

ARCTURUS THERAPEUTICS

Building the Next Generation of RNA Medicines

March 2020

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; the date that an IND may be filed with the FDA; 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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Investment Highlights



Arcturus is an mRNA Medicines Drug Development Company Focused on Rare Diseases

LUNAR[®] Delivery Platform Validated by Multiple Strategic Partners

- More than \$1 Billion in potential milestones and royalties

Broad and Strong Intellectual Property Portfolio

- 182 Patents & Patent Applications
- LUNAR[®] Delivery Technology
- RNA Drug Substance & Drug Product Process Manufacturing



HQ: **San Diego**; Founded: **2013**; Nasdaq: **ARCT**
Outstanding Shares: **15.1M**; Employees: **90**;
Insider Ownership: **33%**

Promising Preclinical Safety Data for LUNAR[®] Delivery and mRNA Drug Products

2019 Summary



Ultragenyx Collaboration Expanded, \$30M 

Cystic Fibrosis Foundation Increased Commitment to \$15M



Fundraising Completed, \$23M from Institutional Investors

Advanced Pipeline

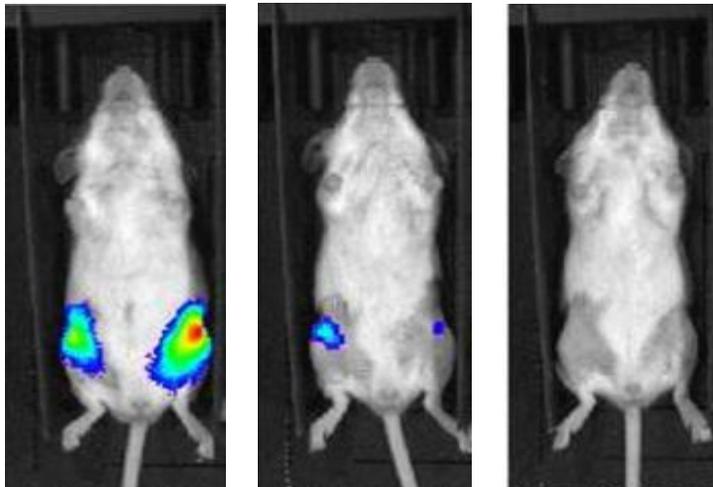
- **LUNAR-OTC:** ARCT-810 Nominated, Received Orphan Drug Designation from FDA, GMP Manufacturing of Drug Product Completed and Released, On-track for Q1-2020 IND
- **LUNAR-CF:** Preclinical Lung Data Collected, CF Foundation Financial Support Received

Expanded Platform to include STARR Technology™

STARR Technology™ Superior to mRNA *in vivo* (mouse)

Self-Transcribing and Replicating RNA (STARR) delivered with LUNAR® provides longer-lasting, higher protein expression

