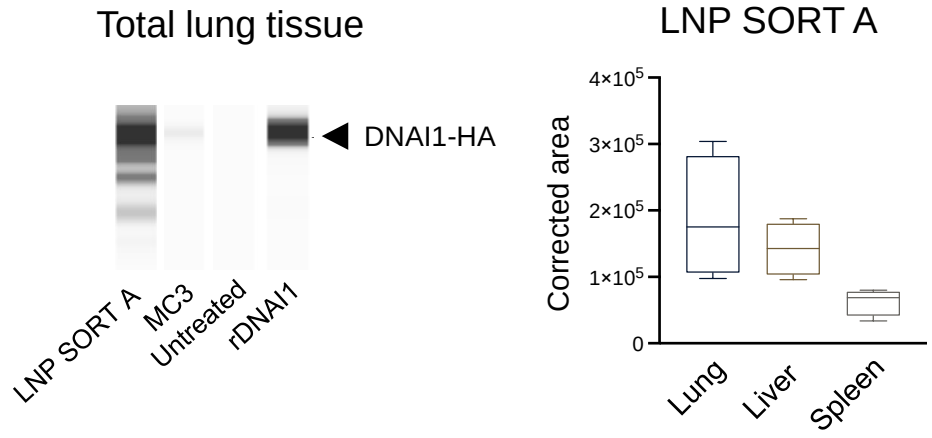


IV SORT LNPs demonstrate differential extrahepatic selectivity

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)

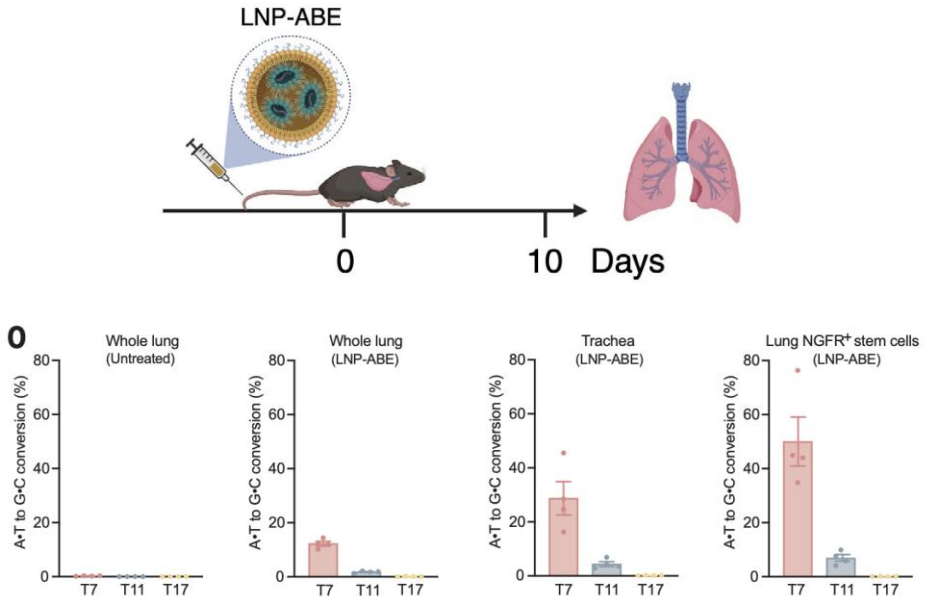
Direct and Persistent in vivo Gene Editing of Mouse Lung Epithelial Cells

Science

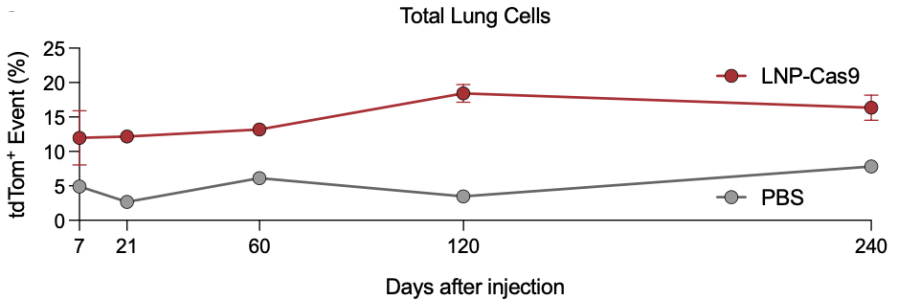
GENE EDITING

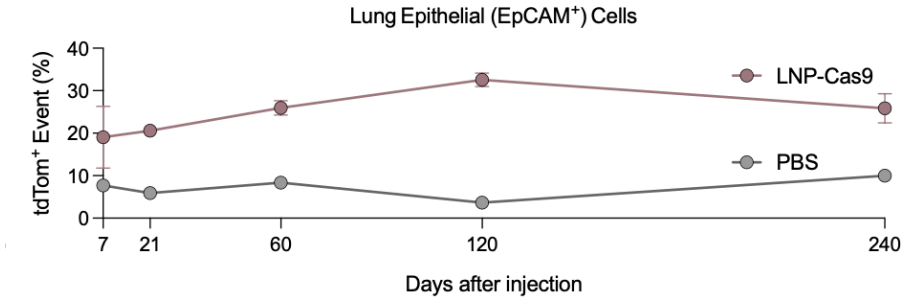
In vivo editing of lung stem cells for durable gene correction in mice

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*





- 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.

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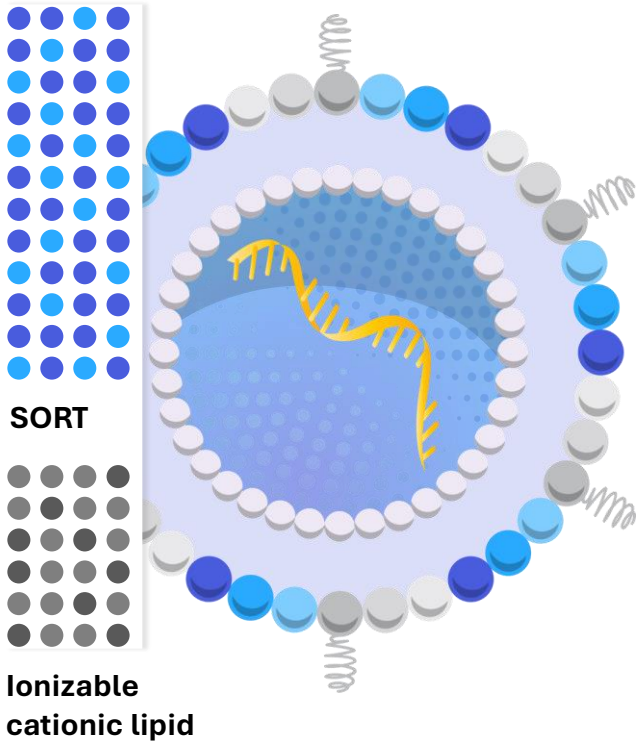
* Data from Science (2024)

Only LNP platform that provides **FTO** with a **large and chemically diverse library** of LNPs **without** requirement for **stacked-licenses**

Library

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



Patents

New lipids, SORT LNPs, Formulations, MOAs, Therapeutics, Manufacturing

150+	40+	30+	300+ class
applications	issued patents	patent families	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

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Corporate Overview

July 2024