ARCTURUS THERAPEUTICS

Building the Next Generation of RNA Medicines

March 2021

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This presentation contains forward-looking statements. These statements relate to future events and involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future performances or achievements expressed or implied by the forward-looking statements. Each of these statements is based only on current information, assumptions and expectations that are inherently subject to change and involve a number of risks and uncertainties. Forward-looking statements include, but are not limited to, statements about: expectations regarding our capitalization and resources; the adequacy of our capital to support our future operations and our ability to successfully initiate and complete clinical trials; our strategy and focus; our efforts to develop a vaccine against COVID-19, the safety, efficacy or reliability of our COVID-19 vaccine candidate; the development and commercial potential of any of our product candidates; the timing and success of our development efforts; the success of any of our trials and our ability to achieve regulatory approval for any product candidate; the entry into or modification or termination of collaborative agreements and the expected milestones and royalties from such collaborative agreements; the potential market or clinical or commercial success of the clinical development programs of Arcturus; and any statements other than statements of historical fact, including those related to Arcturus' future cash, market or financial position.

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Company Highlights

BUILDING INNOVATIVE
RNA MEDICINES

Arcturus is a Clinical-Stage mRNA Vaccines and Medicines Company

Publicly Traded (Nasdaq: ARCT)

- Headquarters: San Diego, CA
- Number of Employees: 124
- Founded: 2013

Promising Therapeutic Candidates

- LUNAR-COV19 (COVID-19 Vaccine)
- LUNAR-OTC (Ornithine Transcarbamylase Deficiency)
- LUNAR-CF (Cystic Fibrosis)
- Additional Earlier Stage Programs

Arcturus Technologies Validated by Multiple Strategic Partners

Johnson & Johnson · Takeda · ultragenyx pharmaceutical · Cystic Fibrosis Foundation · DukeNUS Medical School · Catalent · Recipharm

Proprietary mRNA Technologies Driving Promising Therapeutic Programs

Broad and Strong Intellectual Property Portfolio

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- mRNA & STARR™ mRNA
  - mRNA Chemistry
  - mRNA Design & Modifications
  - mRNA Manufacturing Process
- LUNAR® Delivery
  - Lipid Chemistry
  - Formulation Design
  - LUNAR® Drug Product Manufacturing
- 209 Patents & Patent Applications

Program	Indication
LUNAR-COV19	COVID-19 Vaccine
LUNAR-FLU	Flu Vaccine
LUNAR-OTC	Ornithine Transcarbamylase (OTC) Deficiency
LUNAR-CF	Cystic Fibrosis

ADDITIONAL EARLIER STAGE PROGRAMS

Arcturus Pipeline of mRNA Medicines

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Franchise	Product Name	Indication	Route of Administration	Cell Target	Prevalence Worldwide	Stage	Anticipated Milestones
VACCINES	**LUNAR-COV19** (ARCT-021)	COVID-19	Intramuscular	Myocytes & Dendritic Cells	Global	Phase 2	Phase 3 Initiation Q2 EUA H2 2021
	LUNAR-FLU	Influenza	Intramuscular	Myocytes & Dendritic Cells	Global	Preclinical	IND/CTA H1 2022
HEPATIC	**LUNAR-OTC** (ARCT-810)	Ornithine Transcarbamylase Deficiency	Intravenous	Periportal Hepatocytes	> 10,000	Phase 1b	Phase 2 Multiple Dose Study CTA Q2 2021
RESPIRATORY	**LUNAR-CF** (ARCT-032)	Cystic Fibrosis	Inhaled	Bronchial Epithelial Cells	> 70,000	Preclinical	CTA Q4 2021

EUA = Emergency Use Authorization; CTA = Clinical Trial Application; IND = Investigational New Drug Application

Multiple mRNA Therapeutic and Vaccine Programs in Clinical Development with Milestones

Partnerships Maximize Platform

Program	Partner	Indication
LUNAR-HBV	Johnson & Johnson	Hepatitis B Virus (HBV)
LUNAR-NASH	Takeda	Nonalcoholic Steatohepatitis (NASH)
LUNAR-GSD3	ultragenyx pharmaceutical	Glycogen Storage Disease Type III
LUNAR-RARE	ultragenyx pharmaceutical	Undisclosed Rare Disease
LUNAR-RPL	Undisclosed Large Pharma	Vaccines
LUNAR-AH	Undisclosed Animal Health Pharma	Vaccines

Greater than $1 Billion in Potential Milestones & Royalties

LUNAR® Delivery Technology

Biodegradable, highly optimized for each cell type

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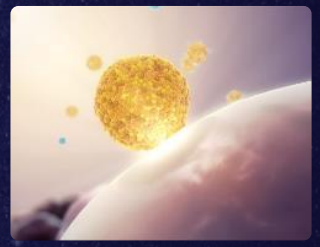
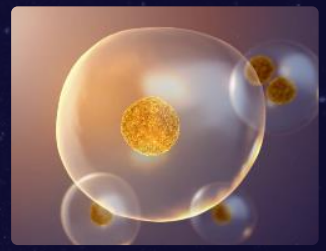
LUNAR Associates with Cell Membrane



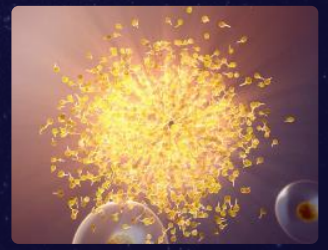
Enters Cell
Via Endocytosis

Lipid Particle in Endosome



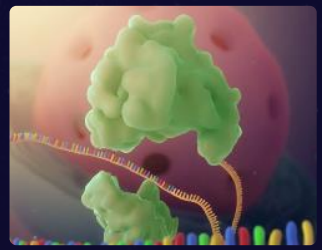
Increased Acidity as
Endosome Ages

pH-Mediated Disruption



Rapid Biodegradation
of Vehicle

RNA in Cytosol



RNA Processing
and Translation

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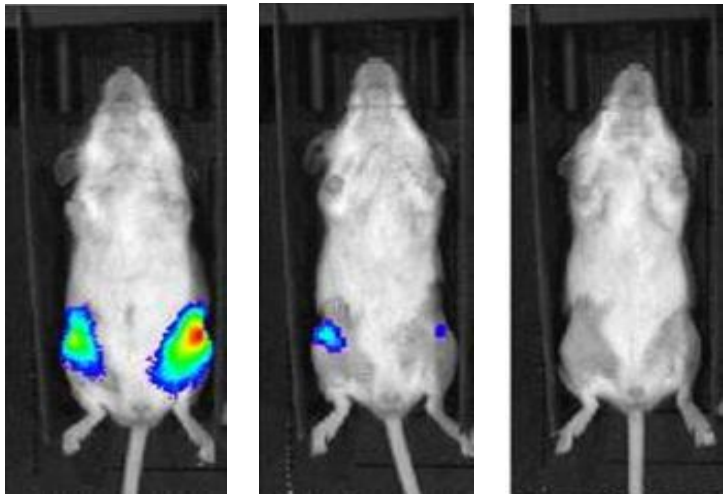
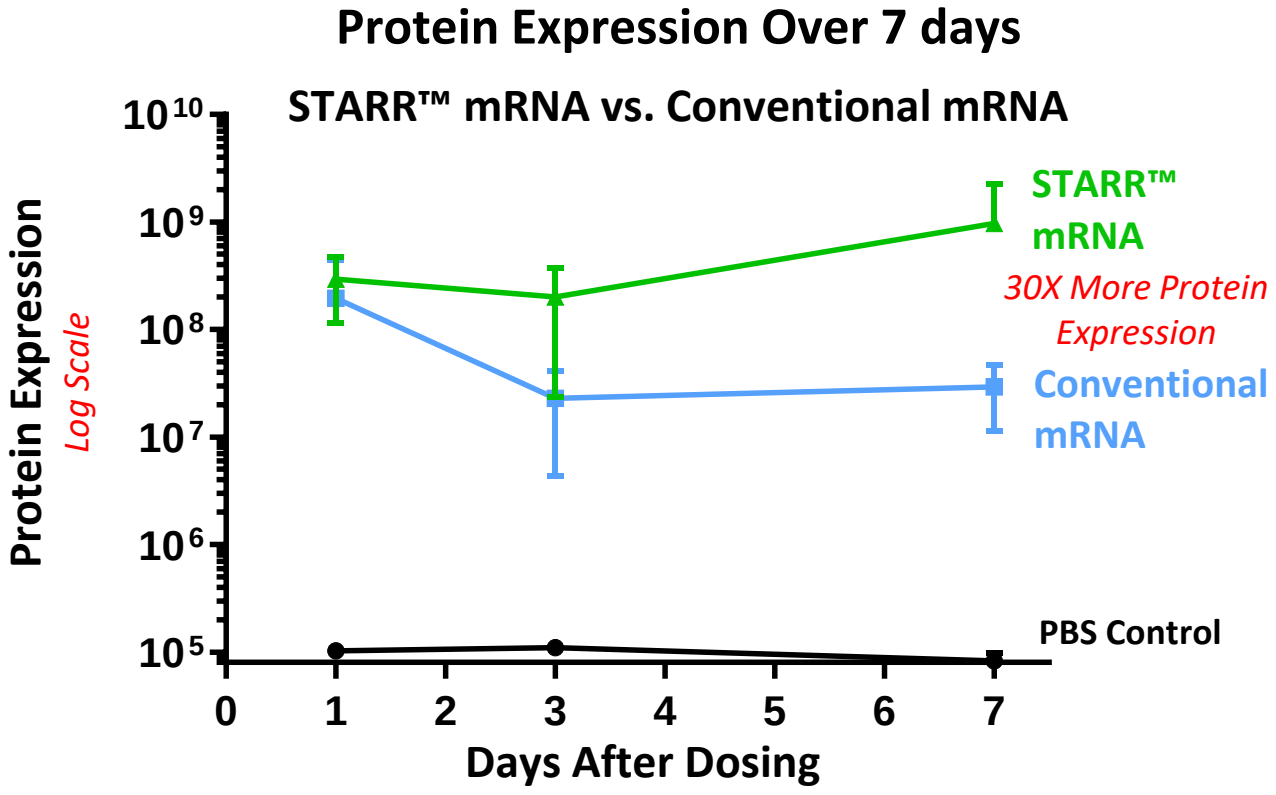
STARR™ mRNA Expression Superior to Conventional mRNA