**STARR Technology™
30-Fold Higher Protein Expression**



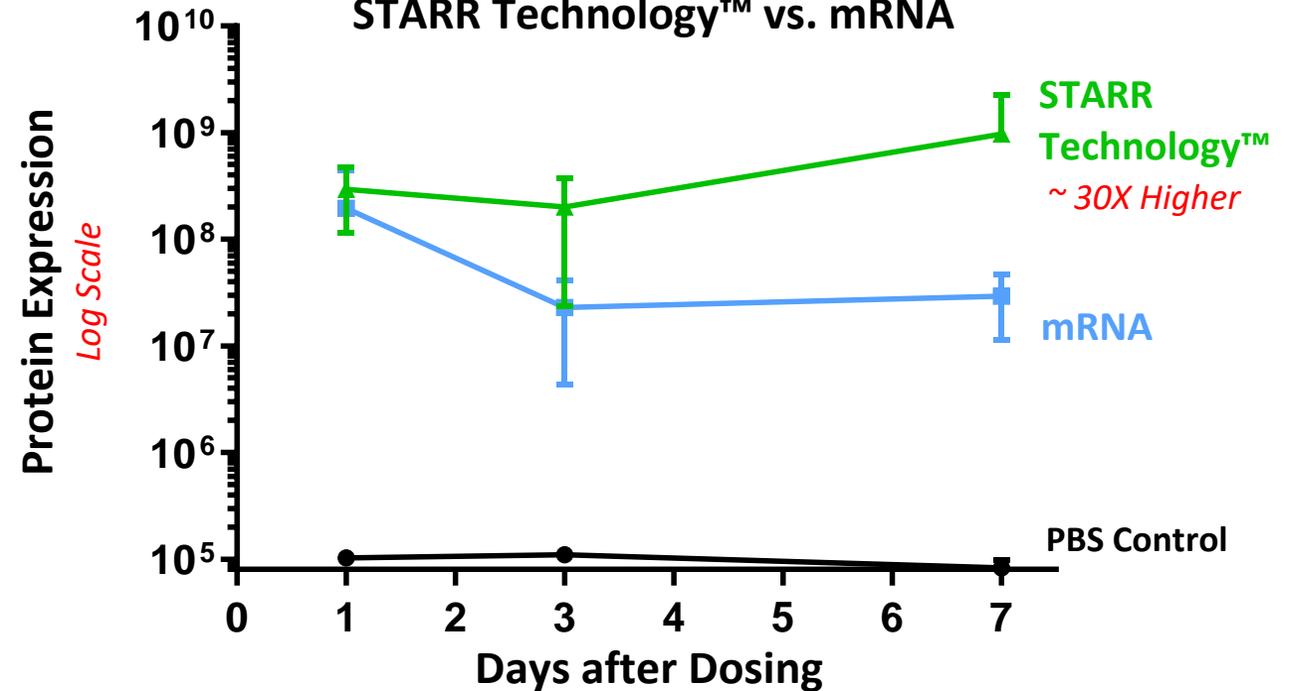
STARR
Technology™

mRNA

PBS Control

Protein Expression Over 7 days

STARR Technology™ vs. mRNA



Single Dose of STARR Technology™ with LUNAR® Provides Enhanced and Prolonged Protein Expression

Key Value Drivers → Platform & Pipeline



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Platform: LUNAR® Delivery, mRNA Drug Substance, and STARR (Self-Transcribing And Replicating RNA) Technology™



SYNTHETIC GENOMICS



Strategic Partners: More than \$1 Billion in Potential Milestones & Royalties

Pipeline: Arcturus mRNA Medicines

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

OTC Deficiency Market Potential \$500M Annual Sales

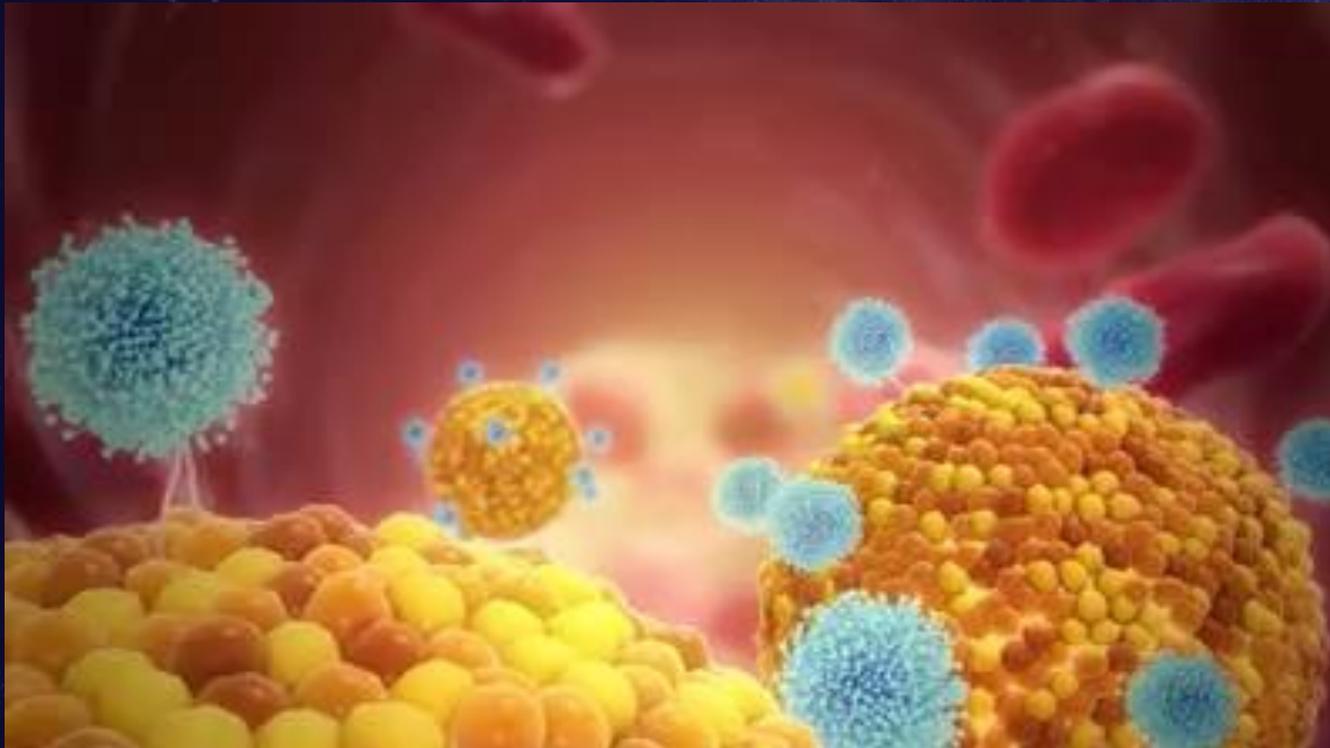
Orphan Drug Designation is received from U.S. FDA

