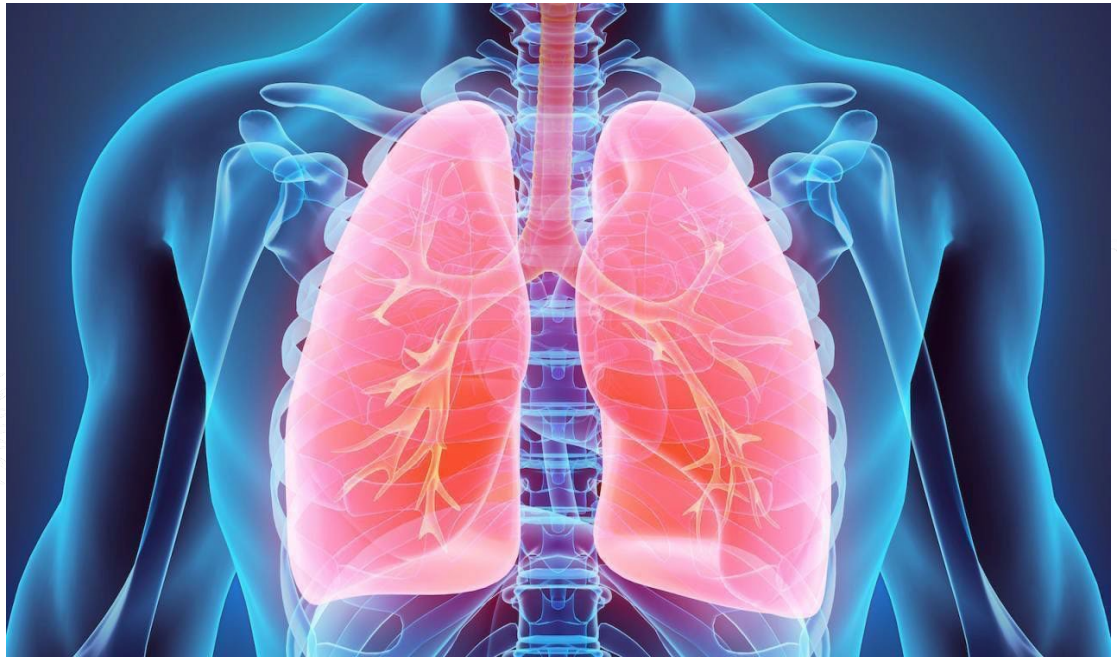


RIGImmune

Targeted non-LNP Delivery of RNA Therapeutics

Non-Confidential Overview
June 2024

Investment Opportunity

NEED™ (Nano Emulsion for Enhanced Delivery) Platform Technology

Effective Delivery of RNA Therapeutics for the Treatment of Diseases with High Unmet Needs

- **RIG-101 – pan-viral inhibitor of the transmission of respiratory diseases in at-risk patient populations**
  - **RIG-101 intranasal (IN)** (RIG-I agonist) advancing to clinic in 3Q2025 for viral transmission inhibition in asthma patients
- **RIG-301 Solution for Inhalation - CFTR mRNA for the treatment of cystic fibrosis (CF)**
  - Efficient delivery of Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) mRNA with the potential to produce wild-type CFTR protein in lung bronchial epithelial of CF patients, **independent of genotype**
  - Phase 1-ready inhaled formulation proceeding through preclinical POC studies with potential to enter clinic in 1Q'26
- **Advancement of non-LNP NEED platform technology**
  - Multiple routes of administration with an aqueous formulation in development – intranasal for upper respiratory tract, nebulized solution for lower respiratory tract, and subcutaneous
  - Utilization for ocular and dermal diseases with high unmet clinical needs
  - Potential capability to deliver gene therapies, DNA, and other modalities

Experienced Management Team & Solid Investor Support

RIGImmune

Martin Driscoll
Chief Executive Officer & Chair

spring bank pharmaceuticals · onconano · Javelin · Schering-Plough · ViroPharma Incorporated

Jag Shur, PhD
Chief Technology Officer

Sub Intro · nanopharm · gsk

Susan Sobolov, PhD
President and COO

CAELUM BIOSCIENCES · Pfizer · ALEXION · NOVARTIS

Kazuhiro Ito, PhD, DVM
Co-founder, Subintro

Sub Intro · Imperial College London · RespiVert

Garth Rapeport, M.D.
Co-founder, Subintro

Sub Intro · gsk · RespiVert · PULMOCIDE

Brett Haumann MD
Clinical adviser

Theravance Biopharma · gsk

F-PRIME CAPITAL PARTNERS · Alembic Touching Lives over 100 years · Bill & Melinda Gates foundation · connecticut innovations · YALE UNIVERSITY

NEED™ PLATFORM

Delivery of nucleic acids critical for therapeutic success

RIGImmune

Transfection efficiency required

- RNA must cross cell membrane to reach cytoplasm.
- Respiratory epithelium presents significant barrier to intracellular delivery.
- Ideal formulations should promote rapid cellular endocytosis and cytoplasmic entry.

Site targeting

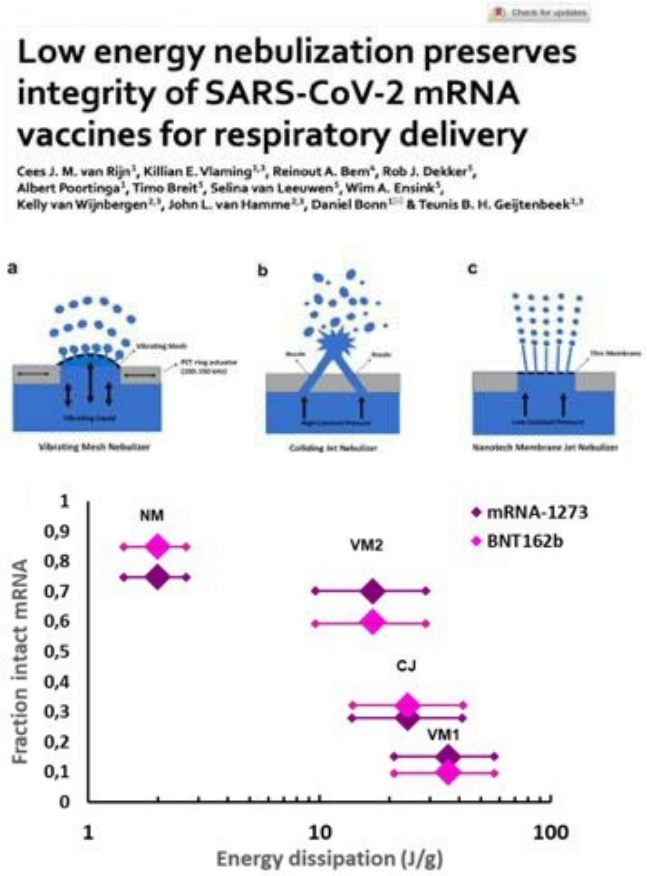
- Effective formulations must deliver modality to site of viral replication in the respiratory tract via nasal or inhaled routes.
- Formulations must be well tolerated, non-irritant and promote sustained cellular entry.
- Targeting factors include viscosity, thixotropic properties and surface tension in addition to emitted dose volume, spray pattern, plume geometry, droplet size distribution and velocity of emitted droplets

scientific reports

OPEN

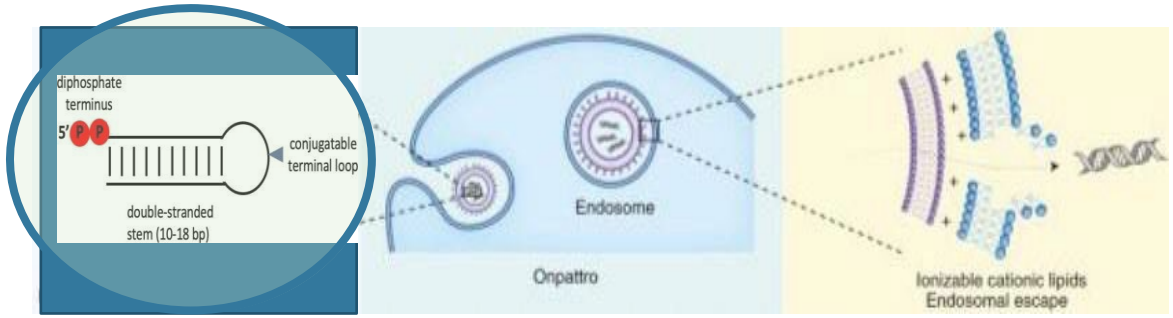
Low energy nebulization preserves integrity of SARS-CoV-2 mRNA vaccines for respiratory delivery

