

ARCTURUS THERAPEUTICS

Building the Next Generation of RNA Medicines

M a r c h 2 0 2 0

FORWARD LOOKING STATEMENTS

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; 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.

In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “could,” “would,” “expects,” “plans,” “anticipates,” “believes,” “estimates,” “projects,” “predicts,” “potential” and similar expressions (including the negative thereof) intended to identify forward looking statements. Arcturus may not actually achieve the plans, carry out the intentions or meet the expectations or projections disclosed in any forward-looking statements such as the foregoing, and you should not place undue reliance on such forward-looking statements. The forward-looking statements contained or implied in this presentation are subject to other risks and uncertainties, including those discussed under the heading "Risk Factors" in Arcturus' Annual Report on Form 10-K for the fiscal year ended December 31, 2019, filed with the SEC on March 16, 2020 and in subsequent filings with, or submissions to, the SEC. Except as otherwise required by law, we disclaim any intention or obligation to update or revise any forward-looking statements, which speak only as of the date they were made, whether as a result of new information, future events or circumstances or otherwise.

Company Highlights



BUILDING INNOVATIVE
RNA MEDICINES

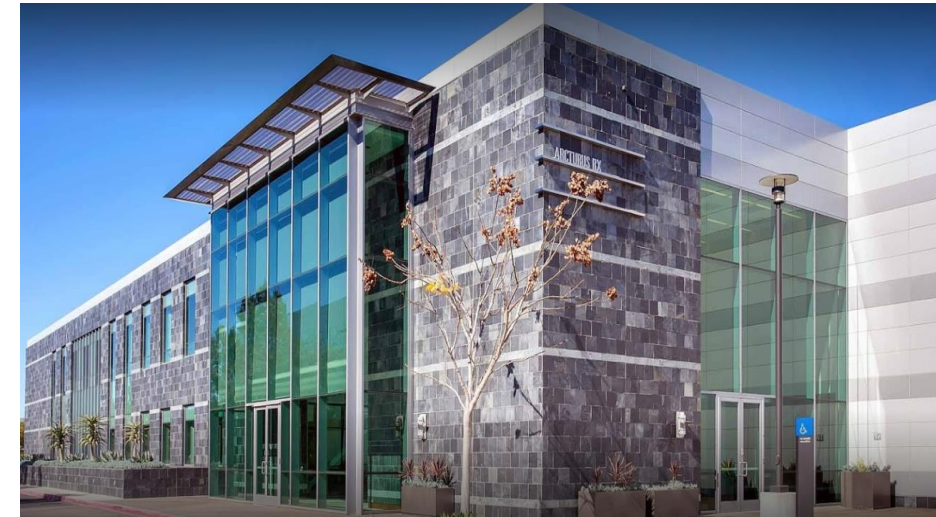
Arcturus is an mRNA Medicines and Vaccines Company

Publicly Traded (NASDAQ:ARCT)

- Headquarters: San Diego, CA
- Number of Employees: 90
- Founded: 2013

Strong Intellectual Property Technology Portfolio

- 187 Patents & Patent Applications
- LUNAR® Delivery Technology
- STARR™ RNA Manufacturing Process
- Drug Product (LUNAR® + STARR™) Manufacturing Process



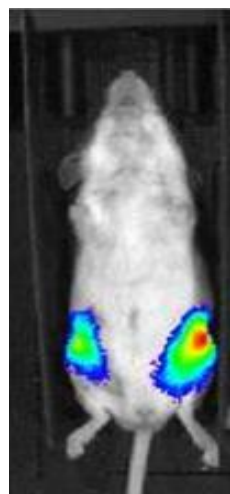
Arcturus Technologies Validated by Multiple Strategic Partners



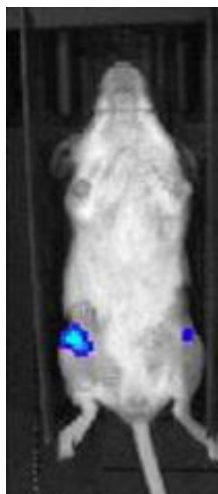
STARR™ mRNA Superior to Conventional mRNA