LUNAR-CF to treat Cystic Fibrosis (CF)

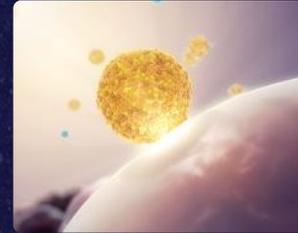


Class I CF Market Potential \$900M Annual Sales

LUNAR[®] Delivery Technology



LUNAR Associates
with Cell Membrane



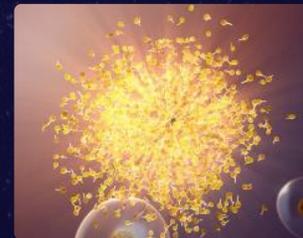
Enters Cell
Via Endocytosis

Lipid Particle in
Endosome



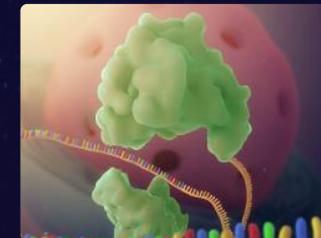
Increased Acidity as
Endosome Ages

pH-Mediated
Disruption



Rapid Biodegradation
of Vehicle

RNA
in Cytosol



RNA Processing
and Translation

Arcturus Platform: Enabling Genetic Medicines



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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	SGI's Replicon RNA	LUNAR®	Preclinical
LUNAR-AH	Large Animal Health Pharma	Infectious Disease Prophylactic Vaccines	SGI'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-OTC (ARCT-810)	Ornithine Transcarbamylase (OTC) Deficiency	Q1 2020	Intravenous (i.v.)	Liver	Hepatocytes	> 10,000
LUNAR-CF	Cystic Fibrosis	2021	Nebulized Aerosol	Lung	Bronchial Epithelial Cells	> 70,000
LUNAR-COV19	Coronavirus COVID-19 Vaccine	2020+	Intramuscular (i.m.)	Muscle	Myocyte	N/A
LUNAR-CV	Rare Cardiovascular Disease	Preclinical	Intravenous (i.v.)	Liver	Hepatocytes	Undisclosed
LUNAR-MD	Rare Metabolic Disease	Preclinical	Intravenous (i.v.)	Liver	Hepatocytes	Undisclosed

- Pipeline programs focus on messenger RNA (mRNA) drug products for rare diseases
- LUNAR-OTC (ARCT-810, intravenous mRNA medicine): IND Filing Target Q1 2020
- LUNAR-CF is funded by the Cystic Fibrosis (CF) Foundation: IND Filing Target 2021