Cees J. M. van Rijn[1], Killian E. Vlaming[1,3], Reinout A. Bem[2], Rob J. Dekker[1], Albert Poortinga[1], Timo Breit[1], Selina van Leeuwen[1], Wim A. Ensink[1], Kelly van Wijnbergen[2,3], John L. van Hamme[2,3], Daniel Bonn[1,✉] & Teunis B. H. Geijtenbeek[2,3]



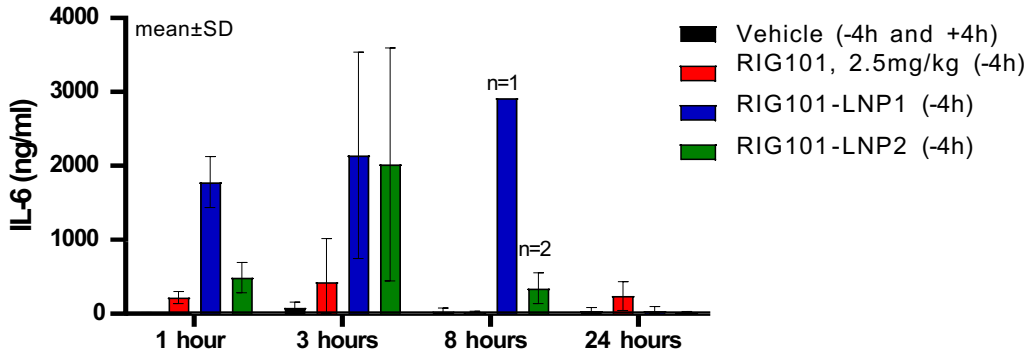
LNPs - unlikely option for respiratory delivery of nucleic acids

Lipid nanoparticle (LNPs) delivery systems are highly pro-inflammatory in the respiratory tract



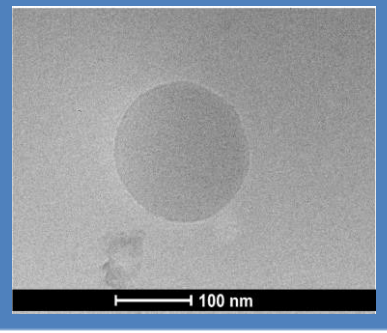
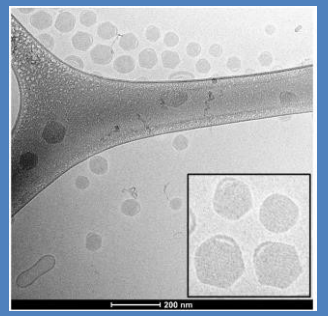
- Cells are protected by their lipid bilayer from allowing in highly charged and large molecules like RNA therapeutics
- LNPs evolved to neutralize and compact RNA molecules to enable uptake by endosomal process **BUT**
- LNP release of cargo into cytoplasm is highly toxic to respiratory epithelium due to highly ionizable components
- The LNP components activate multiple inflammatory pathways and induce IL- 1b and IL-6 which leads to inflammation, sickness and death in animals

RIG-101 formulated into LNPs & dosed IN in mice showed poor tolerability and no antiviral effects



- Greater mortality rates in animals treated intranasally by LNPs
- Animals dosed IN with LNP showed increase in IL-6, IL-10 and TNF-a relative to controls and formulation related

NEED™ Technology Compares Favorably with LNPs

Feature	NEED™ 	LNP 
Structure	Amorphous structure supported by an internal mesh structure.	Well-defined hexagonal internal structure.
Number of Components (excluding Buffers)	2	4+
Tolerability	GRAS excipients and know-use in respiratory medicines.	Pro-inflammatory.
Tensile Strength	Highly compressible.	Cubsomic rigid structure.
Size	80 - 200 nm.	40-200 nm in diameter with internal striations with spacing of 5-10 nm.
Aerosolization Viability	Diffuse structure enables viable aerosolization from respiratory inhaler devices.	High surface free energy and prone to disruption upon aerosolization, leading to lower aerosol viability.

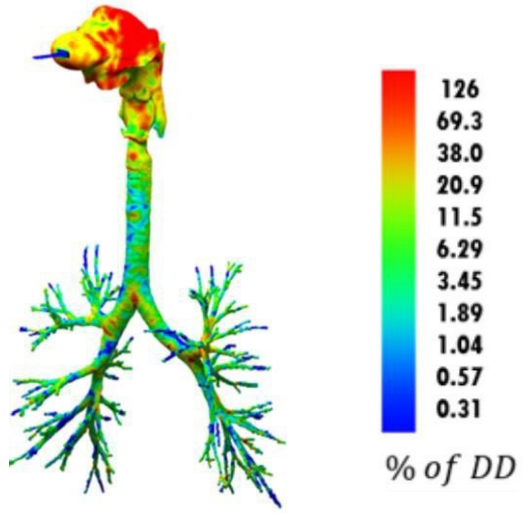
NEED™ (Nano-Emulsion Effective Delivery)

RIGImmune

Proprietary transformation of surfactants and fatty acids into a nano-emulsion complex (non-LNP) that encapsulates a nucleic acid payload with control of particle size and charge.

- **Aerosolization of RNA Cargo**: NEED can effectively aerosolize RNA cargo, ensuring that it can be delivered as an aerosol for tracheobronchial administration.
- **Enhanced RNA Transfection**: NEED aids in RNA transfection, allowing for the RNA to enter cells more efficiently after delivery to the target area.
- **Particle Integrity Preservation**: Despite the process of aerosolization, the integrity of the RNA and nano-emulsion particles is maintained, which is critical for therapeutic effect.
- **Versatile Formulation**: The same formulation that is optimized for aerosol delivery can also be used for subcutaneous (SubQ) administration, demonstrating the versatility of the NEED platform.

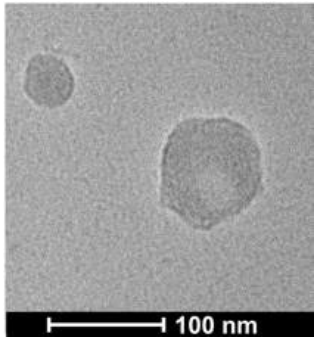
NEED Delivery from VMN



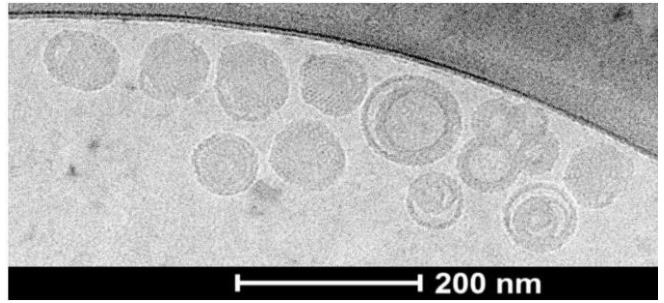
MMAD = 2.69 µm
FPF% = 55.8%

Predicted Regional Deposition of RIG-101 in NEED Platform upon Nebulization

Pre Aerosolization-Delivery

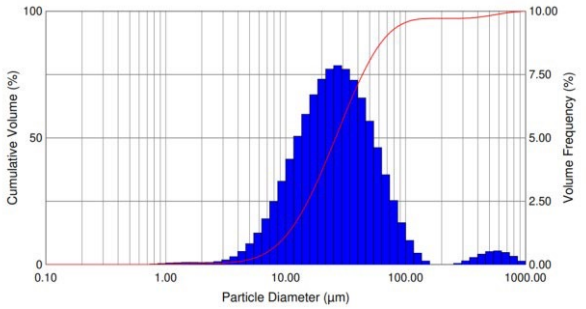


Post Aerosolization Delivery



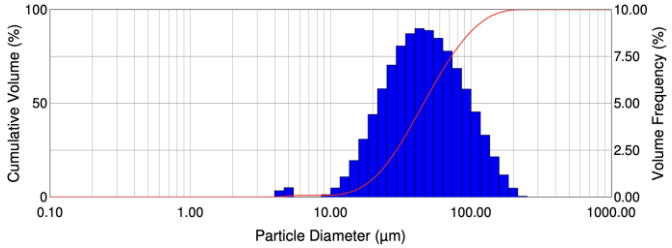
Intranasal Delivery – 1st NEED™ Clinical Formulation