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**



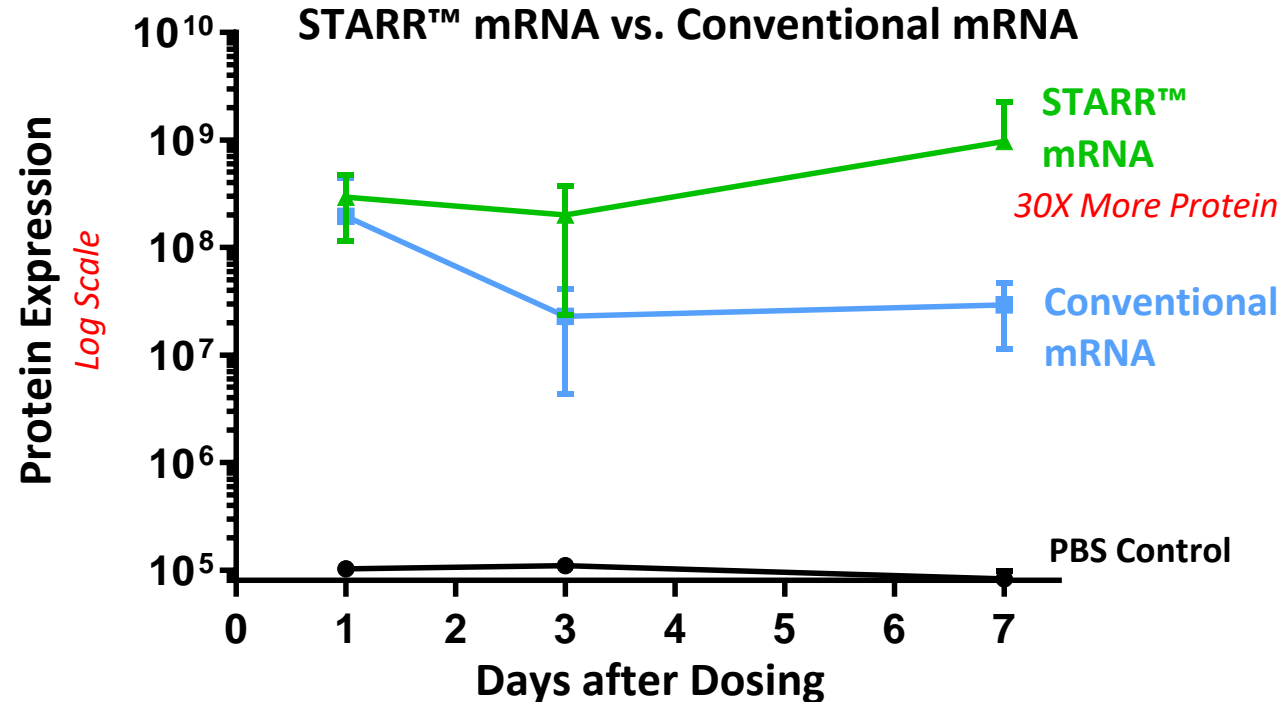
**Conventional
mRNA**



**PBS
Control**

Protein Expression Over 7 days

STARR™ mRNA vs. Conventional mRNA



Single Dose of STARR™ mRNA with LUNAR® Delivery Provides Enhanced Protein Expression

Arcturus COVID-19 Vaccine has Significant Advantages



Very Low Dose

- Result of combining Arcturus' LUNAR® and STARR™ technologies
- Means potentially more people vaccinated per manufactured batch

Potential Single Shot

- Small, single intramuscular injection
- Simpler logistics for vaccinating large populations

Utilizes STARR™ mRNA

- STARR™ mRNA produces 30X more protein than conventional mRNA
- Lasts longer, booster shot may be unnecessary

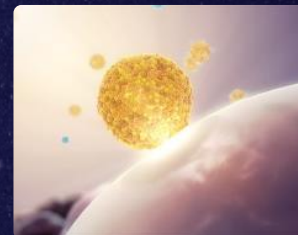
Contains No Viruses or Viral Material

- No dead viruses, no attenuated viruses, no virus or viral vectors (AAVs) used to deliver the RNA vaccine
- LUNAR® Delivery Technology is Non-Viral

LUNAR[®] Delivery Technology



**LUNAR Associates
with Cell Membrane**



Enters Cell
Via Endocytosis

**Lipid Particle in
Endosome**



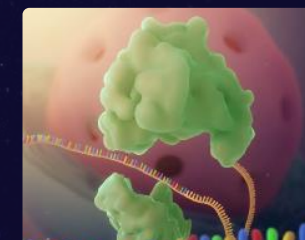
Increased Acidity as
Endosome Ages

**pH-Mediated
Disruption**







Rapid Biodegradation
of Vehicle

**RNA
in Cytosol**



RNA Processing
and Translation

Arcturus Platform: Enabling Genetic Medicines

Program	Partner	Indication	Arcturus Chemistry	Arcturus Delivery	Program Status
LUNAR-GSD3		Glycogen Storage Disease Type III	mRNA	LUNAR® Hepatocytes	Target IND 2020+
LUNAR-RARE		Undisclosed Rare Disease	mRNA	LUNAR® Hepatocytes	Preclinical
LUNAR-HBV		Hepatitis B	RNA	LUNAR® Hepatocytes	Preclinical
LUNAR-NASH		NASH	RNA	LUNAR® Stellate Cells	Preclinical
LUNAR-RPL	Large Pharma	Infectious Disease Prophylactic Vaccines	SGL's Replicon RNA	LUNAR®	Preclinical
LUNAR-AH	Large Animal Health Pharma	Infectious Disease Prophylactic Vaccines	SGL's Replicon RNA	LUNAR®	Preclinical

- Greater than \$1 Billion in Potential Milestones & Royalties
- Enabling Different Types of RNA – Messenger RNA, Gene Editing RNA, Replicon RNA
- Multiple Cell Types Targeted
- LUNAR-GSD3 (UX053) partnered with Ultragenyx – IND Target 2020+



Arcturus Pipeline of mRNA Medicines

Name	Indication	Expected Regulatory Filing Date	Route of Administration	Target Organ	Target Cells	Prevalence Worldwide
LUNAR-COV19	Coronavirus COVID-19 Vaccine	H2 2020 (CTA, Singapore)	Intramuscular (i.m.)	Muscle	Myocyte	Global
LUNAR-OTC (ARCT-810)	Ornithine Transcarbamylase (OTC) Deficiency	IND Filed March 2020	Intravenous (i.v.)	Liver	Hepatocytes	> 10,000
LUNAR-CF	Cystic Fibrosis	2021	Nebulized Aerosol	Lung	Bronchial Epithelial Cells	> 70,000
LUNAR-CV	Rare Cardiovascular Disease	Preclinical	Intravenous (i.v.)	Liver	Hepatocytes	Undisclosed
LUNAR-MD	Rare Metabolic Disease	Preclinical	Intravenous (i.v.)	Liver	Hepatocytes	Undisclosed

- **LUNAR-COV19: CTA (Singapore) Filing Target H2 2020**
- **LUNAR-OTC (ARCT-810): IND Filed; Next Milestone Human Data**
- **LUNAR-CF (Funded by the Cystic Fibrosis Foundation): IND Filing Target 2021**

Arcturus Developing COVID-19 Vaccine with Duke-NUS



Partnership Initiated March 4, 2020

- Funded, up to \$10M



Arcturus COVID-19 Vaccine Benefits From Duke-NUS Genetic Correlation System

- Helps Arcturus learn more quickly about the LUNAR-COV19 efficacy and safety profile
- Specific gene changes correlate with efficacy and safety
 - Level of neutralizing antibody titers
 - Safety-related adverse events (headache, fever)
- Gene expression changes can be measured within the first 5 days following vaccination