Self-Transcribing and Replicating mRNA (STARR™) delivered with LUNAR® provides higher protein expression and potentially longer-lasting duration of protein expression in mouse

STARR™ Technology
30-Fold Higher Protein Expression



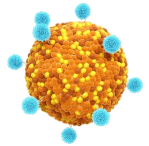
STARR™ Technology | Conventional mRNA | PBS Control



Single dose of STARR™ mRNA technology with LUNAR® delivery provided enhanced protein expression *in vivo* (mouse)

LUNAR-COV19 (ARCT-021)
COVID-19 Vaccine Candidate

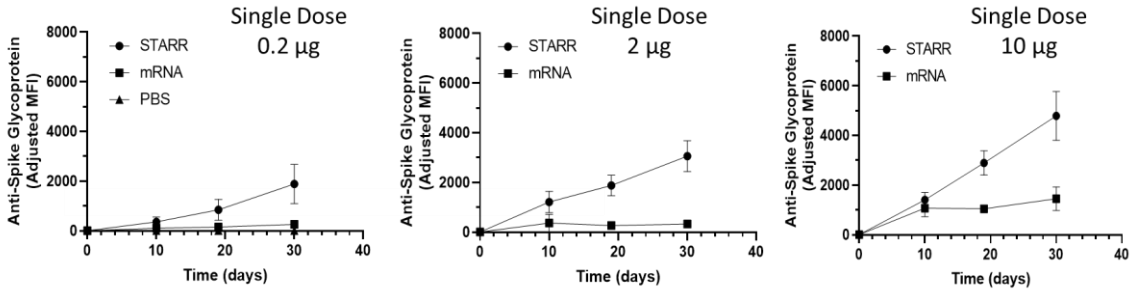
Arcturus COVID-19 Vaccine Candidate has Significant Advantages

- Duke-NUS Partnership DukeNUS Medical School
- mRNA Vaccine: No Adjuvants, No Viral Vector Used, Readily Updatable as New Variants Arise
- Self-amplifying (STARR™) mRNA and LUNAR® Non-viral Delivery Technology 
- Promising Clinical Data Demonstrate Humoral and Cellular Immunogenicity, and Tolerability Data
- Potential Single-Shot: Simpler Logistics for Vaccinating Large Populations
- Very Low Dose: Enables Rapid Global Scale-up
- Readily Manufactured: Arcturus Processes + Strategic Partnerships Catalent Recipharm
- Lyophilized Formulation: No need to be stored at ultra-cold temps, improved supply chain & distribution benefits

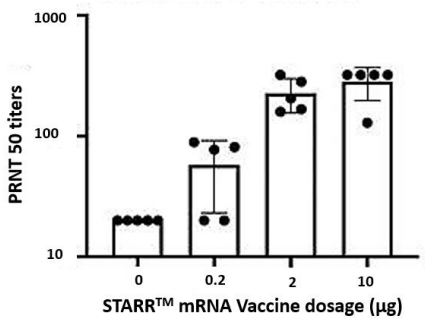
Preclinical Data: Robust Immune Response

Humoral Immunity

STARR™ induces more robust titers compared to conventional mRNA



Neutralizing antibody titers and high seroconversion at low doses

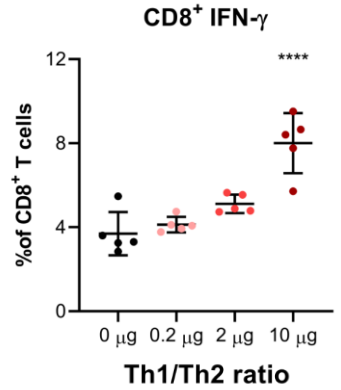


Single Dose (µg)	Seroconversion	Neutralizing Antibody Titers (Geometric Mean)
0.2	80 %	58
2	100 %	218
10	100 %	≥ 320

Cellular Immunity

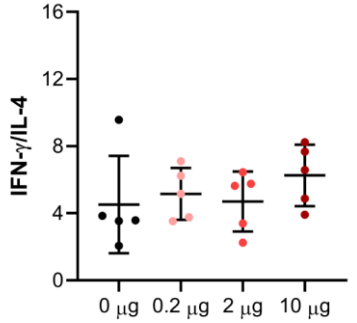
7 Days Post Single Dose

Adaptive Cellular Response (CD8+ cells)



Th1/Th2 ratio

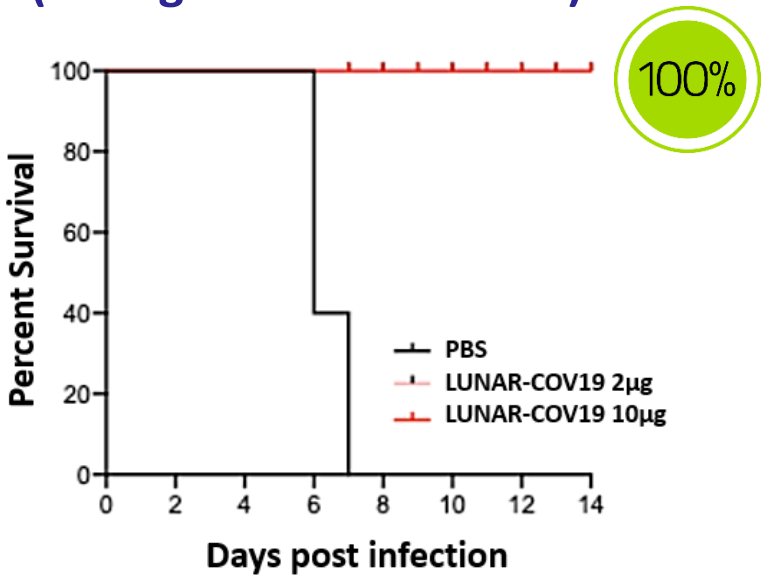
Balanced Th1/Th2 Immune Response (CD4+ cells)



- **Single administration with a very low dose of Arcturus COVID vaccine results in potent immune reaction**
- **STARR™ mRNA generates neutralizing antibodies (anti-SARS-CoV-2 Spike Glycoprotein IgG) and a cellular T-cell mediated immune response at a much lower dose level compared to conventional mRNA**

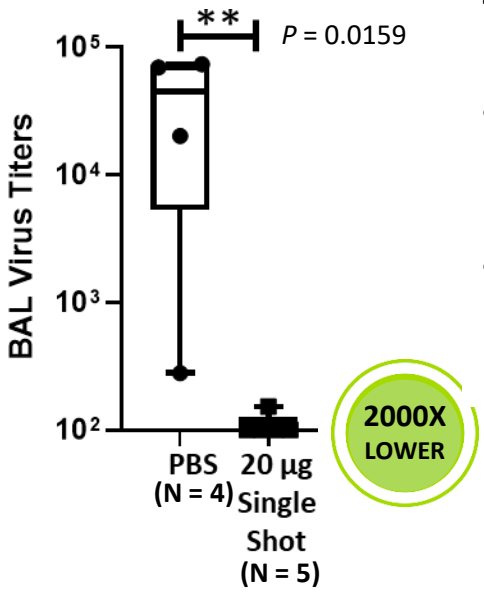
ARCT-021 Significantly Effective in Challenge Models

Mouse Model (transgenic human ACE2)



ARCT-021 significantly effective in a virus challenge study in the human ACE2 transgenic mouse model; single dose provided complete protection from SARS-CoV-2 infection and death, compared to control mice which experienced 100% mortality

Primate Model (macaque)



7 Days After SARS-CoV-2 Virus Challenge

- Lung viral titers exceeded 13,100 (median) in non-vaccinated primates (PBS)
- Lung viral titers = 6.5 (median); more than 2000X lower in primates administered a single shot of ARCT-021

Single administration of ARCT-021 significantly effective in primate model (macaque); vaccinated macaques show substantial (3.30 log lower) reductions in median lung viral titers

ARCT-021 Clinical Trial and Manufacturing Update

Phase 1/2 Clinical Trial

- Completed dosing all subjects (n=106), including older adults
- At interim analysis, observed high seroconversion rates for IgG binding antibodies, and Th1 dominant CD4+ immune responses, neutralizing antibodies (PRNT50) Geometric Mean Titer (GMT) levels in the range of titers observed in convalescent serum
- Favorable safety and tolerability observations; no subjects have withdrawn from dosing

Phase 2 Clinical Trial Ongoing

- More than 500 participants dosed across USA and Singapore
- Two dose levels being evaluated: 5 µg and 7.5 µg

Phase 3 Clinical Trial; EUA

- Expect to commence Phase 3 clinical trial Q2 2021; targeting Emergency Use Authorization H2 2021
- Lyophilized (freeze-dried) version of ARCT-021 vaccine product on track to be evaluated in Phase 3 clinical trial