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

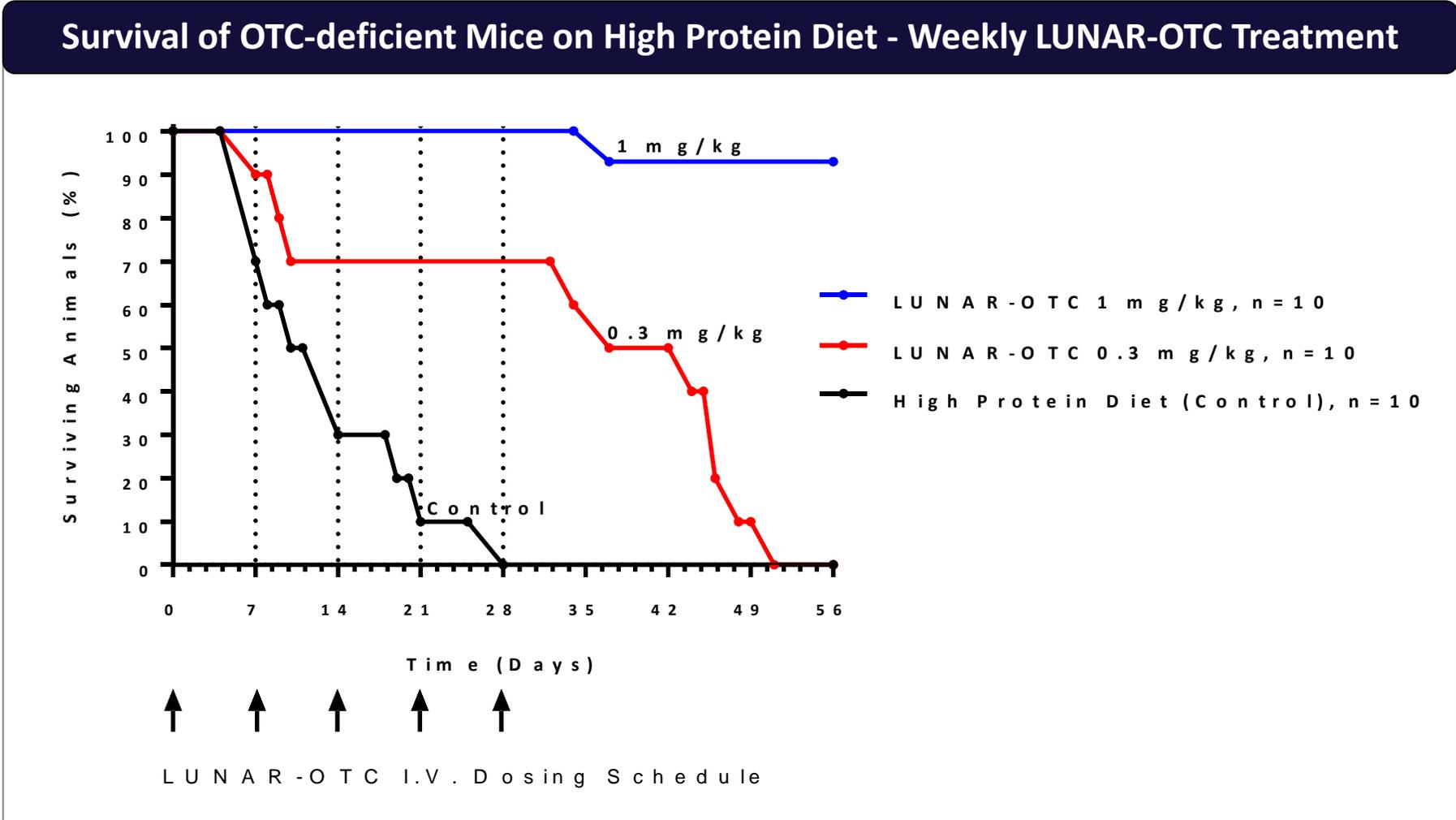


LUNAR-OTC Aims to Restore Enzyme Function

- 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



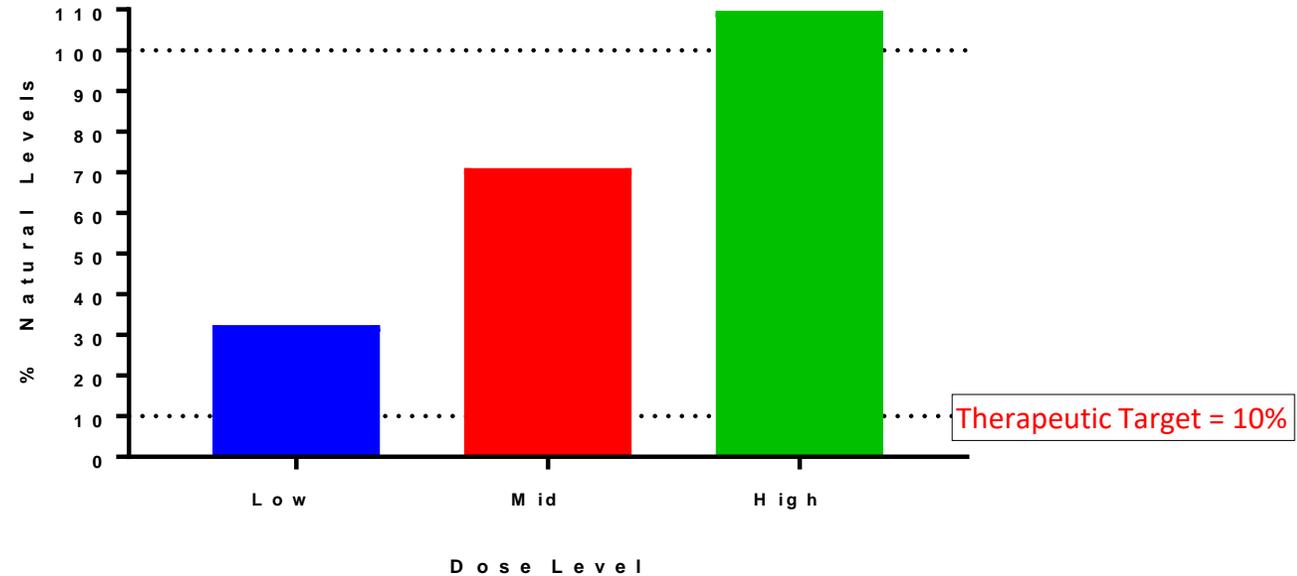
LUNAR-OTC



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

Periportal Expression in the Liver of OTC Protein



*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