The data generated from the Duke-NUS system gives Arcturus the ability to more efficiently select the dose and help streamline the vaccine development program, and potentially accelerate timeline

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

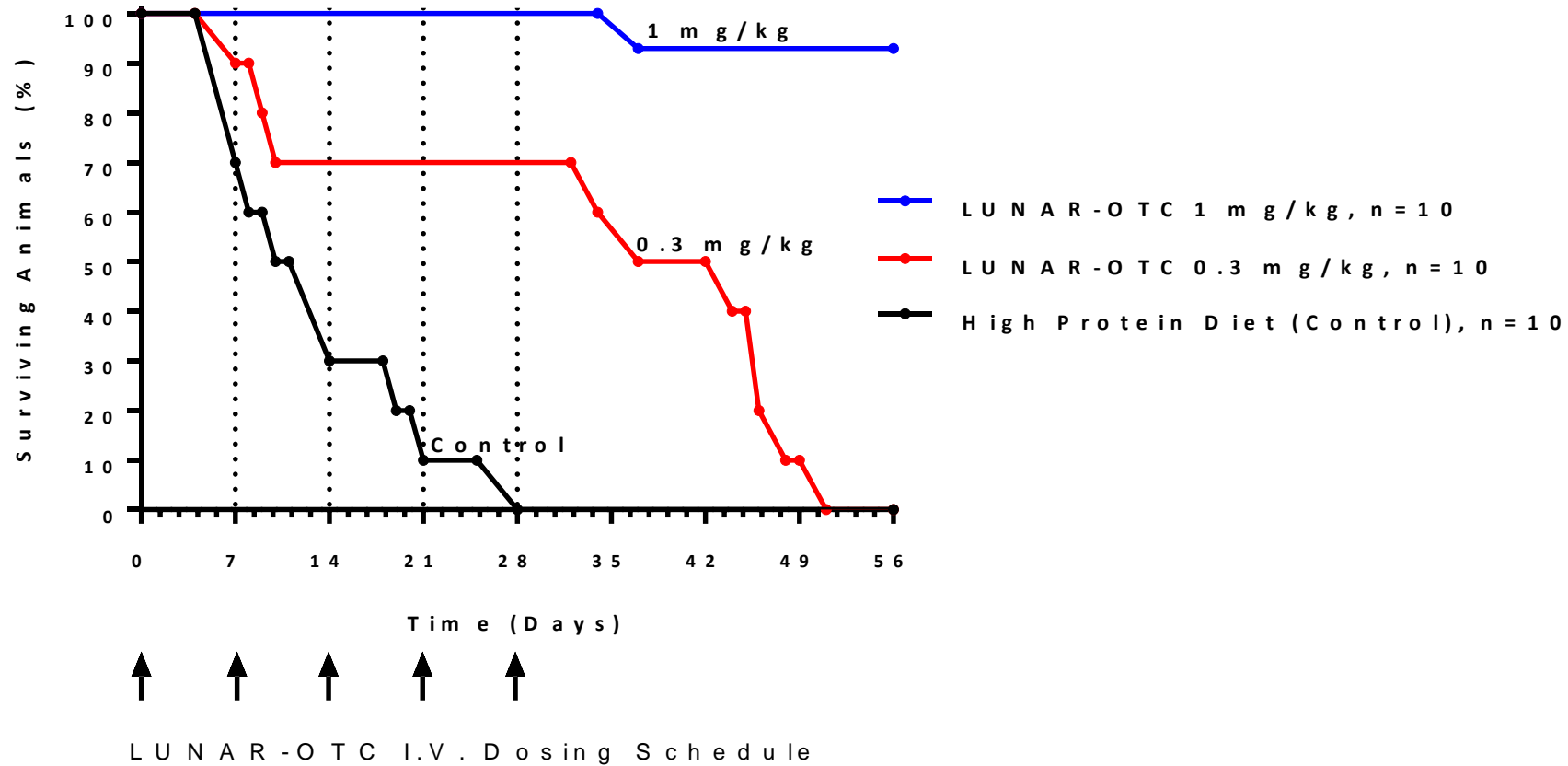
LUNAR[®]-OTC

Disease Normalization Following Single and Repeat Dosing in OTC Mouse Model



BUILDING INNOVATIVE
RNA MEDICINES

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

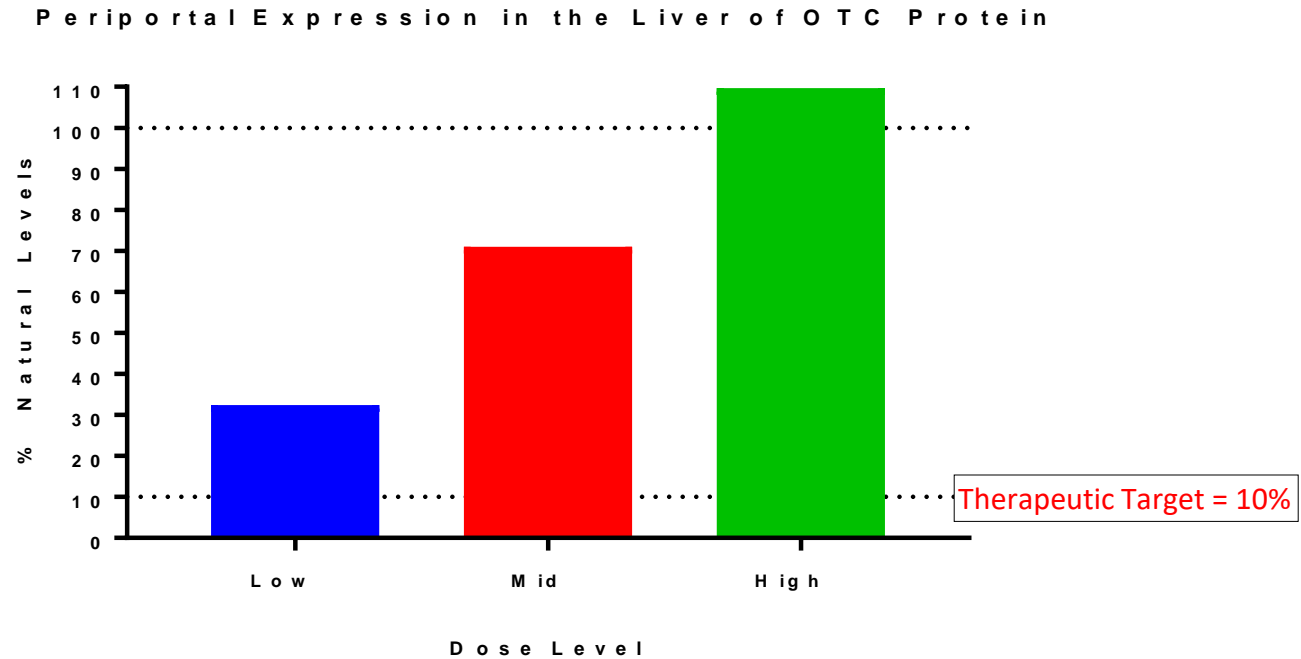


LUNAR-OTC



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