Manufacturing

- With our global manufacturing partners, we are on track to manufacture finished doses of lyophilized ARCT-021 in Q1 2021 for stockpiling purposes, and have laid the foundation to produce hundreds of millions of doses of lyophilized ARCT-021 over the next 18 months

Lyophilization Process Advantage Over Conventional Frozen Liquid

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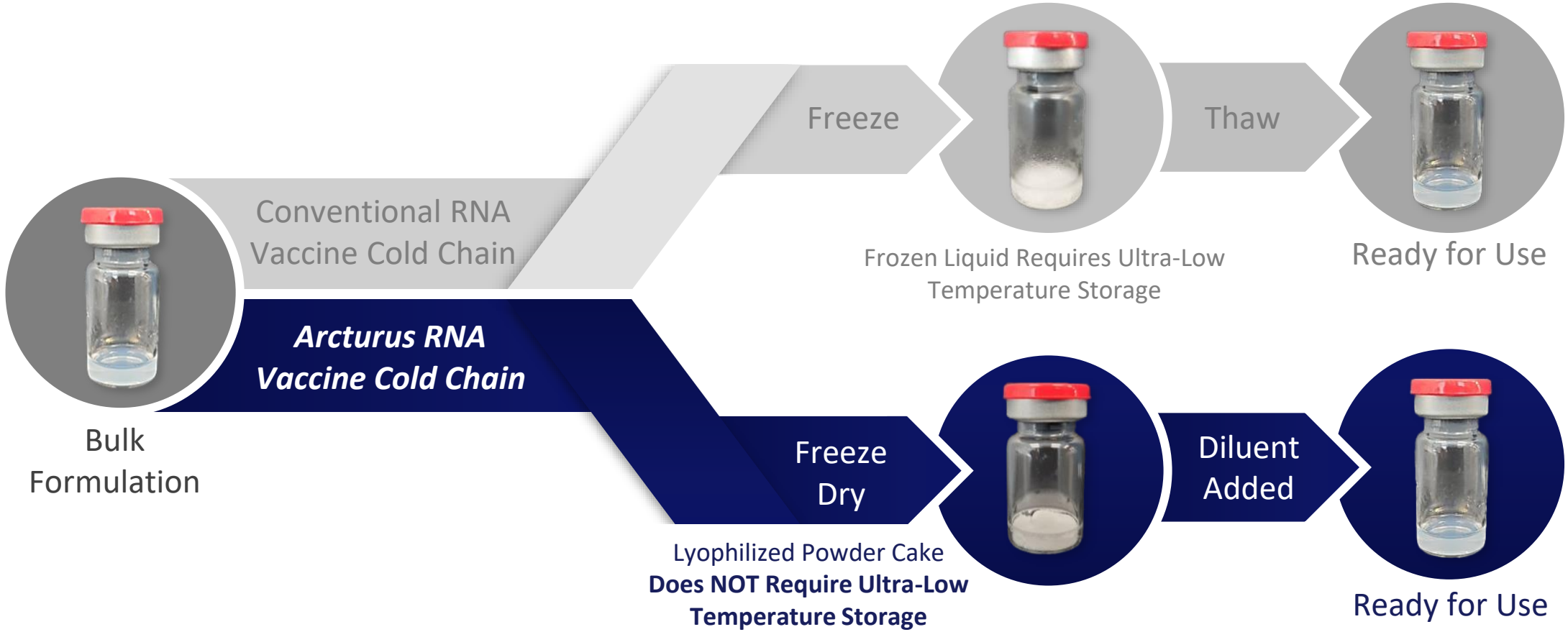


- **Lyophilized version of ARCT-021 maintains key quality attributes of the frozen liquid equivalent**
- **Collecting stability data at -20°C, 2-8°C, and Room Temperature**
- **Simpler handling: No dry ice at point of care, lower risk of degradation from uncontrolled temperature fluctuation**

LUNAR-OTC (ARCT-810)
Ornithine Transcarbamylase (OTC) Deficiency

OTC Deficiency Market Opportunity

Ornithine Transcarbamylase (OTC) Deficiency: The most common urea cycle disorder

- The urea cycle converts neurotoxic ammonia to water-soluble urea that can be excreted in urine
- Deficiency in OTC causes elevated blood ammonia, which can lead to neurological damage, coma, and death
- 10,000 worldwide prevalence

Unmet Medical Need

- Present standard of care involves a strict diet (low protein, high fluid intake) plus ammonia scavengers (sodium phenylbutyrate)
- Present standard of care does not effectively prevent life-threatening spikes of ammonia
- Severe OTC Deficiency patients are typically referred for liver transplant, currently the only cure

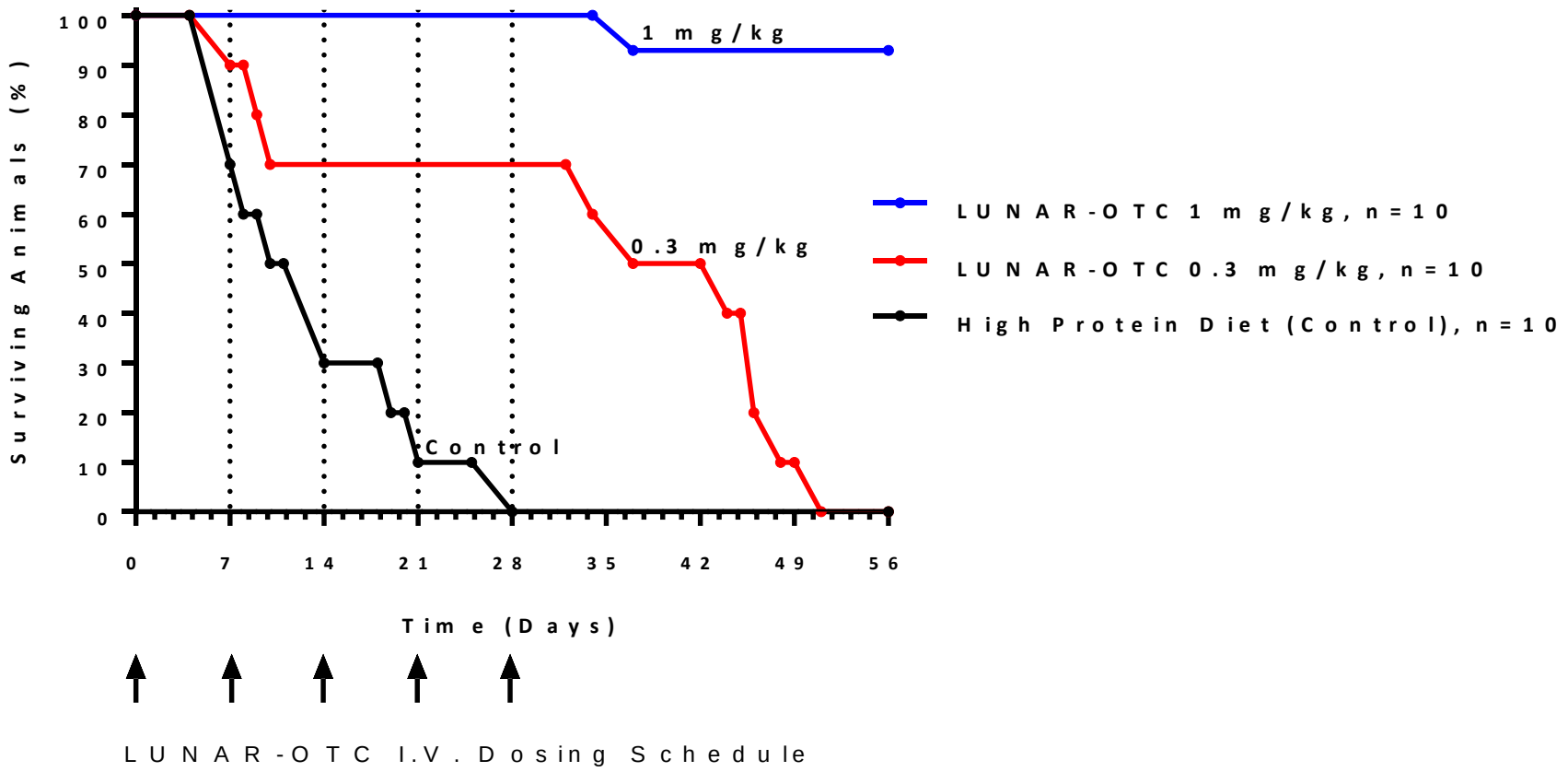
LUNAR-OTC Aims to Restore Enzyme Function

- Expression of OTC enzyme in liver has potential to restore normal urea cycle activity to detoxify ammonia, preventing neurological damage and removing need for liver transplantation

LUNAR-OTC

Disease Normalization Following Single and Repeat Dosing in OTC Mouse Model

Survival of OTC-deficient Mice on High Protein Diet - Weekly LUNAR-OTC Treatment



LUNAR-OTC

Exceeds Therapeutic Target of 10% Enzyme Replacement at all Doses in OTC-Deficient Mouse Model