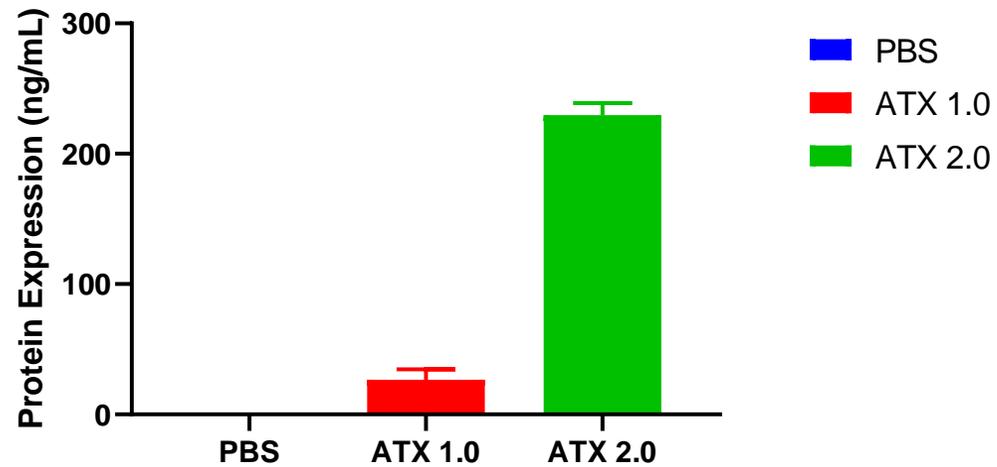
*Lamers, W.H., Hakvoort, T.B.M., and Köhler, E.S. 'Molecular Pathology of Liver Diseases' in Monga S.P.S. (ed.), *MOLECULAR PATHOLOGY LIBRARY SERIES*, Springer Publishing, New York, pp. 125-132 | DOI: 10.1007/978-1-4419-7107-4

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

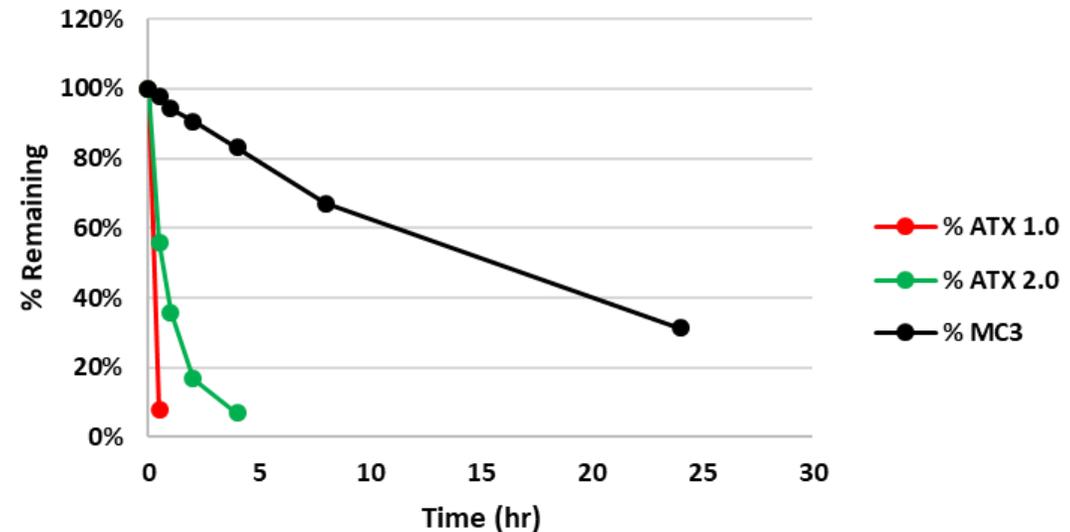
ATX Lipids are Effective and Degrade Rapidly



Protein Expression (*in vivo*)