- 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-1 α Promotes Ureagenesis in Mouse Periportal Hepatocytes through SIRT3 and SIRT5 in Response to Glucagon. Scientific Reports. 6:24156 | DOI: 10.1038/srep24156, April 2016

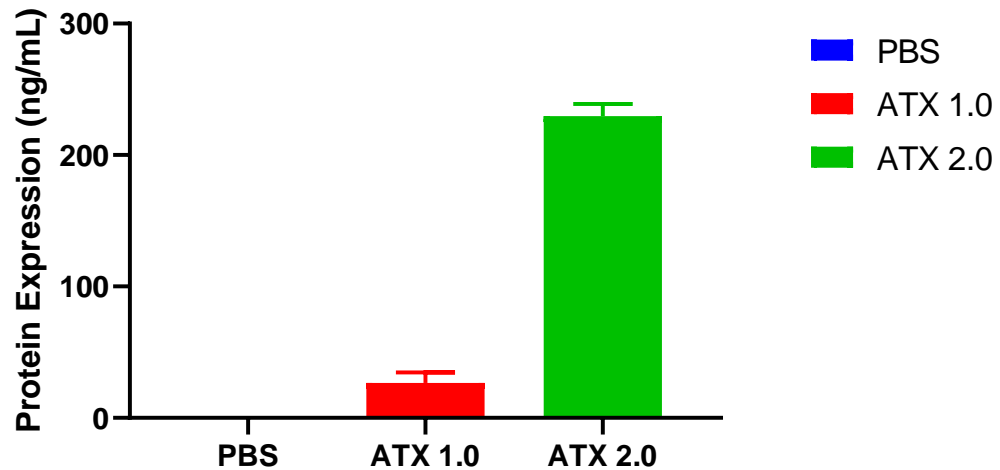
*Lamers, W.H., Hakvoort, T.B.M., and Köhler, E.S. 'Molecular Pathology of Liver Diseases' in Monga S.P.S. (ed.), MOLECULAR PATHOLOGY LIBRARY SERIES, Springer Publishing, New York, pp. 125-132 | DOI: 10.1007/978-1-4419-7107-4

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

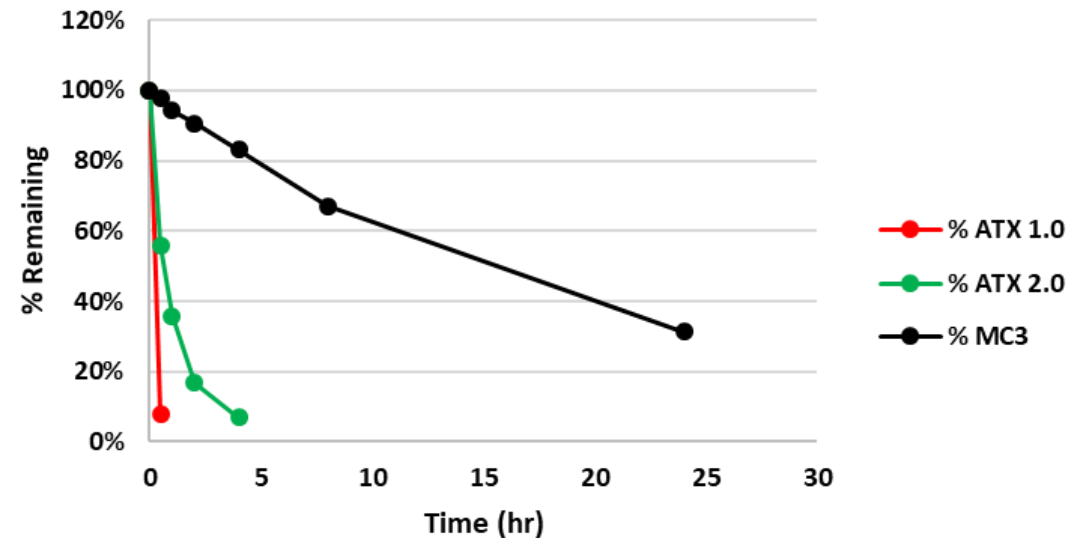
ATX Lipids are Effective and Degrade Rapidly

BUILDING INNOVATIVE
RNA MEDICINES

Protein Expression (*in vivo*)