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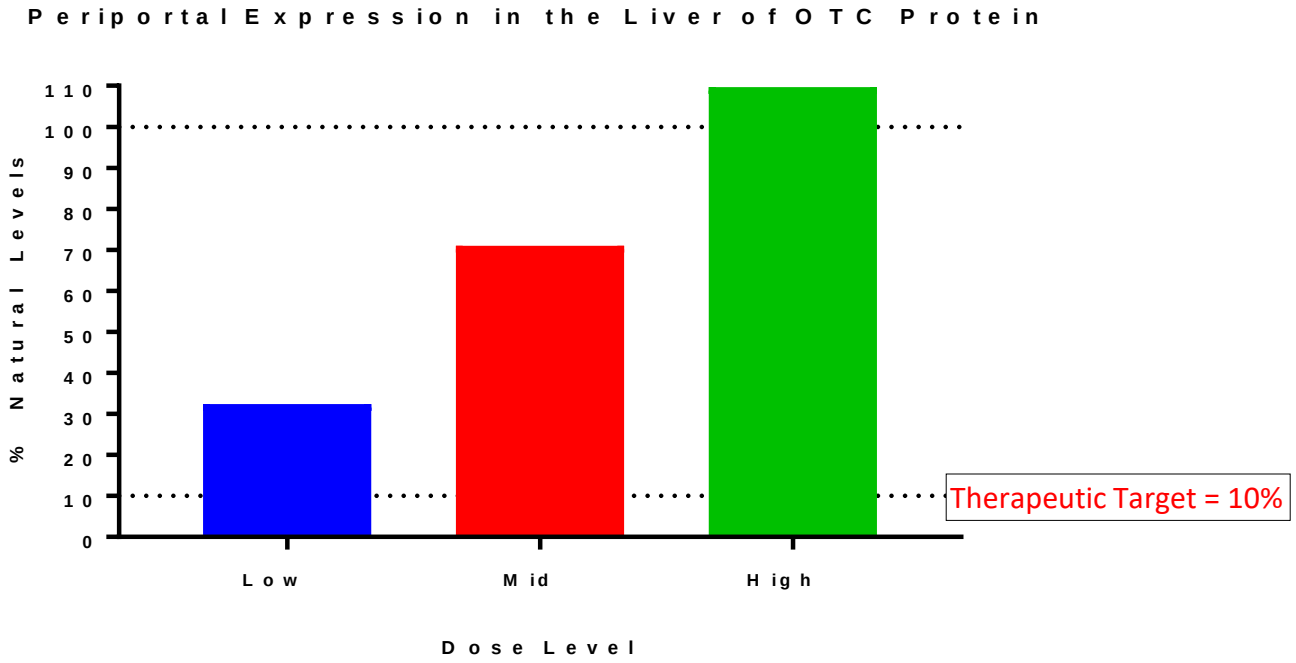
- OTCD impacts ureagenesis (ammonia detoxification)
- The main site of ureagenesis is the periportal region of the liver*
- Establishing 10% of natural enzyme levels is expected to be therapeutically significant



*Li, L. et al. PGC-1α Promotes Ureagenesis in Mouse Periportal Hepatocytes through SIRT3 and SIRT5 in Response to Glucagon. Scientific Reports. 6:24156 | DOI: 10.1038/srep24156, April 2016
*Lamers, W.H., Hakvoort, T.B.M., and Köhler, E.S. 'Molecular Pathology of Liver Diseases' in Monga S.P.S. (ed.), *MOLECULAR PATHOLOGY LIBRARY SERIES*, Springer Publishing, New York, pp. 125-132 | DOI: 10.1007/978-1-4419-7107-4

LUNAR-OTC treatment increases OTC expression in mouse periportal hepatocytes (main site of ureagenesis)

ARCT-810 Clinical Update

Phase 1 Clinical Trial Completed

- Double blind, randomized 2:1 active to placebo, dose-escalation trial in healthy adult volunteers
- All Adverse Events (AEs) mild or moderate
- Favorable PK profile: No LUNAR® lipids detectable after 48 hours following drug administration
- No steroid premedication
- Completed dose escalation of all cohorts (0.1, 0.2, 0.3, and 0.4 mg/kg)

Phase 1b Clinical Trial in OTC-Deficient Patients Ongoing

- Commenced patient enrollment
- First subject has been dosed
- Up to 12 patients; up to 3 dose levels
- All doses within anticipated range for therapeutic biological effect

Primary Goal: Identify safest doses to take forward into multiple dose clinical trials
Primary Endpoints: Safety and tolerability
Secondary Endpoints: Pharmacokinetics
Exploratory Endpoints: Biomarkers include ureagenesis, plasma ammonia levels and plasma OTC enzyme activity, and urine orotic acid levels

Next Milestone: CTA submission in Q2 2021 for Phase 2 Multiple Dose Study in OTC Deficient Patients

LUNAR-CF (ARCT-032)
Cystic Fibrosis

Cystic Fibrosis Market Opportunity

Cystic Fibrosis: The most common rare disease in the United States

- Caused by genetic mutations in the CFTR gene, resulting in aberrant flux of ions in and out of cells, causing thick mucus buildup in lung airways
- Chronic airway obstruction leads to infection and inflammation, which causes permanent tissue scarring and respiratory failure
- 70,000 worldwide prevalence

Unmet Medical Need

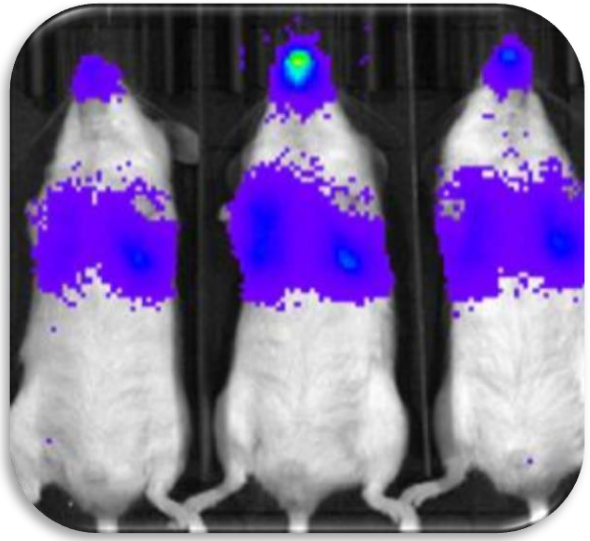
- No CFTR functional corrector is approved for treatment of all patients
- Present standard of care does not effectively prevent long-term effects of mucus accumulation. CF patients with late-stage loss of respiratory function require lung transplant

LUNAR-CF Aims to Restore CFTR Function

- An mRNA replacement therapy has the potential to deliver a new copy of CFTR into the lungs of CF patients, independent of any genotype
- A functional CFTR protein can restore chloride channel efflux in the airways, reducing mucus accumulation, tissue scarring and minimizing the progressive respiratory dysfunction observed in CF patients

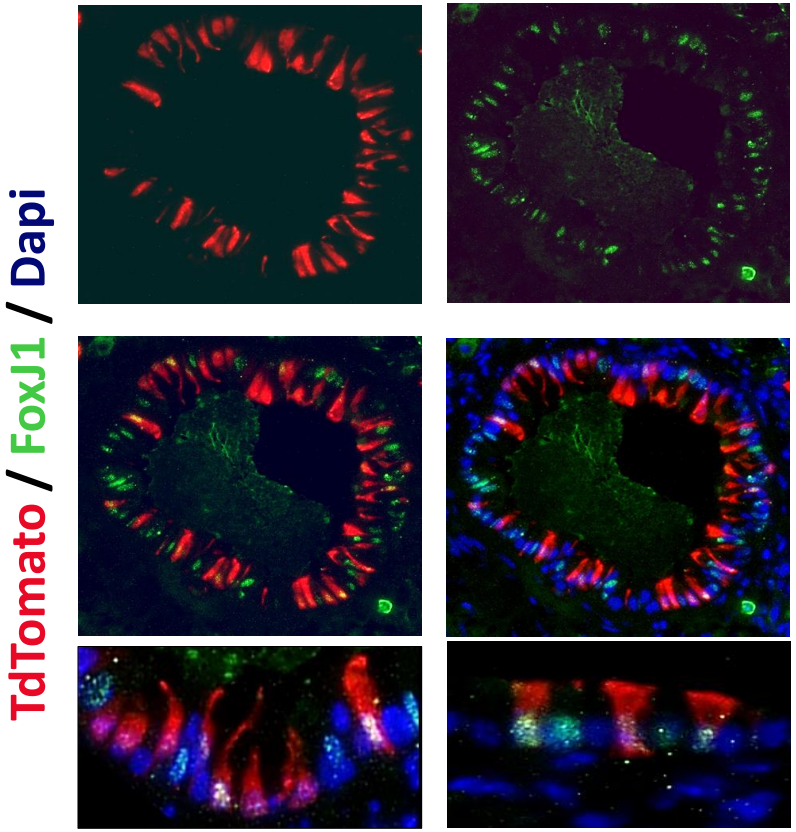
Delivery of LUNAR®-mRNA to Rodent Airways

Nebulization: Upper/Lower Airways



LUNAR® + Luciferase mRNA

LUNAR® Targets Mice Epithelial Airways (TdTomato), Including Ciliated Cells (TdTomato/FoxJ1)