NEED Delivery from MAD

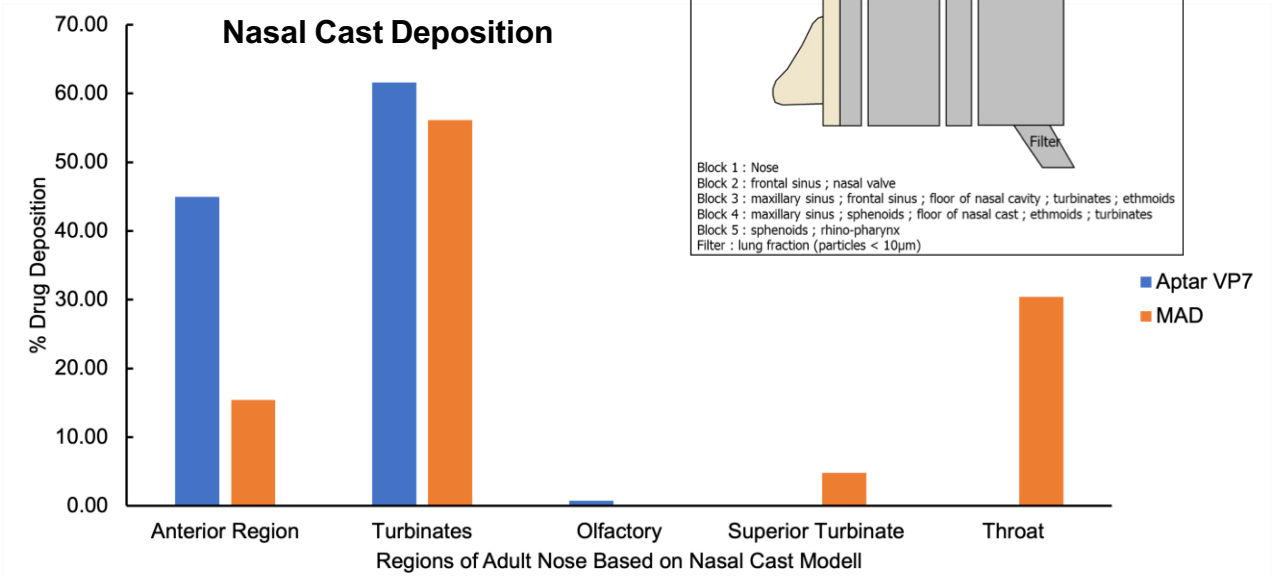


d_{10}= 9.5 µm, d_{50} = 26.0 µm, d_{90} = 68.8 µm

NEED Delivery from VP7



d_{10}= 20.2 µm, d_{50} = 45.9 µm, d_{90} = 105.4 µm



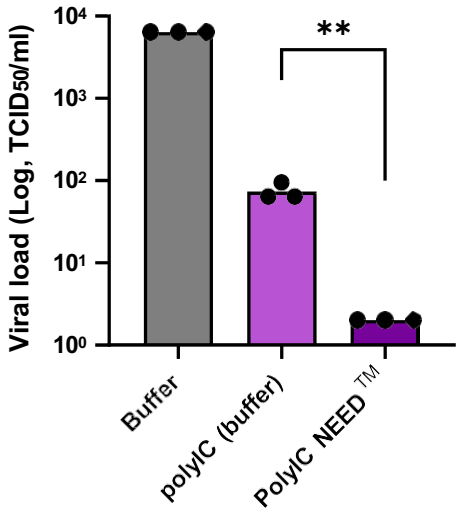
- **Efficient Intranasal Deposition**: Aerosolization using MAD nasal device or Aptar VP7 ensures targeted and efficient delivery of the NEED nanoemulsion directly to the nasal mucosa.
- **Preserved Nano-emulsion and RNA Integrity**: The aerosolization process maintains the stability and functionality of both the nano-emulsion and RNA cargo.
- **"Phase 1 ready" Formulation:** Formulation process has been scaled up and stability demonstrated.

Expansion Opportunities for NEED™ Platform

Poly IC

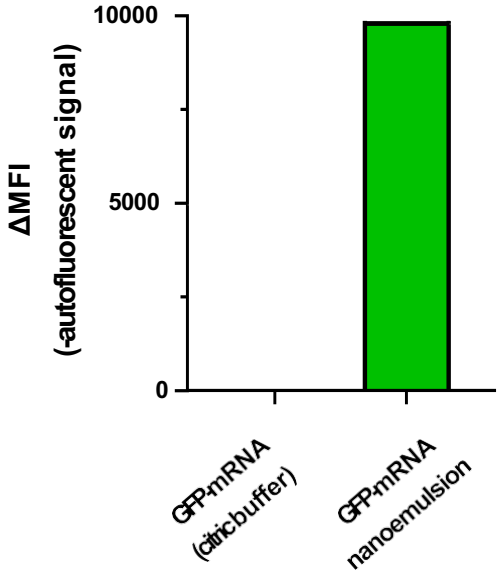
polyI:C (a TLR3 agonist) were applied apically on Day -1 and Day 0 (1hr) before virus inoculation.

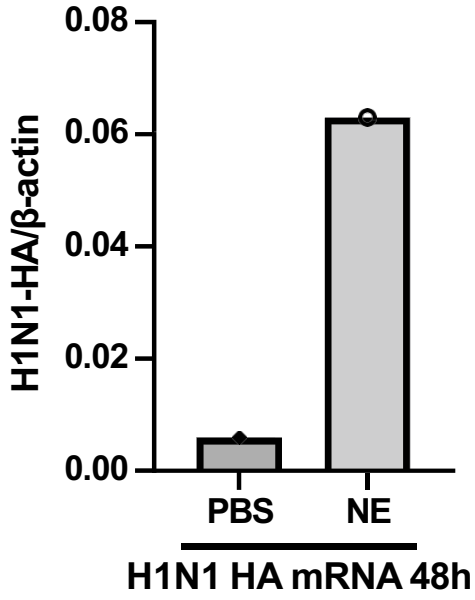
Viral load
[Day 1 post infection]



mRNA

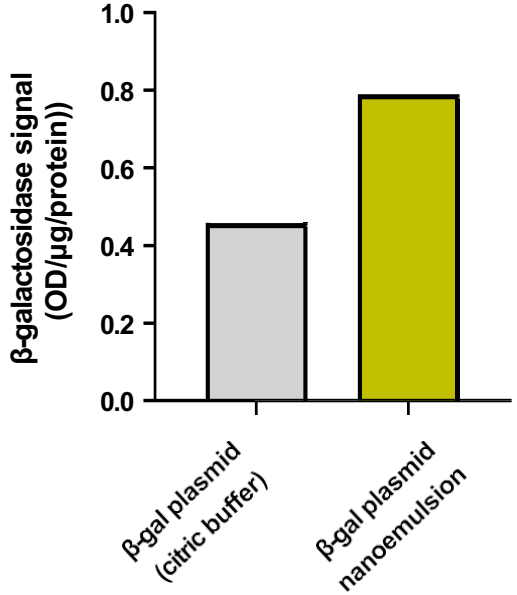
GFP coding mRNA was applied apically and cells were collected 24hrs post treatment for FACS analysis.





dsDNA

β-galactosidase coding plasmid was applied apically and cells were collected 24hrs post treatment for β-galactosidase enzyme activity analysis.



Future development plans – dry powder formulation, delivery of other modalities including DNA and gene therapies, and delivery to broader sites, e.g., ocular and dermal

PAN-VIRAL TRANSMISSION INHIBITION

Company Progress & Strategic Mission

RIGImmune

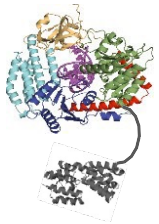
RIGImmune

Anna Marie Pyle, PhD

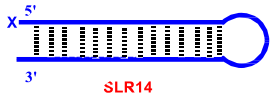
Yale University Sterling Professor, HHMI investigator Co-discoverer of the RIG-I receptor family.

Akiko Iwasaki, PhD

Professor of Immunobiology, Molecular, Cellular and Developmental Biology at Yale University. Demonstrated RIG-I functions as an immunomodulator.