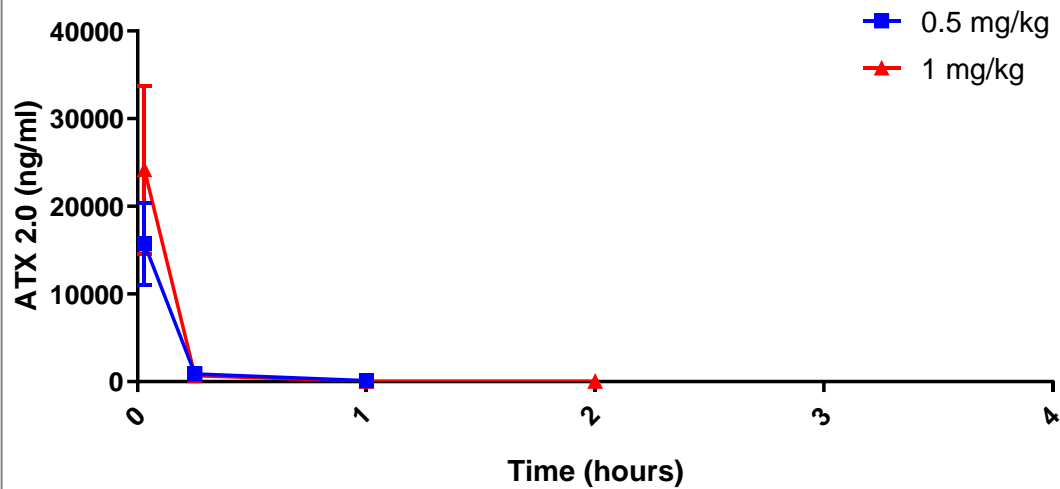
Esterase Catalyzed Degradation (*in vitro*)



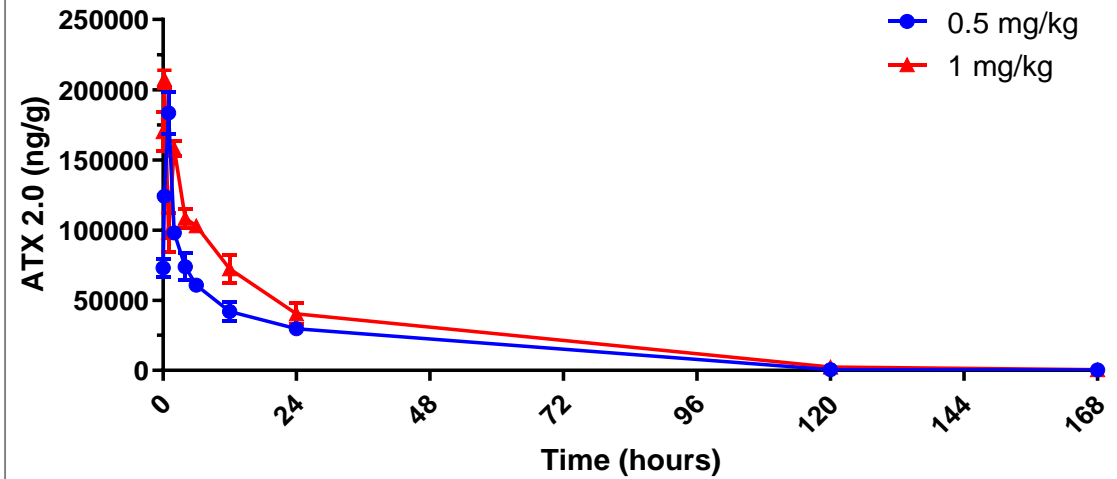
Next Generation ATX Lipids Retain Degradability & Improve Delivery Efficiency

ATX 2.0 Lipid Rapidly Clears *in vivo*

Plasma



Liver



- ATX Lipid (the major component in LUNAR® technology) is rapidly degraded *in vivo*
- ATX Lipid Half-Life in the Liver is Approximately 20 hours

Arcturus Safety Profile



External Validation

- Multiple strategic partnerships over many years confirms the positive 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 Delivery

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

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



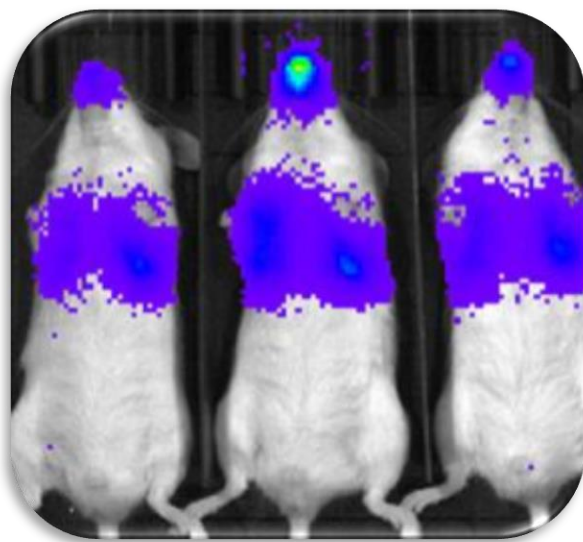
LUNAR-CF Aims to Restore CFTR Function

- 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

LUNAR[®] Delivery of mRNA to Lung (Mouse)