Efficient delivery of LUNAR®-mRNA formulations in rodent airways

LUNAR®, an aerosolized delivery platform for lung

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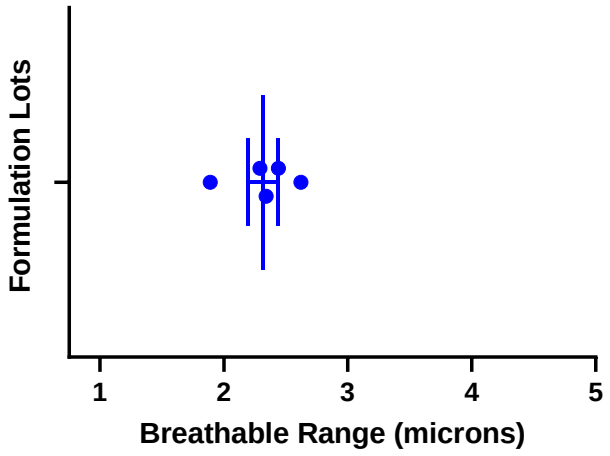
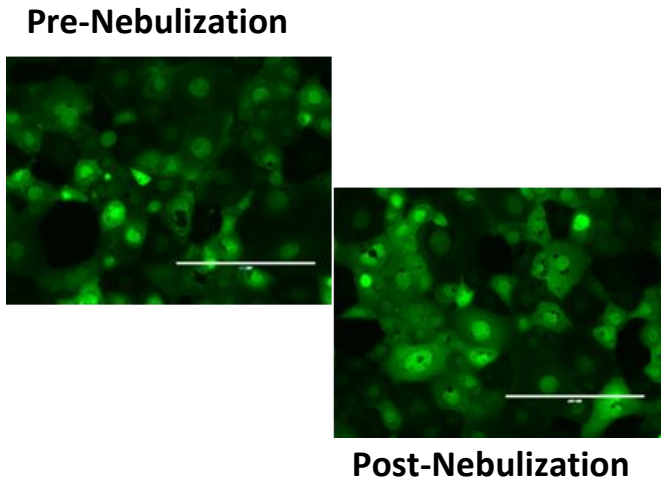
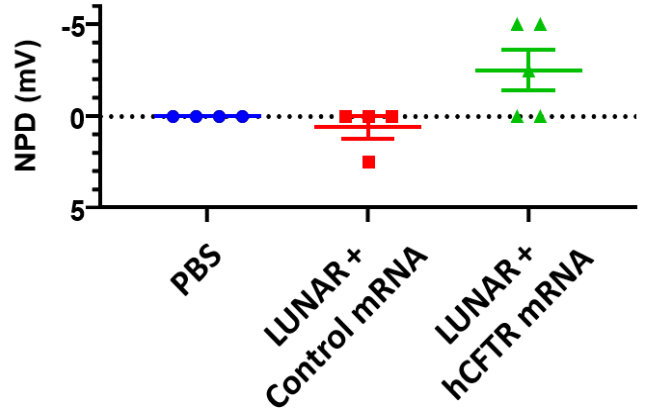
Aerosolized LUNAR® Particles are Breathable



Aerosolized LUNAR® -mRNA (EGFP) maintains activity



LUNAR®-mRNA (hCFTR) is biologically active *in vivo* (NPD, Mouse)



Aerosolized LUNAR® droplets are in the optimal breathable range (1-5 microns)
Aerosolized LUNAR® maintains activity as measured by EGFP protein expression & Nasal Potential Difference (NPD)

Delivery of LUNAR®-mRNA into Epithelial Airways in Ferret

EGFP conversion in tracheal epithelial airways observed in the ROSA26TG Ferret model

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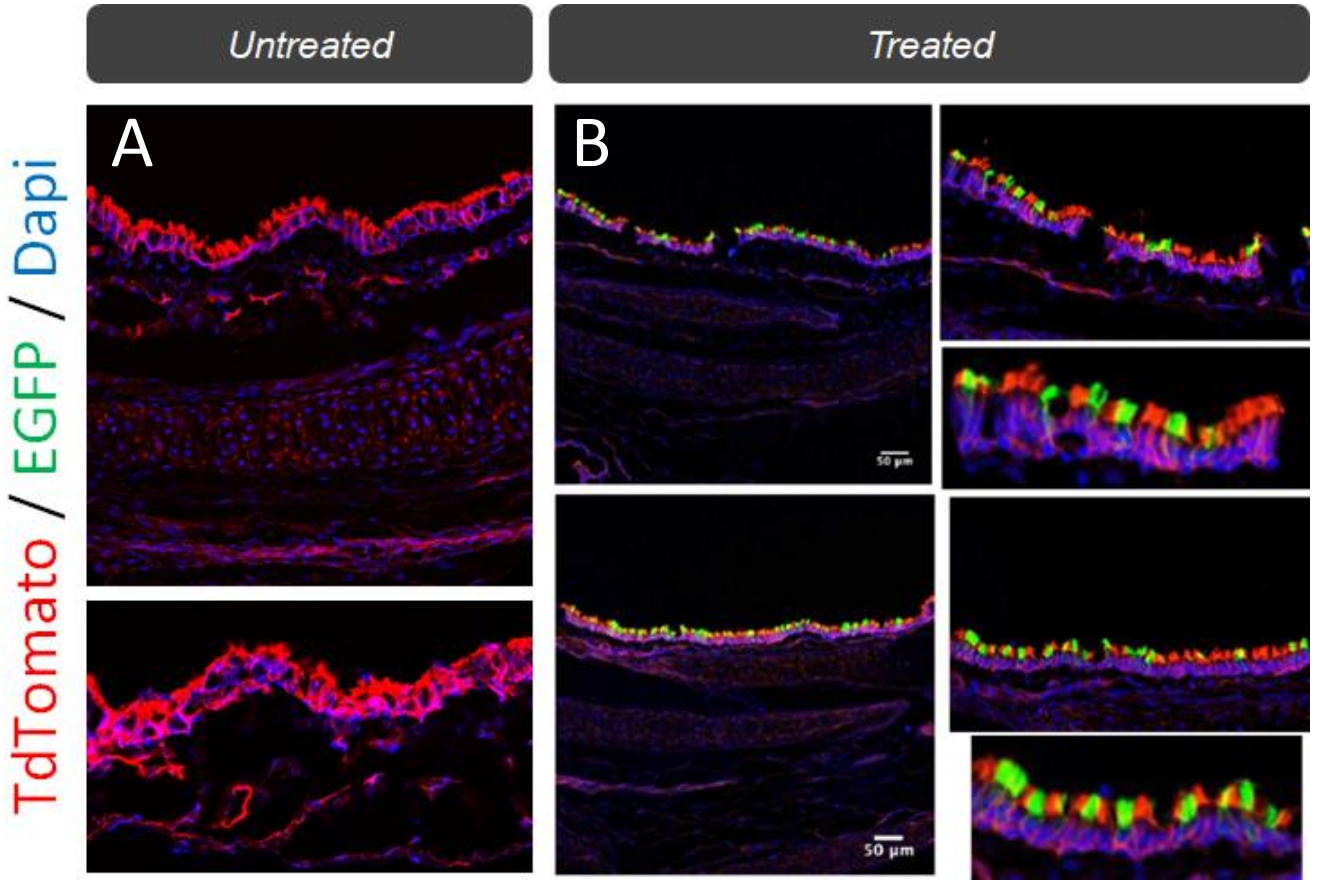
- Ferrets are an excellent species for modeling certain human lung diseases*
- Novel LUNAR® formulations of CRE mRNA were tested in a transgenic ROSA26TG ferret model
- Activation of EGFP expression indicates that LUNAR® targets epithelial airways
- Anticipated next steps: CTA Q4 2021



In collaboration with John Engelhardt

LUNAR® effectively delivered mRNA to the tracheal epithelial airways in a Ferret model

*Yu, M., Sun, X., Tyler, S.R. *et al.* Highly Efficient Transgenesis in Ferrets. *Sci Rep* **9,** 1971 (2019)

Moving Forward

Anticipated Near-Term Milestones and Cash Position

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ARCT-021 (LUNAR-COV19)	
Phase 3 Initiation	**Q2 2021**
Emergency Use Authorization (EUA)	**H2 2021**

ARCT-810 (LUNAR-OTC)	
Phase 2 Multiple Dose Study Clinical Trial Application	**Q2 2021**

ARCT-032 (LUNAR-CF)	
Clinical Trial Application (CTA)	**Q4 2021**

Cash Position
$463.0 Million as of December 31, 2020

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Management Team

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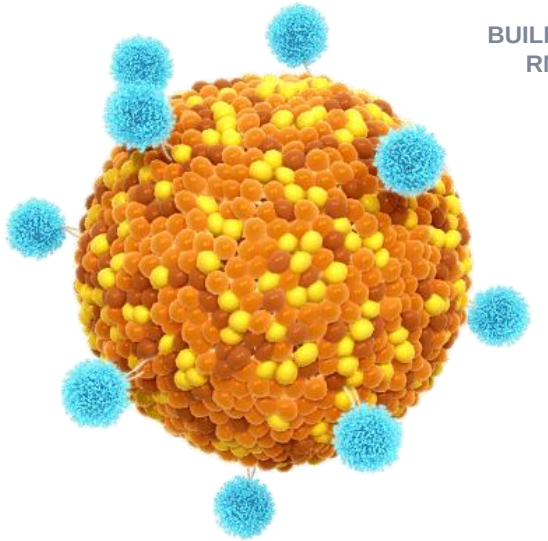
MERCK

Pad Chivukula, Ph.D.
CSO & COO
Nitto

Andrew Sassine, MBA
CFO
Fidelity INVESTMENTS

Steve Hughes, M.D.
Chief Medical Officer
IONIS PHARMACEUTICALS

Lance Kurata, J.D.
Chief Legal Officer
MINTZ



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amplyx

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Perelman School of Medicine
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ARCTURUS therapeutics