RIG-I activated state



Stem Loop RNA Therapeutics *("SLRs")*

Novel oligonucleotides for diseases caused by RNA viruses

Combined in 2022 with…

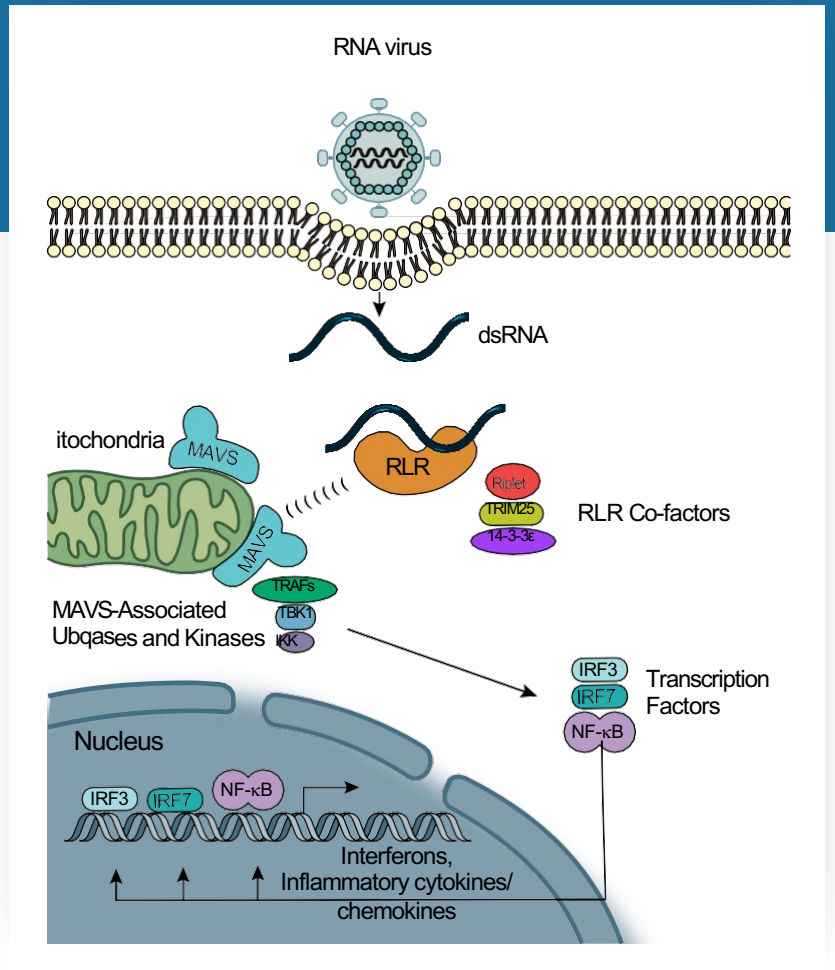
Sub Intro

- **Novel complex of surfactants & fatty acids to encapsulate payloads w/o LNPs**
- **World class respiratory drug and delivery development team**

Advance a platform technology to effectively deliver RNA therapeutics for respiratory diseases with high unmet needs w/o the need for LNP encapsulation

RIG-I Activation Triggers Multifaceted Innate Immune Response

RIGImmune



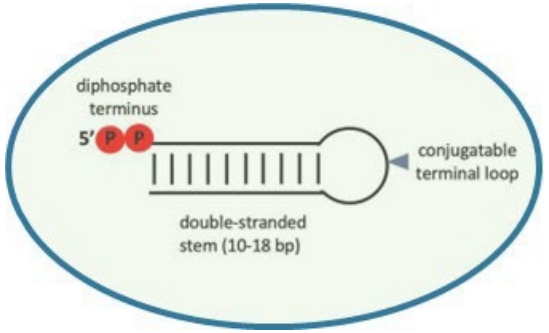
Triggered by double stranded RNA from virus or SLR mimic

Central role in innate immunity and antiviral response

RIG-I – first line of defense against RNA viral pathogens

- Coronaviruses (COVID-19, SARS, MERS)
- Influenza, RSV
- Ebola
- Flaviviruses (Dengue)

"SLRs" – potent ligands to selectively activate RIG-I

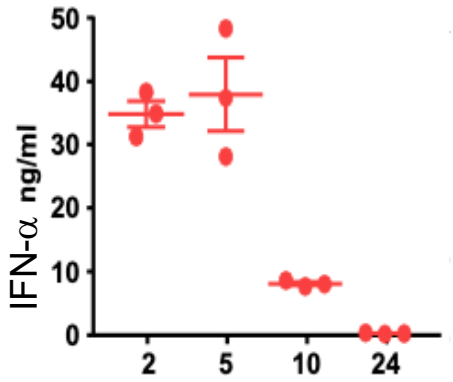


- Viral Respiratory Diseases
- Oncology

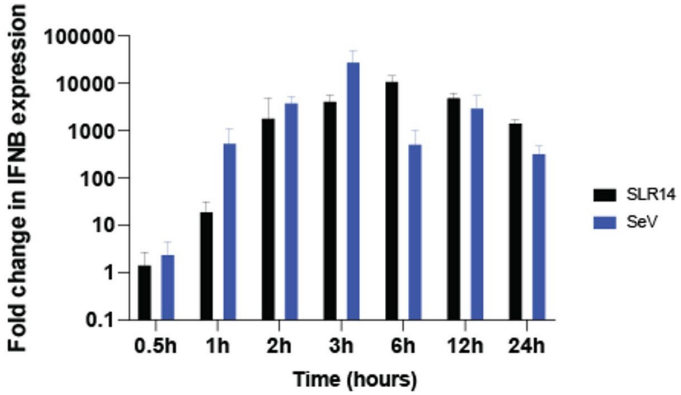
SLRs rapidly activate production of IFN, and also IFN pathway later

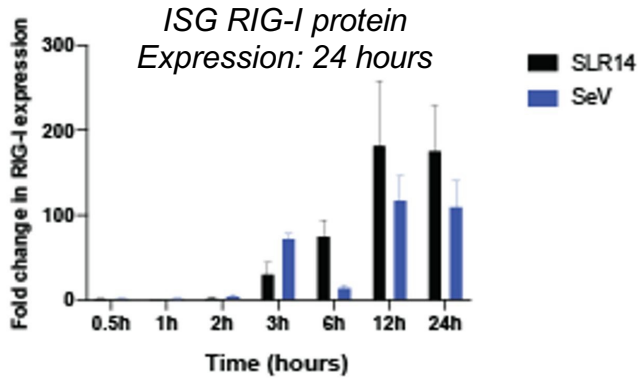
RIGImmune

Mice	A549 cells	ALI nasal epithelium (preliminary)
(Fast interferon production Upon SLR14 IV administration, JETPEI)	(SLR14, Fast interferon production, and 2ndary ISG-gene expression later)	(RIG101 nanoemulsion, Fast interferon production, and associated ISG-gene expression later)