BUILDING INNOVATIVE
RNA MEDICINES

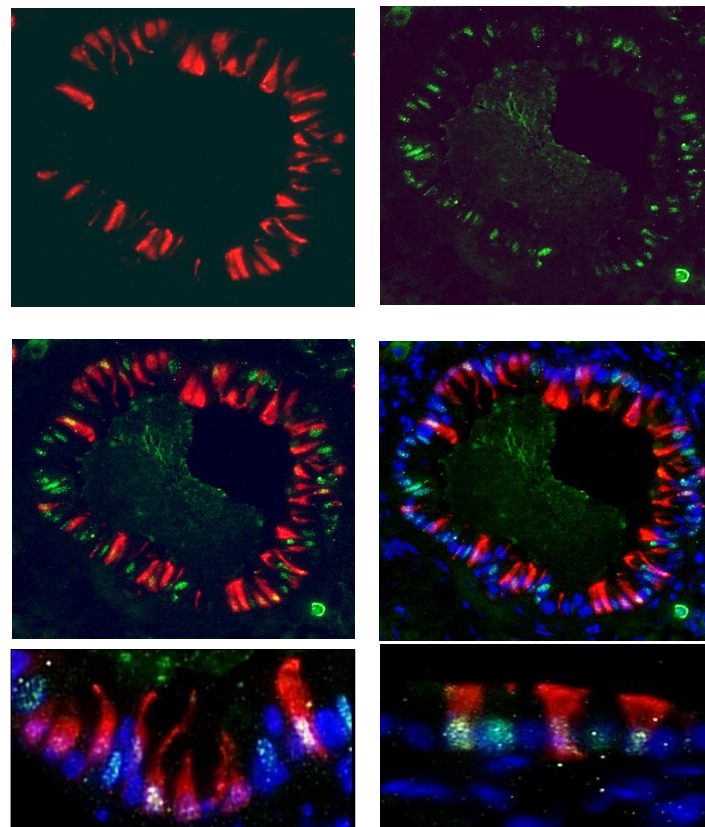
Nebulization



LUNAR[®] + Luciferase mRNA

LUNAR[®] Delivery of mRNA into Bronchial Epithelial Cells (BECs)

TdTomato / FoxJ1 / Dapi

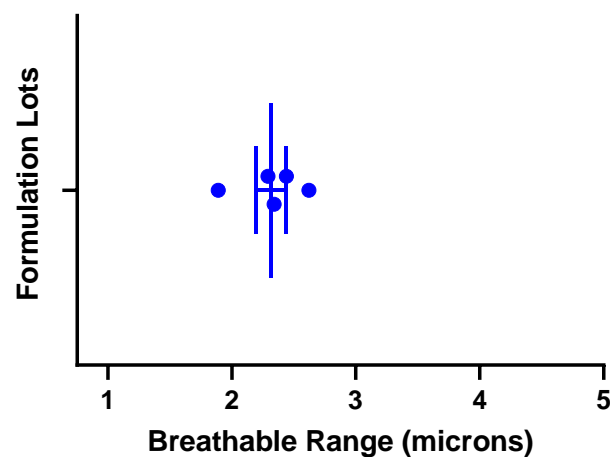


Functional Nebulized Delivery of LUNAR[®]+ mRNA into Lung Epithelial Cells

Aerosolized LUNAR[®]

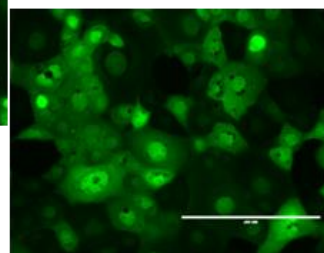
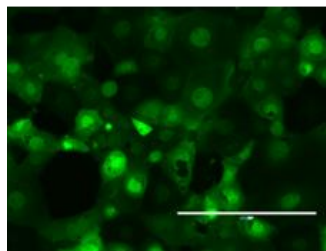
BUILDING INNOVATIVE
RNA MEDICINES

Aerosolized LUNAR[®]
Particles are Breathable



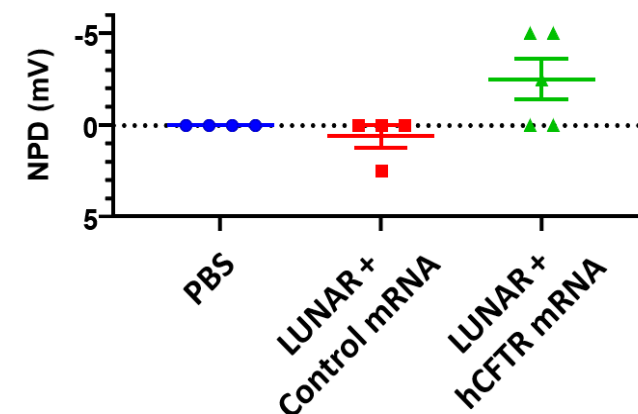
Aerosolized LUNAR[®] -mRNA (GFP)
maintains activity

Pre-Nebulization



Post-Nebulization

Aerosolized LUNAR[®] -CF
is functional *in vivo* (mouse)



Aerosolized LUNAR[®] Droplets are in the Optimal Breathable Range (2-3 microns)

Aerosolized LUNAR[®] Maintains Function as Measured by GFP Protein Expression & Nasal Potential Difference (NPD)

Drug Substance: mRNA Design

BUILDING INNOVATIVE
RNA MEDICINES**Arcturus' proprietary mRNA optimization platform****Sustained hEPO activity in NHPs upon repeat dosing**

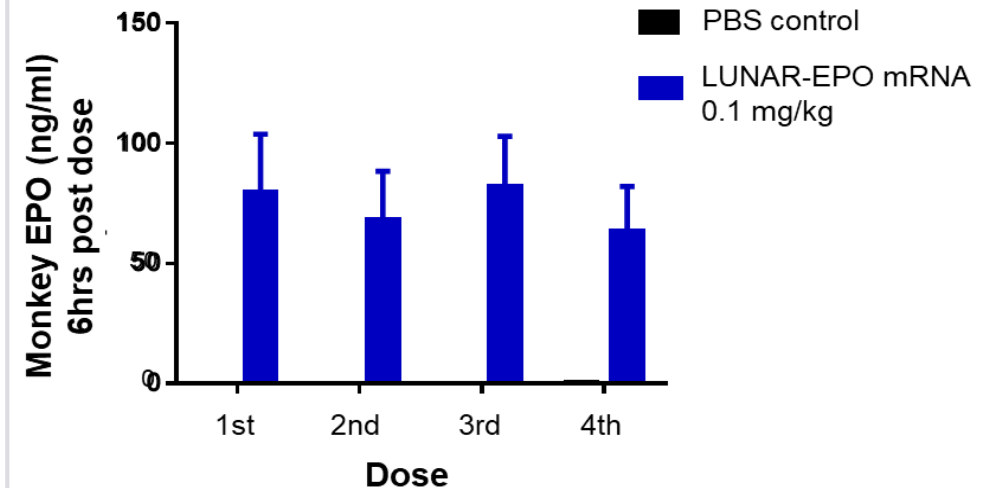
Optimize
mRNA sequence
Chemistry
Process