Appendix

LUNAR-COV19 Preclinical Seroconversion Data

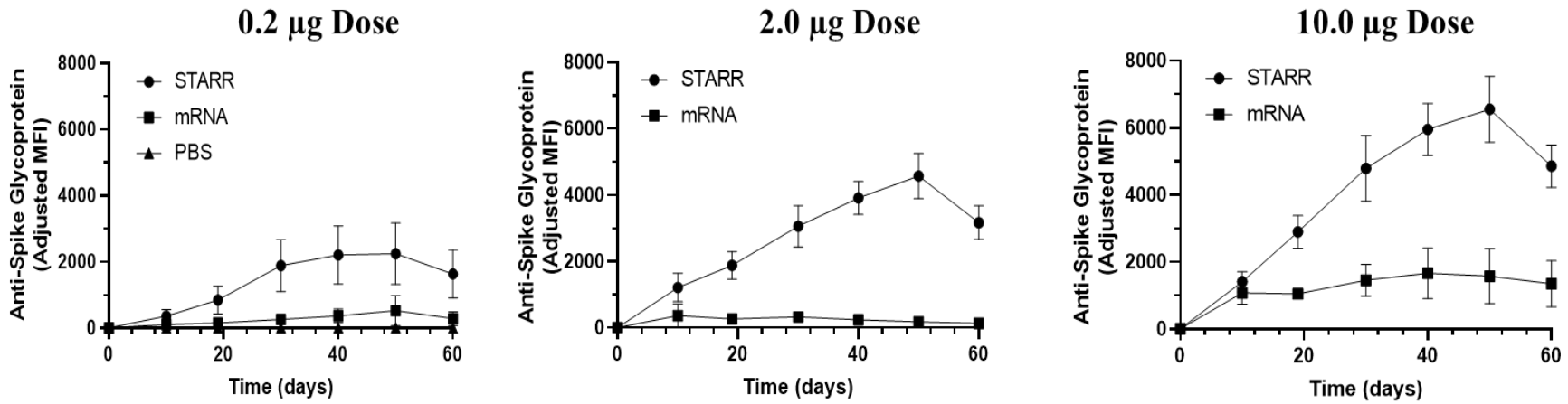
Seroconversion Rate (% of Animals) – STARR™ mRNA vs. Conventional mRNA

Single Dose (µg)	LUNAR® Delivery			
	STARR™ mRNA (%)		Conventional mRNA (%)	
	Day 10	Day 19	Day 10	Day 19
0.2	40	60	20	20
2	80	**100**	20	0
10	100	100	40	80

100% of mouse seroconverted by day 19 at a single low dose (2 µg)

Preclinical Data: Anti-Spike Protein Levels Continue to Increase Up to 50 Days

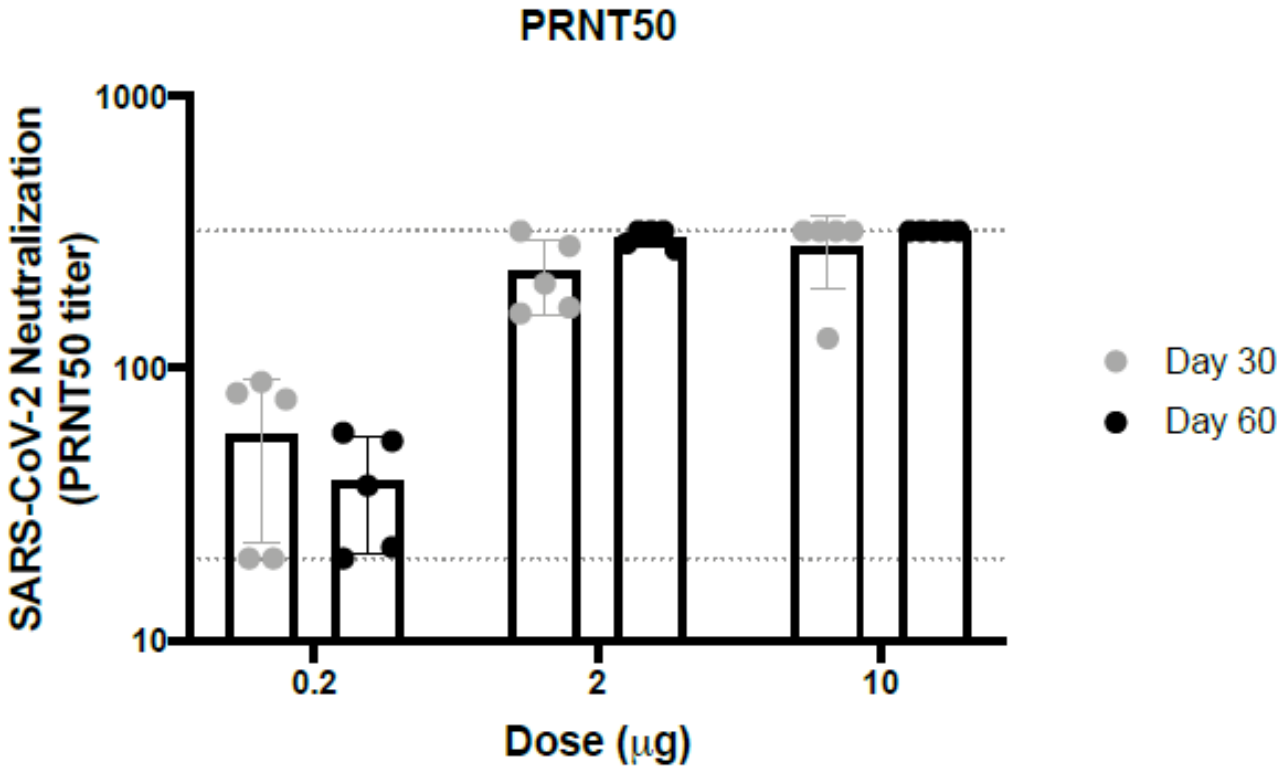
Single Administration of LUNAR-COV19



- **Higher titers** (anti-SARS-CoV-2 Spike Glycoprotein IgG) elicited by STARR™ mRNA
- **Titers continue to increase up to 50 days** with STARR™ mRNA; plateau reached with conventional mRNA
- Dose dependent increase in IgG titers; Luminex bead assay, 1/2000 serum dilution

Preclinical Data: Neutralizing Antibodies Continue to Increase for 60 Days

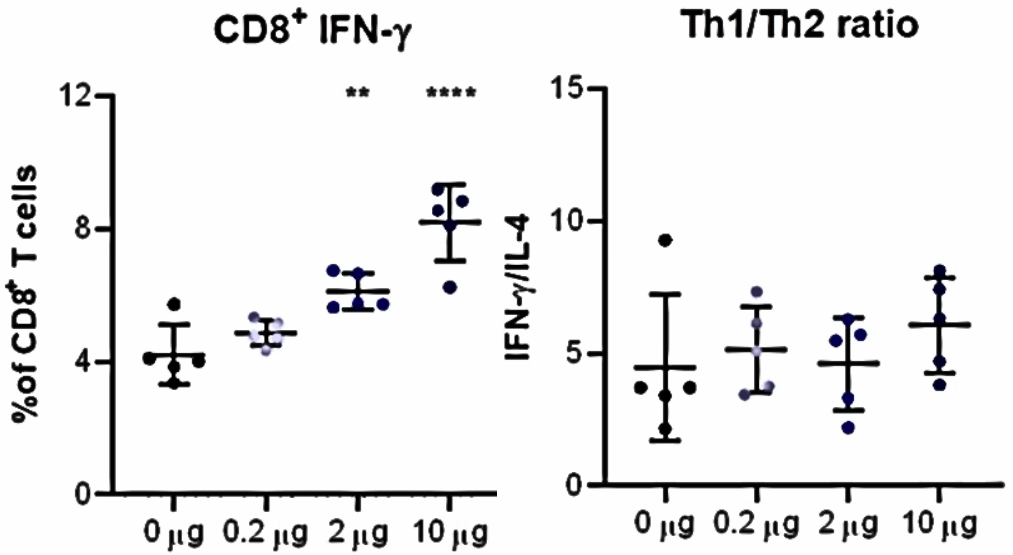
Single Administration (small dose, 2µg) of LUNAR-COV19



Virus neutralization assay:
Serum dilutions are incubated with SARS-CoV-2 virus, then added to cells. The cells die forming plaques, which are counted. The serum dilution that reduces the number of plaques by 50% is recorded (PRNT50). Maximum serum dilution tested was 1/320

**After single dose (2 µg) of LUNAR-COV19,
neutralizing antibodies continue to increase for 60 days (>300 titer)**

Preclinical Data: Arcturus Vaccine elicits a Balanced Cell Mediated Immune Response



RNA Dose (µg)	% IFN-γ+ CD8+ T Cells	CD4+ Th1/Th2 (IFN-γ/IL4)
0	4.0	4.6
0.2	4.5	5.3
2.0	6.0	5.0
10.0	8.0	6.0

Results Summary

- RNA dose dependent increase in IFN-γ positive CD8+ T-cells
- Th1 biased CD4+ response and stable Th1/Th2 ratio with increased RNA dose indicate balanced cell mediated immune response

Arcturus Safety Profile

External Validation

- Multiple strategic partnerships over many years confirms the positive potential safety profile of Arcturus LUNAR® and mRNA

Arcturus is committed to developing safe mRNA products

- 15 studies over several years with strategic partners

Top Safety Concern for RNA Medicines is <u>Delivery</u>

Arcturus LUNAR® Delivery Technology is well tolerated in non-human primates (NHPs)