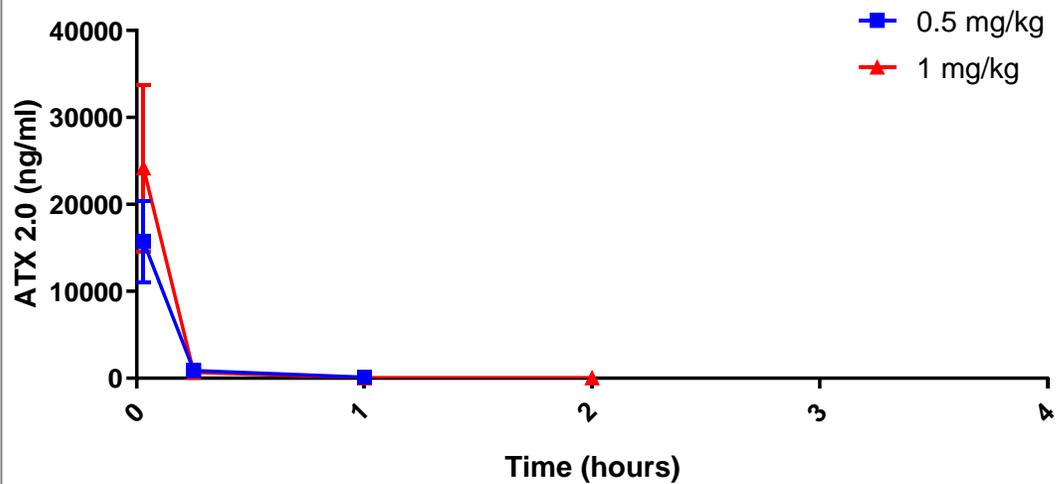
Esterase Catalyzed Degradation (*in vitro*)



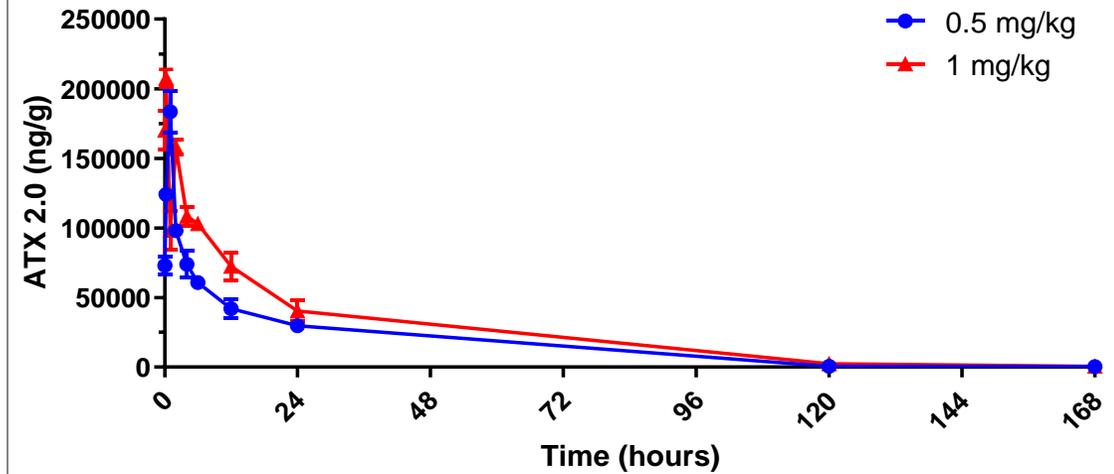
Next Generation ATX Lipids Retain Degradability & Improve Delivery Efficiency

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



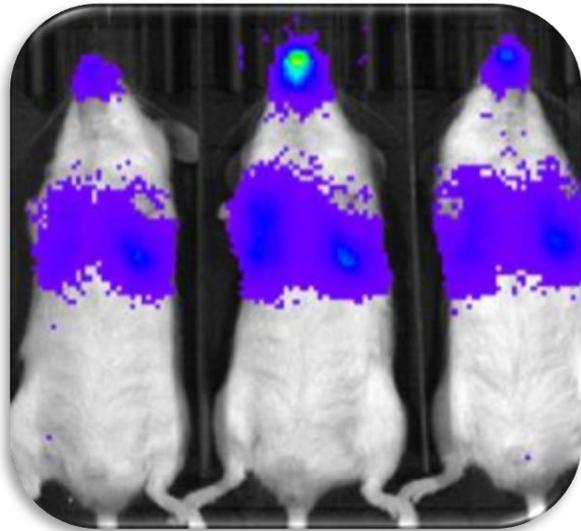
LUNAR-CF Aims to Restore CFTR Function

- 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)