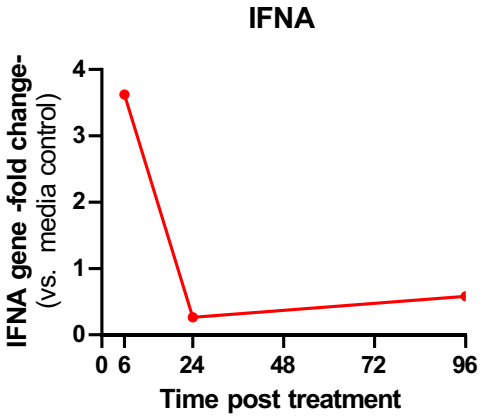


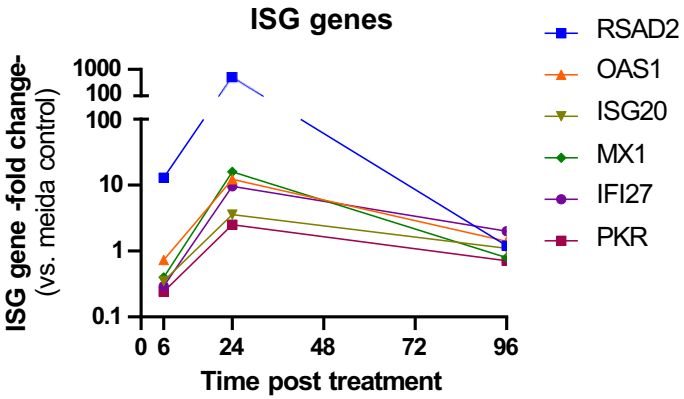
Thoresen, et al. *Molecular Cell* 2022

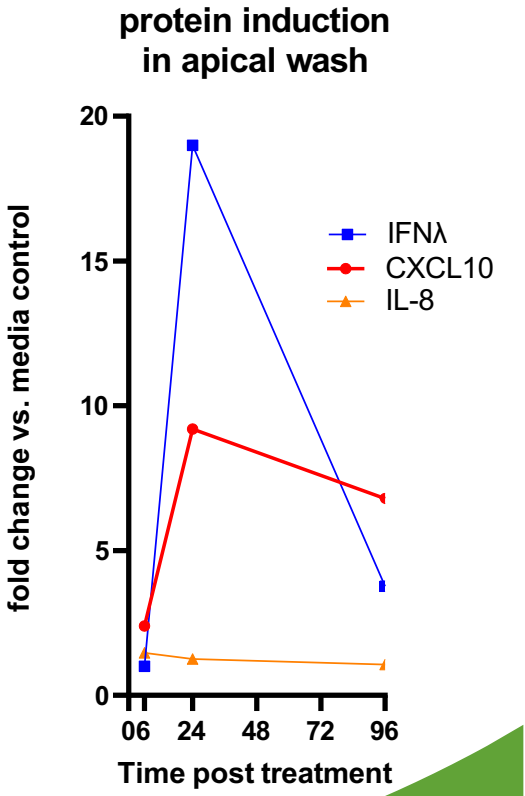




Linehan et al. *Science Advances 2018*





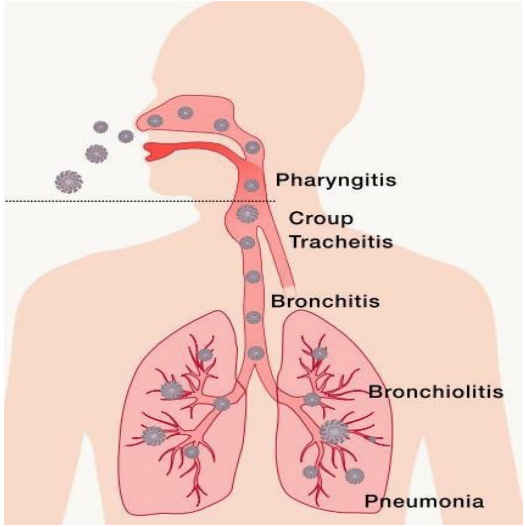


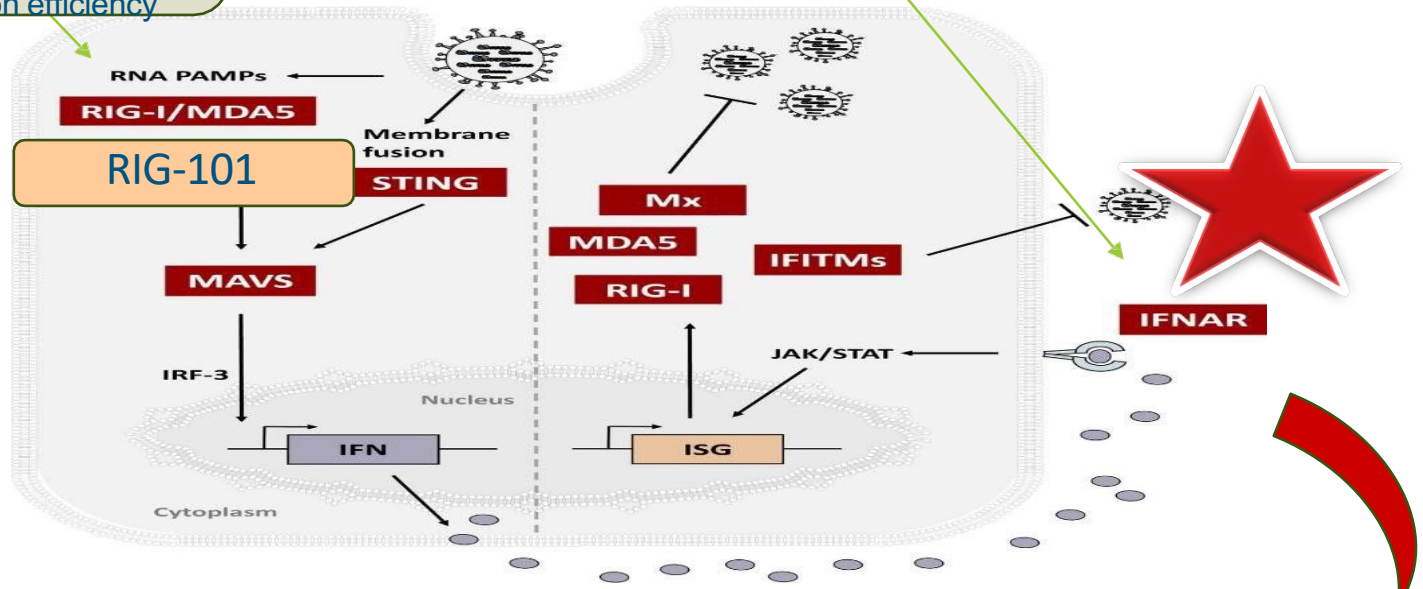
RIG-101 can be delivered to nasal and lung epithelium

RIG-101
Targeted delivery to site of replication
-local concentrations-

Potent activation of RIG-I pathway in nasal epithelium using advanced drug delivery platform
- high transfection efficiency

RIG-101
-Induces local type 1 interferon in respiratory epithelium (via ISG)
- Does not induce inflammatory cytokines

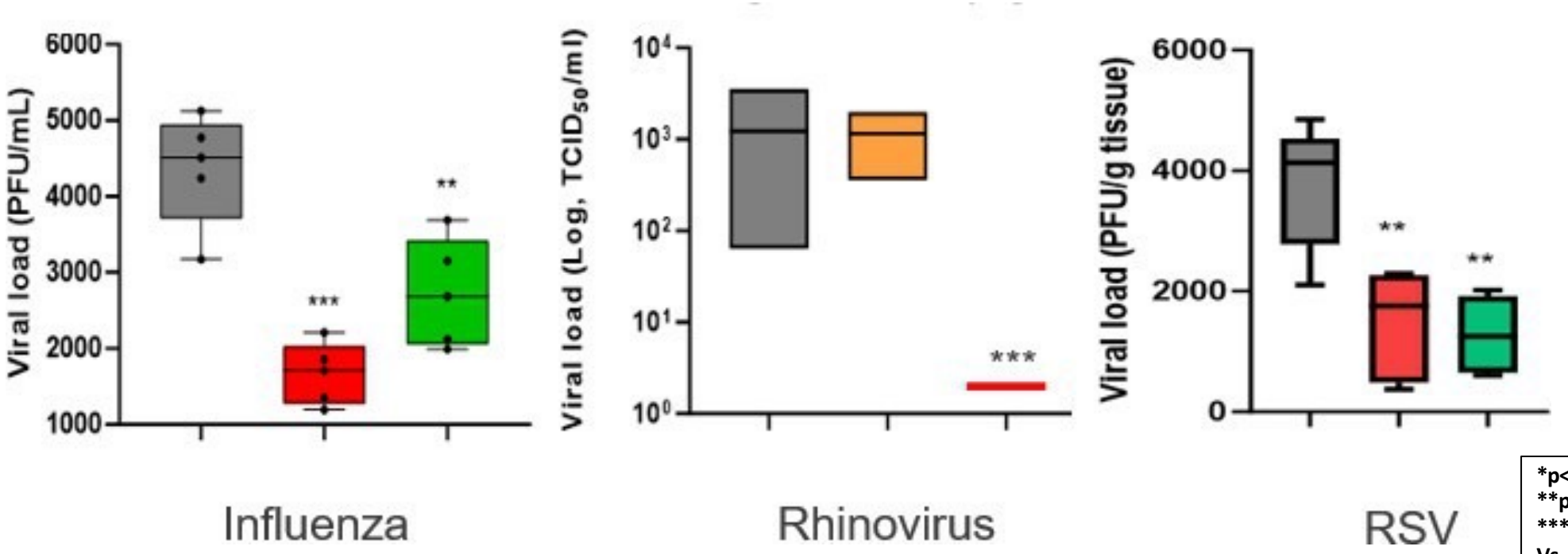




RIG-101 Intranasal (IN)
- pan RNA virus antiviral activity with no risk of emergent resistance
- Local delivery reduces safety and tolerability risks
- Non-LNP Ph 1 ready aqueous spray (reservoir device)

RIG-101 in NEED™ Formulation in Human nasal epithelium (ALI)