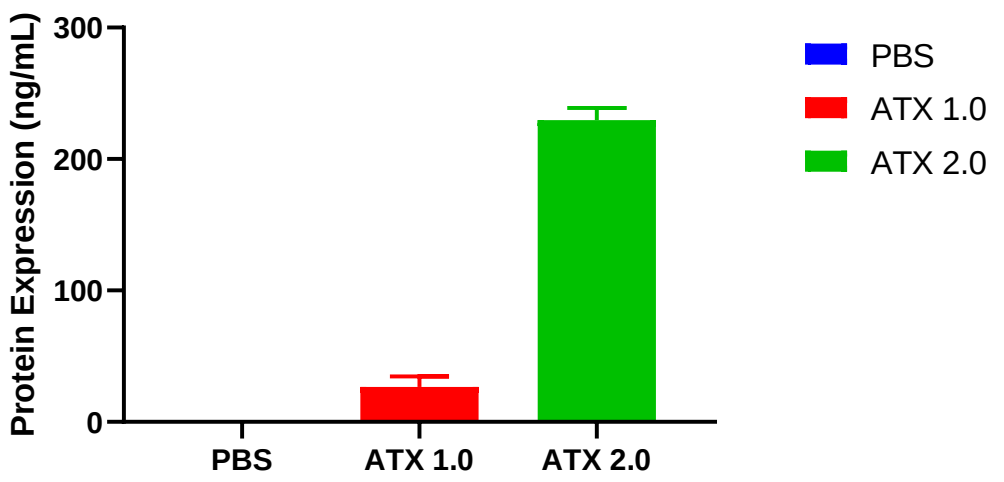
- ✓ **@ 15 mg/kg single dose of non-coding siRNA**
- ✓ **@ 3 mg/kg x eight (8) weekly doses of non-coding siRNA (total of 24 mg/kg over 2 months)**

Arcturus mRNA chemistry shows promising efficacy and tolerability data

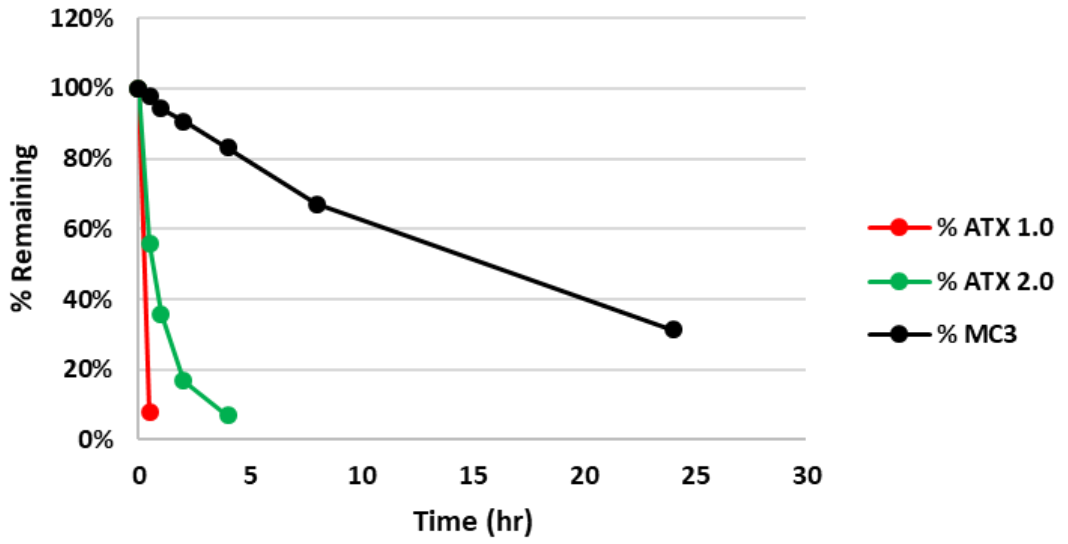
- Efficacy of OTC mRNA in mouse model @ 0.1 – 1 mg/kg

ATX Lipids are Effective and Biodegradable

Protein Expression (*in vivo*)



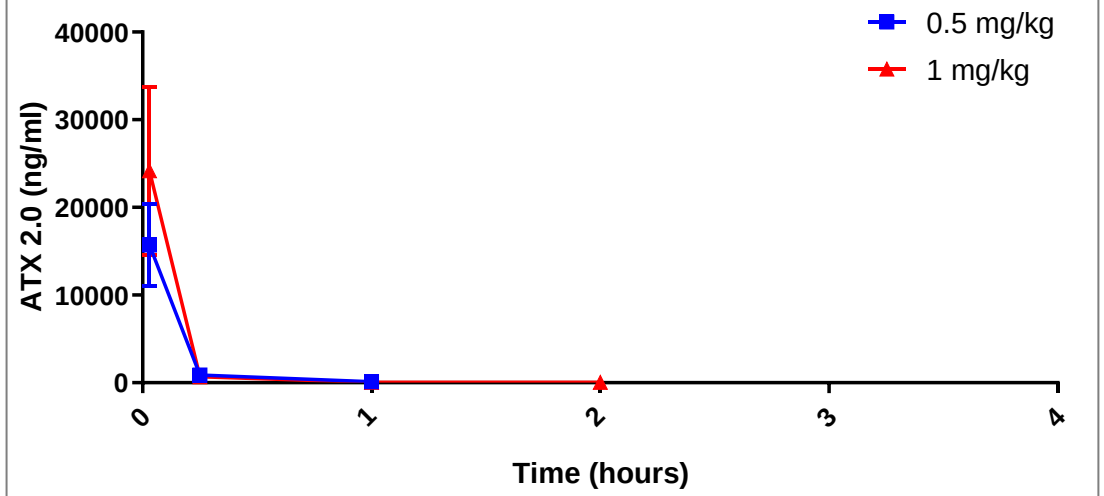
Esterase Catalyzed Degradation (*in vitro*)



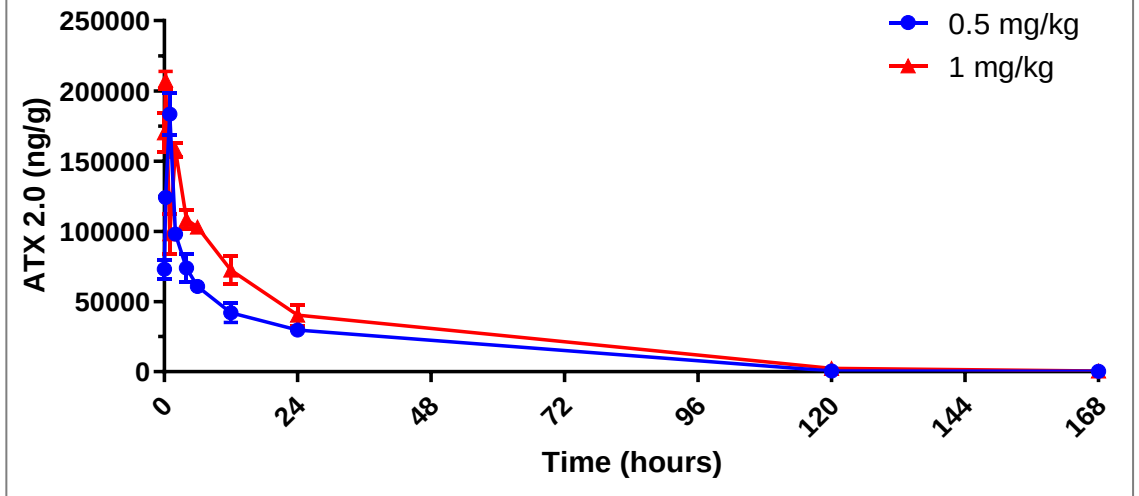
Next Generation ATX Lipids Retain Degradability & Improve Delivery Efficiency

ATX 2.0 Lipid is Biodegradable and Clears *in vivo*

Plasma



Liver



- ATX Lipid (the major component in LUNAR® technology) is degraded *in vivo*
- ATX 2.0 Lipid half-life in the liver is approximately 20 hours

Key Existing Country Relationships

Singapore

Research Partnership with Duke-NUS Medical School

Financial Support from the Economic Development Board of Singapore

- $10 M Grant for Research and Preclinical Work
- $6.7 M Grant for Phase 1/2 Clinical Trial
- Executed Manufacturing Support Agreement for $46.6 Million Non-Recourse Loan
- Up to $175 Million in vaccine purchases

Israel

Supply Agreement with Israel Ministry of Health

- Announced August 18, 2020
- Up to $225 Million in vaccine purchases (with MOH election for 500,000 Initial Reserve Doses)
- $12.5 M Initial Reserve Payment was paid in Oct 2020

Drug Substance: mRNA Design

Arcturus' proprietary mRNA optimization platform

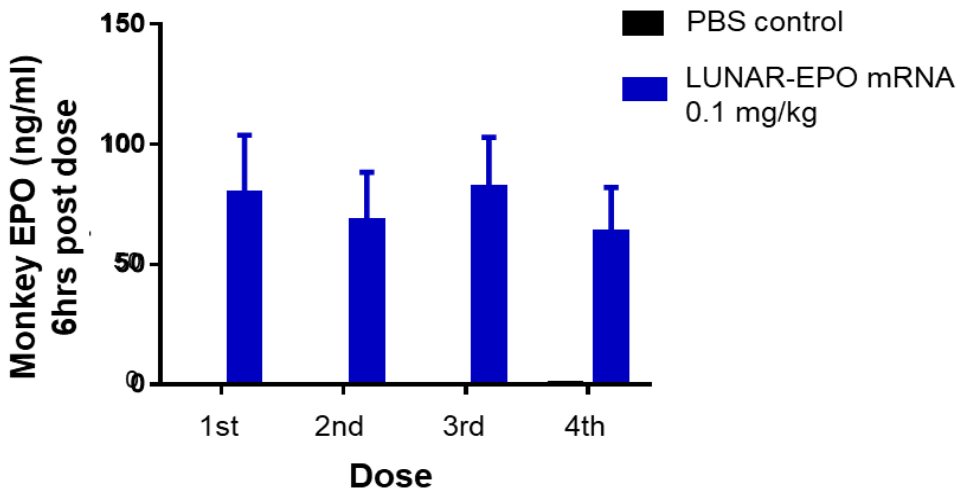
Optimize
mRNA sequence
Chemistry
Process