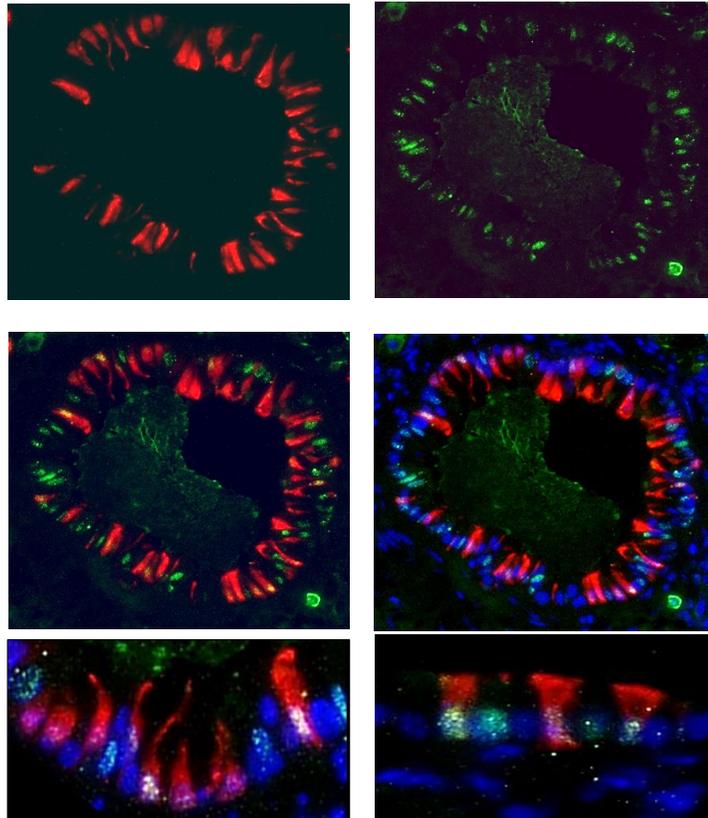
Nebulization



LUNAR[®] + Luciferase mRNA

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

TdTomato / FoxJ1 / Dapi

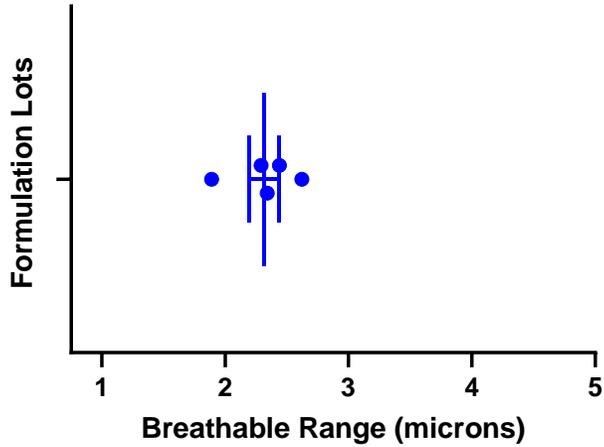


Functional Nebulized Delivery of LUNAR[®]+ mRNA into Lung Epithelial Cells

Aerosolized LUNAR[®]

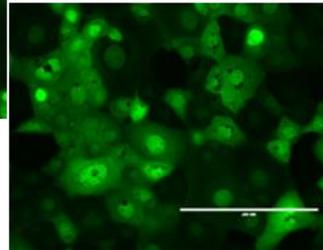
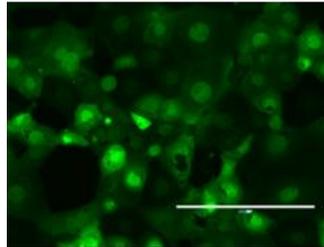


**Aerosolized LUNAR[®]
Particles are Breathable**



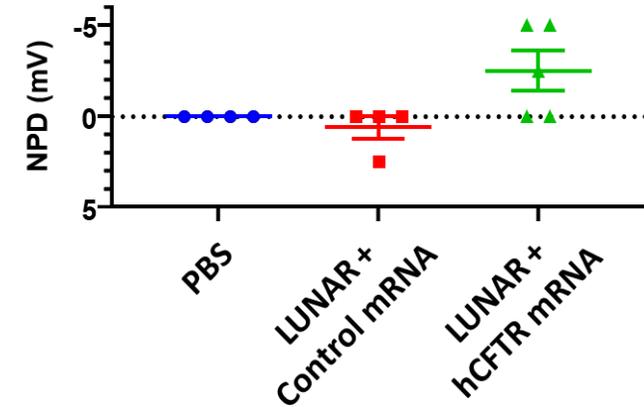
**Aerosolized LUNAR[®] -mRNA (GFP)
maintains activity**

Pre-Nebulization



Post-Nebulization

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



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

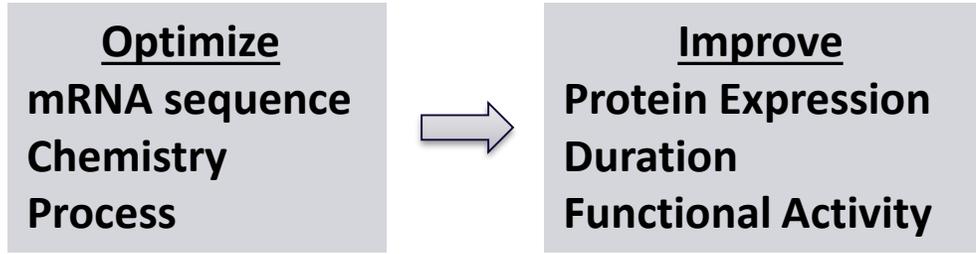
Aerosolized LUNAR[®] Maintains Function as Measured by GFP Protein Expression & Nasal Potential Difference (NPD)