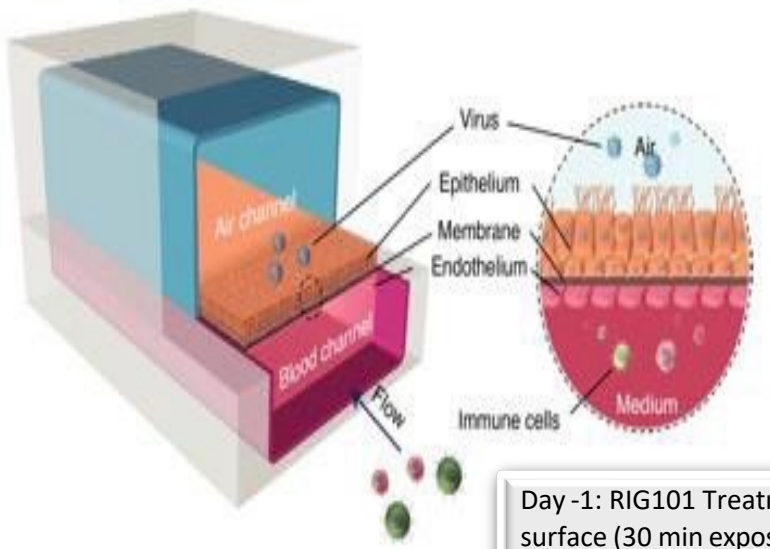
RIG-101 Delivered Intranasally Demonstrated Significant Prophylactic Viral Load Reduction Across Viruses Causing Asthma Exacerbations



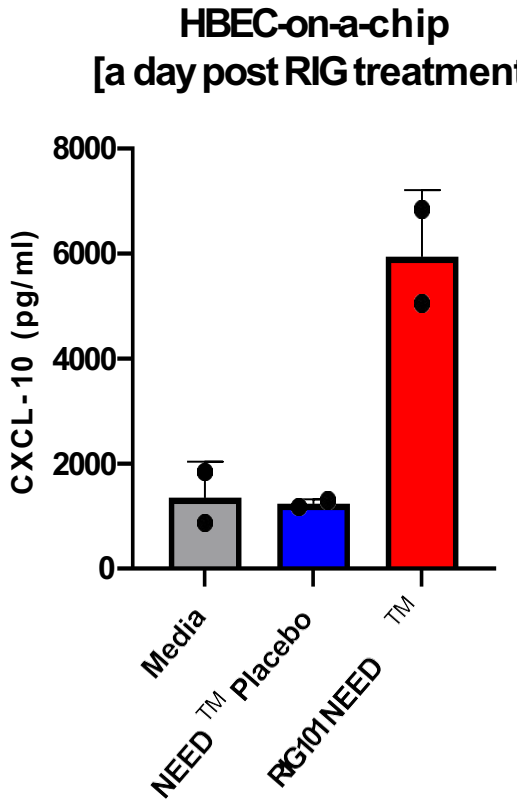
*p<0.05
**p<0.01
***p<0.001
Vs. vehicle control

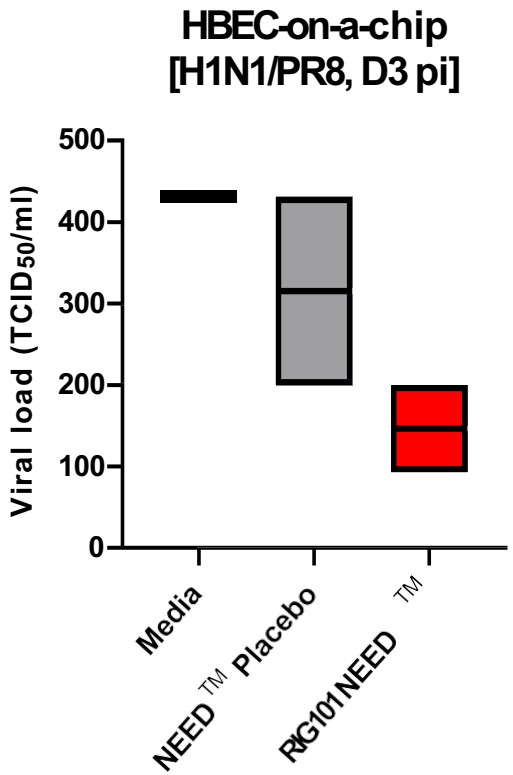
Vehicle control	RIG-101 water	RIG-101 NEED™	Positive control

RIG-101 POC: human lung on a chip against influenza infection



Day -1: RIG101 Treatment at apical surface (30 min exposure)
Day 0: H1N1 infection (1hr +)
Day 1,2,3,6: Apical wash collection





Highly translatable system which closely simulates human breathing

Human bronchial cell line forms pseudostratified epithelium culture

RIG-101 intranasal (IN) Target Product Profile

- Selective RIG-I agonist
  - RNA viruses activate RIG-I, a cellular RNA sensor
- Structurally designed short hairpin RNA oligonucleotide delivers sterilizing immunity
- Pan-viral transmission inhibition pre- and post-exposure
  - RNA virus strain agnostic – the administration of RIG-101 results in potent broad-
    - spectrum antiviral activity, e.g., HRV, RSV, Influenza, & SARS-CoV-2
  - >100 serotypes of HRV circulate thus pan-viral capability essential for use in asthma
- Delivery via NEED™ permits effective local delivery to respiratory tract
- Well-tolerated with ease of intranasal self-administration by the patient
- Once-daily dosing or 2-3x weekly in season (up to 6 months)

RIG-101 IN Progressing to CTA Submission in 2Q'25

- Utilizing highly translatable models of the human nasal epithelium (ALI system and lung on a chip) & multiple mouse studies, RIG-101 has demonstrated viral transmission prevention across HRV, RSV, and influenza with intranasal delivery in the NEED formulation.

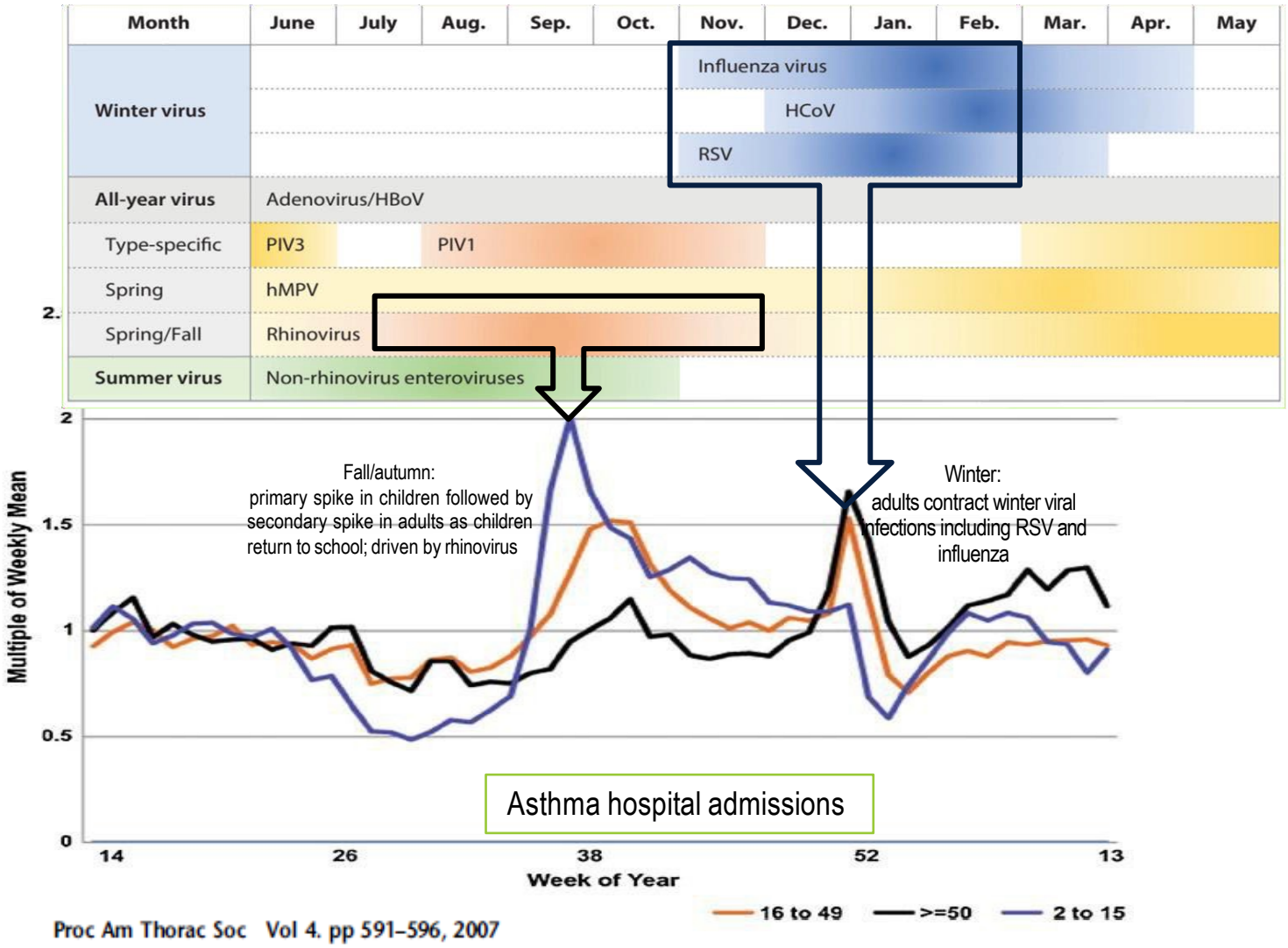
- Non-clinical program has enabled dose and dose regimen projections to design the early clinical development program