Improve
Protein Expression
Duration
Functional Activity



Weekly Dosing in Non-Human Primates (NHPs)

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

Drug Substance (mRNA) Manufacturing

BUILDING INNOVATIVE
RNA MEDICINES

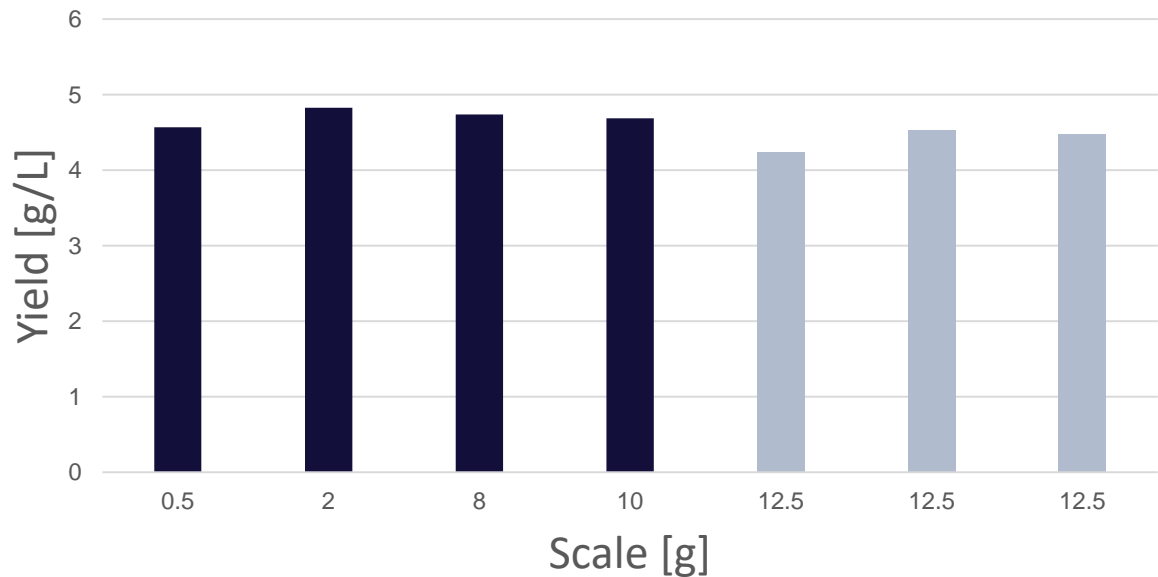
Features	Benefits
Optimized IVT Method	Reduced Cost; Higher Purity
Improved Capping Reaction	Reduced Cost of Goods
Proprietary Purification Process	Higher Purity in a Shorter Time
Efficient	Entire Process Less Than One Week
Scalable to > 1Kg	Access Large Patient Populations
Adaptable	Can Utilize a Variety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

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

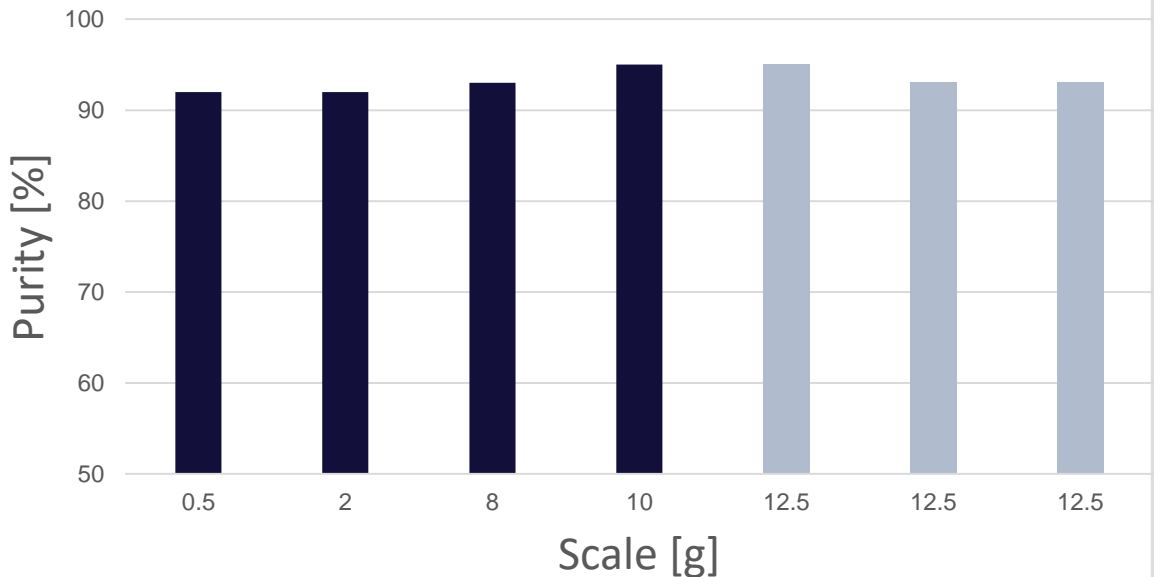
Drug Substance (mRNA) Manufacturing



RNA Yield



RNA Purity



- Non-GMP Lots Produced at Arcturus
- GMP Lots Produced at CMO as part of recent GMP campaign