⇨

Improve
Protein Expression
Duration
Functional Activity

Sustained hEPO activity in NHPs upon repeat dosing

Weekly Dosing in Non-Human Primates (NHPs)



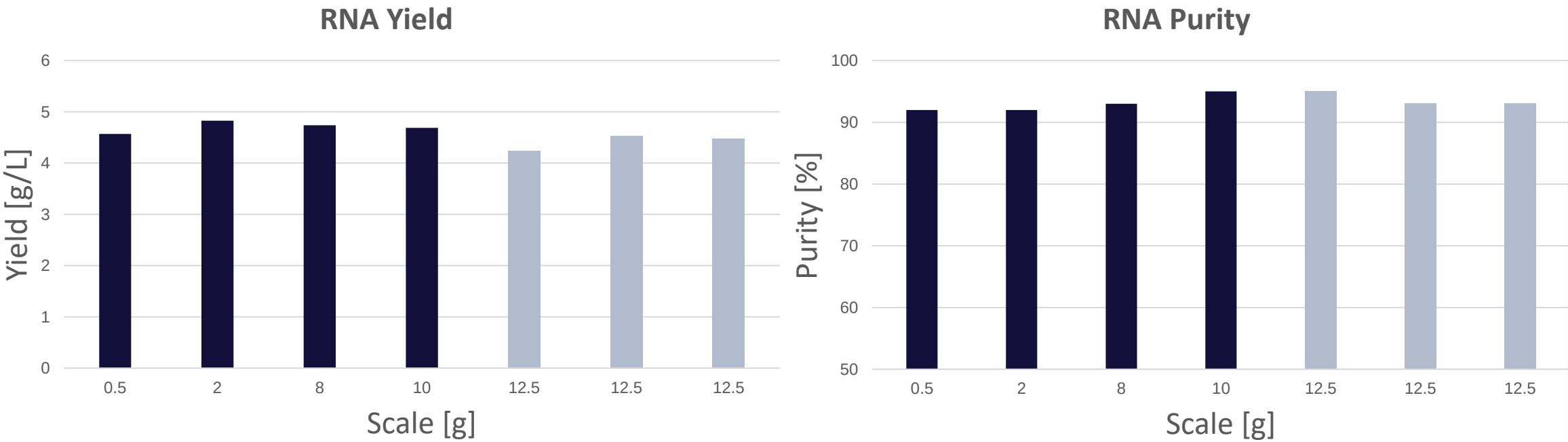
Proprietary mRNA Optimization Platform Demonstrates Sustained Activity Upon Repeat Dosing in NHPs

Drug Substance (mRNA) Manufacturing

Features	Benefits
Optimized IVT Method	Reduced Cost; Higher Purity
Improved Capping Reaction	Reduced Cost of Goods
Proprietary Purification Process	Higher Purity in a Shorter Time
Efficient	Entire Process Less Than One Week
Scalable to > 1Kg	Access Large Patient Populations
Adaptable	Can Utilize a Variety of Modifications

Arcturus Internal non-GMP mRNA Production Capabilities: Up to 30 g in Less Than One Week

Drug Substance (mRNA) Manufacturing



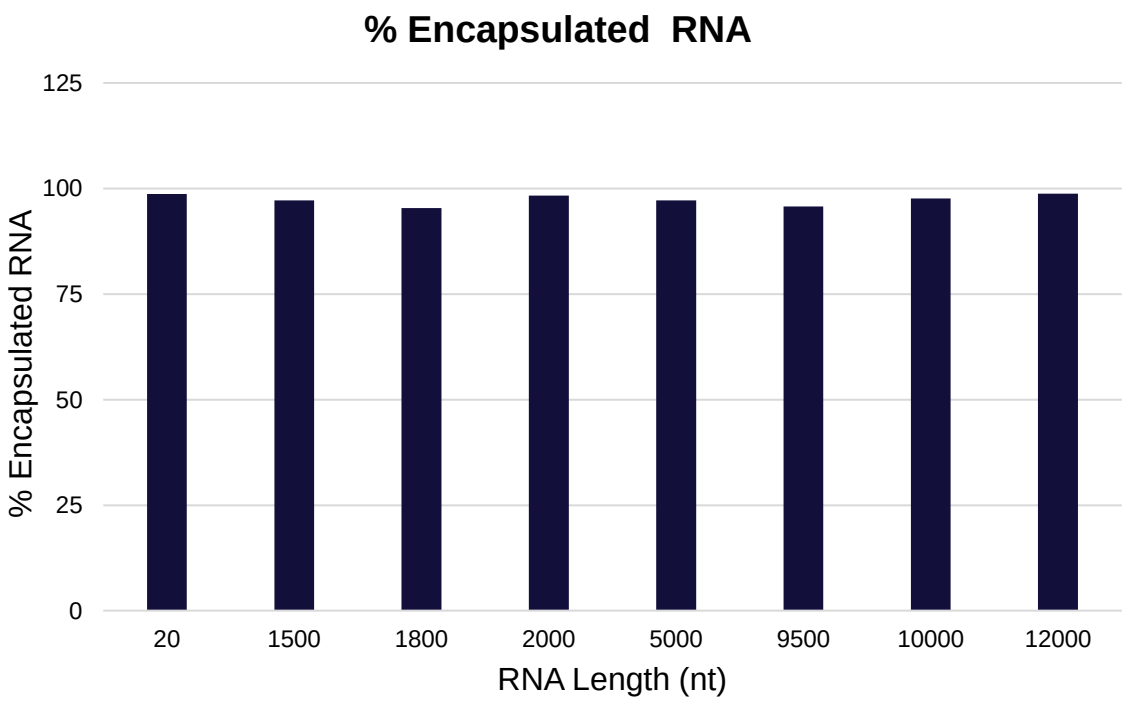
Non-GMP Lots Produced at Arcturus

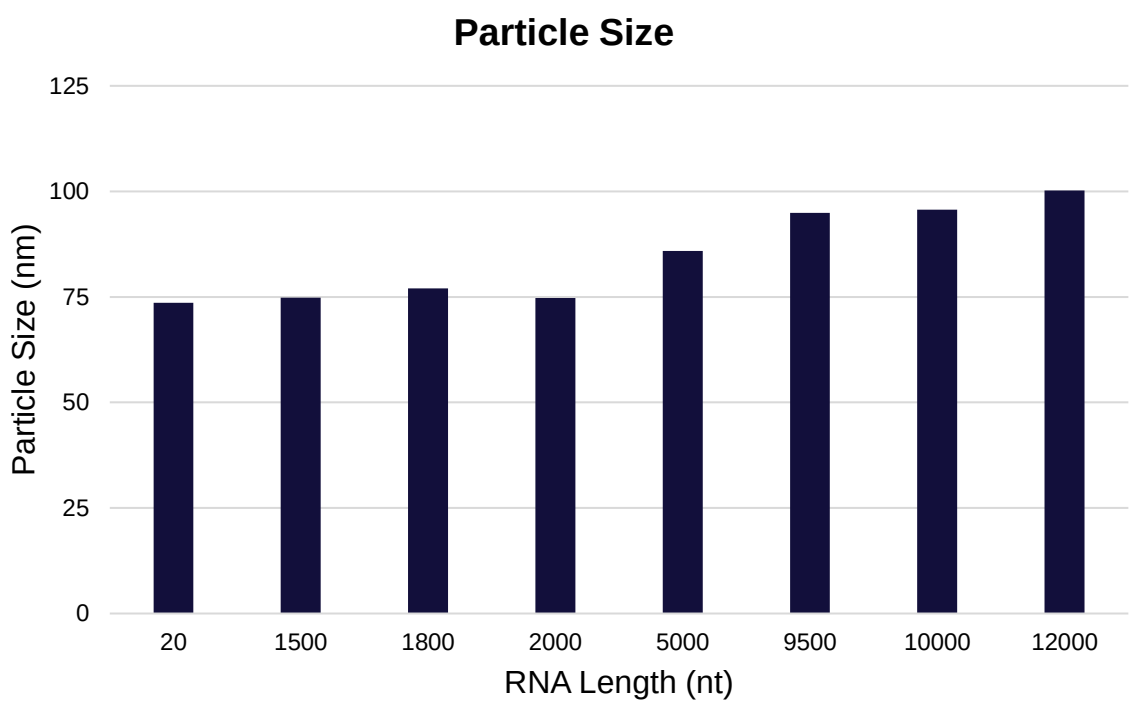
GMP Lots Produced at CMO as part of recent GMP campaign

Three 12.5 g lots produced in recent GMP campaign are of equivalent quality and yield

LUNAR® Versatility

Compatible with RNA of Various size





LUNAR® Formulations Successfully Encapsulate RNA of Varying Sizes and Chemistries