- Rat and dog dose range finding studies with intranasal dosing have completed.
  - RIG-101 IN was well-tolerated and no safety signal
  - Doses set for GLP toxicology study with initiation set for Sept '24

- GMP manufacturing will be starting in 4Q2024 to support FIH in mid-2025

- Plan to submit CTA by mid-2025

Seasonal respiratory viral infections drive asthma hospital admissions



- **Loss of asthma control (asthma exacerbations) has serious consequences**
  - Absenteeism, increased medication use and healthcare visits
  - Increased risk of ER visits, hospitalizations and death
    - *Emergency room care and hospitalizations generate ~80% of asthma care costs*
- **Respiratory viral infections are key cause of loss of asthma control**
- **~80% of exacerbations caused by human rhinovirus (HRV)**
- **Current therapies (including expensive biologics) only reduce exacerbation risk by 50-65%**
- **Existing therapies reduce inflammatory allergic responses but do not address viral infections**

RIG-101 IN Clinical Program Design

RIGImmune

Phase 1 HVT
S, T &P K SAD, MAD
2-10mg/ml Nasal Spray
CXCL10 and IFN time and dose response

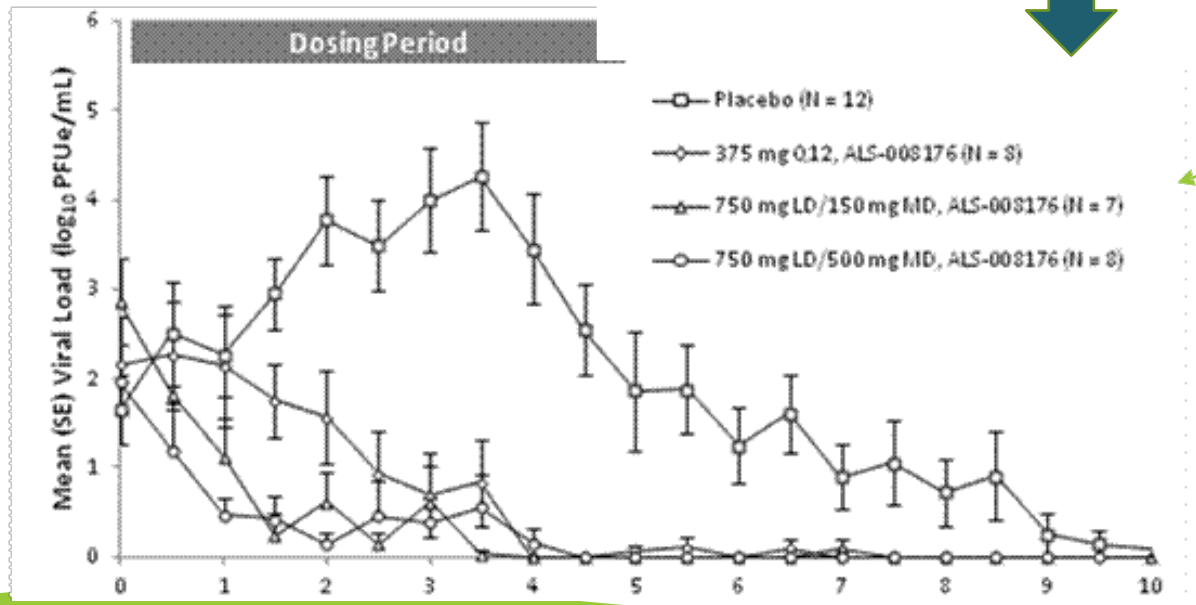
Go / No Go

Phase 2 a
HRV challenge study
n = 40
Cohort 1 HVT Day - 4 and – 7
Cohort 2 HVT Daily dosing
Cohort 3 asthmatics
Viral load , Symptom Scores

Go / No Go

Phase 2 B

Parallel group placebo-controlled seasonal prophylaxis study (12 weeks)
N=400
Protection against loss of asthma control (CompEx)
Viral symptoms, viral load, viral resistance, nasal biomarkers, safety and tolerability