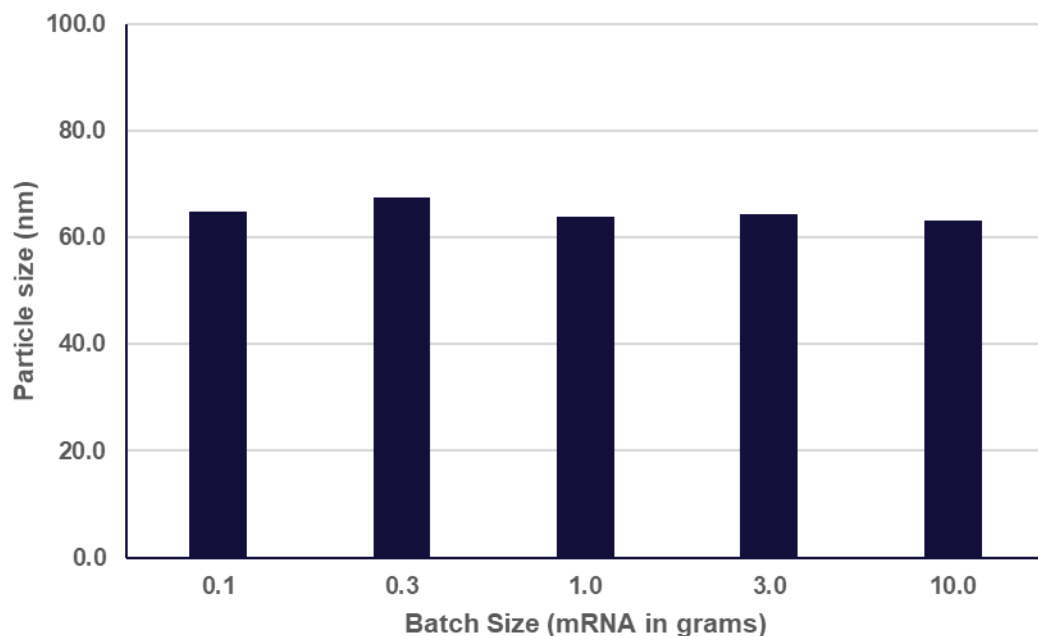
Three 12.5 g lots produced in recent GMP campaign are of equivalent quality and yield

Drug Product (LUNAR[®] + mRNA) Manufacturing

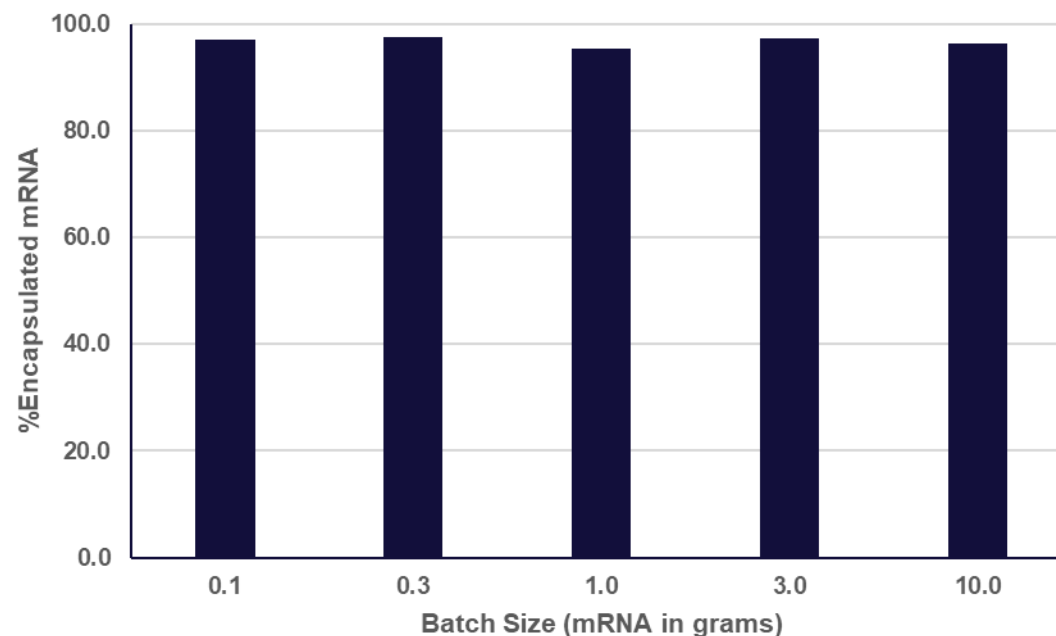


BUILDING INNOVATIVE
RNA MEDICINES

Particle Size



%Encapsulated mRNA



- Manufacturing of Drug Product Demonstrated up to Multigram Scale with Yields $\geq 85\%$
- GMP Batch of LUNAR[®]-OTC (ARCT-810) Drug Product Manufactured and Released

Board of Directors



BUILDING INNOVATIVE
RNA MEDICINES



Peter Farrell, Ph.D.
Chairman of the Board



Karah Parschauer, JD
Director of the Board



Edward W. Holmes, M.D.
Director of the Board



James Barlow, MA
Director of the Board



Magda Marquet, Ph.D.
Director of the Board



Joseph E. Payne, MSc
*Director of the Board,
President & CEO*



Andrew Sassine, MBA
*Director of the Board,
CFO*



Emil D. Kakkis, M.D., Ph.D.
Board Advisor



Management Team



BUILDING INNOVATIVE
RNA MEDICINES



Joseph E. Payne, MSc
President & CEO



Pad Chivukula, Ph.D.
CSO & COO



Andrew Sassine, MBA
CFO



Steve Hughes, M.D.
Chief Development Officer