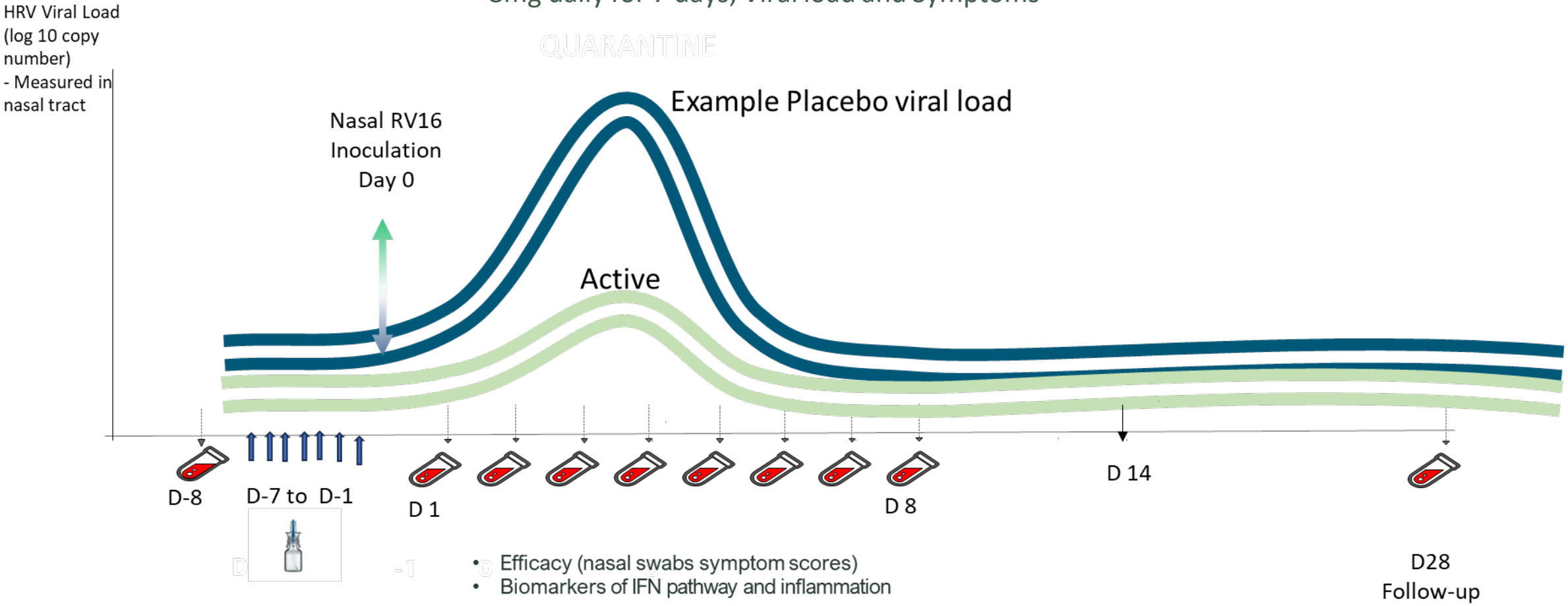


N= 10 per group

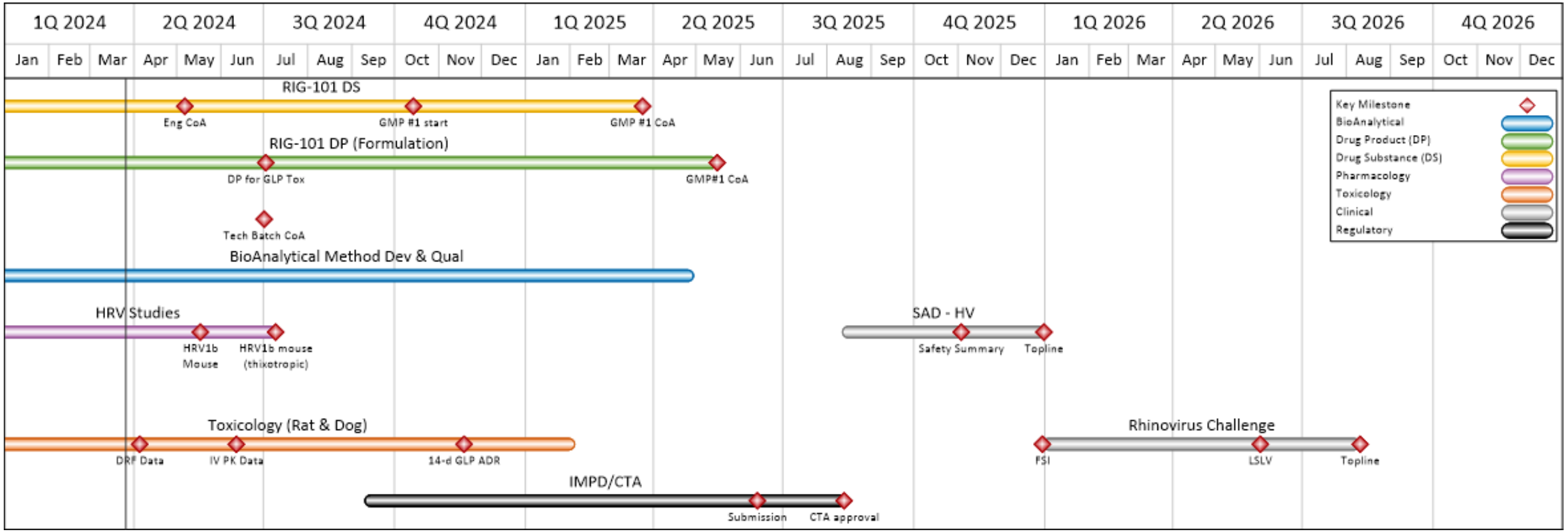
- **Seasonal viral infections are predictable and a good motivation for preventative treatment**
- **Pan-virus protection eliminates the need to identify the causative agent**
- **The direct intranasal delivery with NEED™ provides opportunity for good safety/tolerability**
- **Asthma patients are familiar with intranasal delivery of their medicine**
- **No known competitors in development using this unique pan-viral mechanism-of-action**

RIG-101 IN HRV (Rhinovirus) Challenge

Part B n= 40 Healthy Volunteers; n=40 Asthmatics Intranasal delivery
8mg daily for 7 days; Viral load and Symptoms



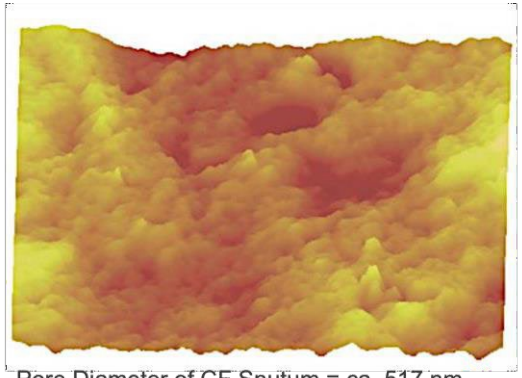
RIG-101 IN Development Plan



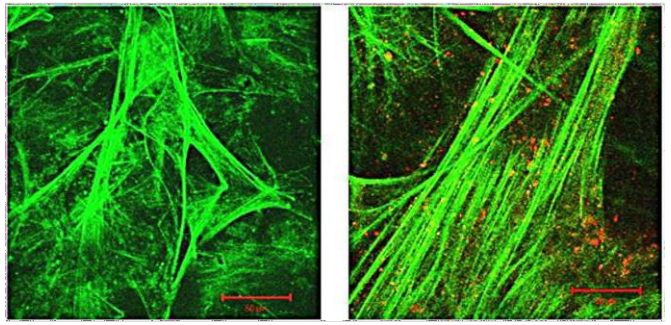
CYSTIC FIBROSIS

Effective delivery of CF treatments to the lungs remains a significant challenge

- **Cystic Fibrosis (CF) is a rare genetic disease caused by a variety of mutations in the CF Transmembrane Conductance Regulator (CFTR) gene**
  - ~40,000 patients in the US
- **CFTR modulator therapies on the market correct the malfunctioning CFTR protein but address only certain CFTR mutations**
  - CF market size ~$6B in 2022
- **A variety of genetic medicines (e.g., AAV gene therapy, mRNA delivery, base editing) are in development but effective delivery of these modalities to the lungs is a significant challenge**



Pore Diameter of CF Sputum = ca. 517 nm



Mucins: 10 – 50 mg/ml; DNA: 1 – 15 mg/ml; Actin: 0.1 – 1 mg/ml

NEED™ formulation overcomes challenges of drug delivery to the CF airways

Inhaled RIG-301 – CFTR mRNA therapeutic formulated with NEED™

- **RIG-301 - a CTFR mRNA therapeutic that will deliver a full length CFTR protein to treat all CF patients, agnostic of mutation**
- **Optimized CFTR mRNA will be delivered as an inhaled aerosol using our proprietary NEED™ formulation**
- **CFTR mRNA production and NEED™ experiments are completed**
  - **RIG-301 (NE) shows significant amounts of CFTR being produced after 72H**
- **Ongoing efforts to demonstrate restoration of normal function in CF human bronchial epithelium (Air Liquid Interface model) and uptake distribution of RIG-301**

Pipeline of Platform & Product Opportunities

RIGImmune

Program	Therapeutic Use	Delivery	Discovery	Preclinical	Phase 1/2
Platform Technology **NEED™** **(Nano-Emulsion Enhanced Delivery)**	Pan-viral prevention of viral respiratory diseases in high-risk populations	Intranasal			
	Rare pulmonary diseases	Solution for Inhalation			
	Ocular diseases				
RIG-101 **(RIG-I agonist)**	Pan-viral transmission inhibition in at risk patients	Intranasal			
RIG-301 **(CFTR mRNA)**	Cystic Fibrosis	Solution for Inhalation			

Financing History & Plan

Capital raised to date:

- **Gates Foundation grants - $3.5M**
- **Private investors - $15M**

Series A Round launched in 2Q'24

Primary Use of Proceeds / Key Objectives

- **Achieve Ph 2a POC viral transmission inhibition for RIG-101 IN**
- **Achieve Ph 1b POC (CF marker data) for RIG-301 Solution for Inhalation**
- **Expand capabilities for the NEED platform to enhance strategic business development opportunities**
- **General corporate purposes & fund company to YE 2027**

Series A Investment Opportunity Summary

STRATEGIC OBJECTIVES

- Demonstrate Ph 2a POC for lead product development candidate, **RIG-101 IN**, as a pan-viral transmission inhibitor in “at risk” patient populations
- Demonstrate Ph 1b POC for 2nd product development candidate, **RIG-301 Solution for Inhalation**, as a novel treatment for a broader set of cystic fibrosis patients than currently-available modalities
- Further advance and expand the capabilities of the proprietary **NEED ™ platform** to demonstrate the effective delivery of a broad range of nucleic acid payloads

GOAL

- Raise new capital in the range of **$45M - $50M**
  - Series Seed Round post-money of **$18.25M** (1H’2022)

USE OF PROCEEDS

- Fund RIG-101 IN through Ph 2a POC
- Fund RIG-301 solution for inhalation through Ph 1b POC
- Further expand NEED™ platform capabilities to include dry powder formulation, aqueous formulation for ocular use, and effective encapsulation and delivery of multiple payloads, e.g., DNA and selected gene therapies
- Extend cash runway through YE 2027

RIGImmune Strategic Opportunities

RIGImmune

RIG-101 IN

- Pan-viral transmission inhibition
- Multiple routes of administration
- Large addressable markets
- Ph 2 POC mid-2026

RIGImmune

RIG-301 Inhaled

- Potential to address broader CF patient population
- Overcomes challenges for CF treatments with respiratory delivery
- Ph 1b POC mid-2027

NEED™ Platform

- Non-LNP delivery of nucleic acids
- Formulations expansion
- Capability to deliver diverse payloads
- Monetization via strategic business development for monetization