Drug Substance: mRNA Design

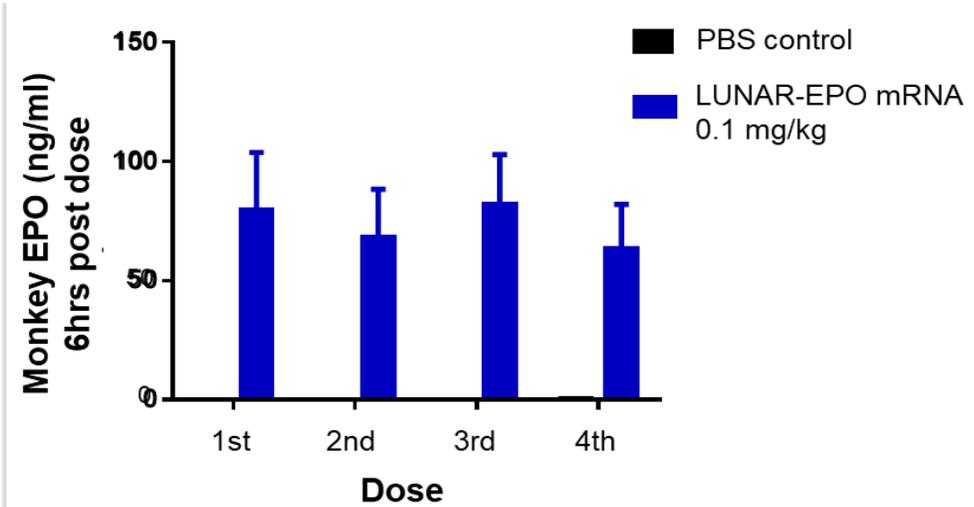


Arcturus' proprietary mRNA optimization platform

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



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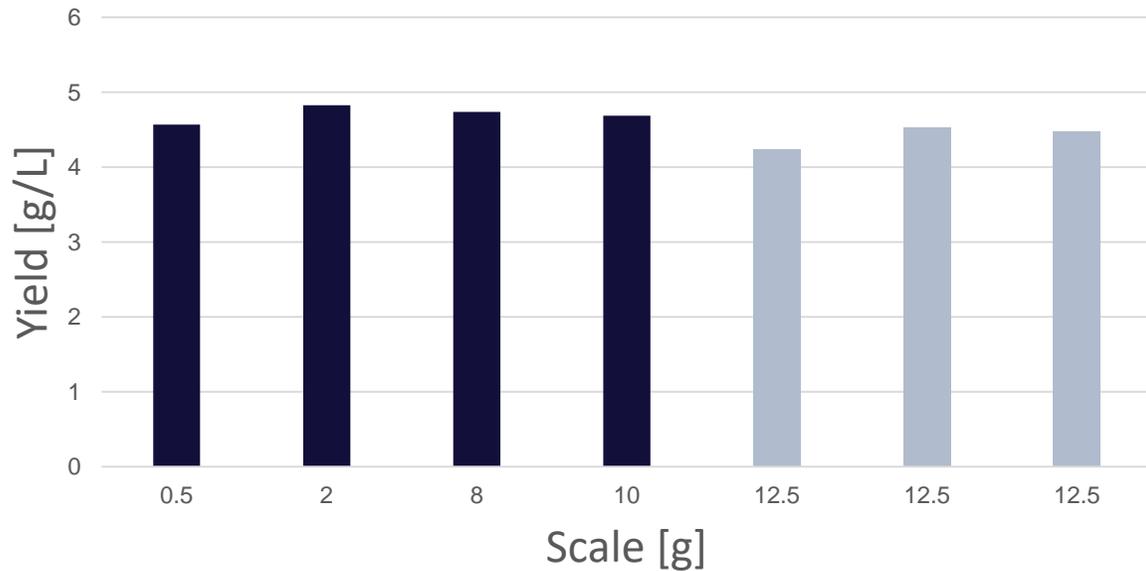
Features	Benefits
Optimized IVT Method	Reduced Cost; Higher Purity
Improved Capping Reaction	Reduced Cost of Goods
Proprietary Purification Process	Higher Purity in a Shorter Time
Efficient	Entire Process Less Than One Week
Scalable to > 1Kg	Access Large Patient Populations
Adaptable	Can Utilize a Variety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

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

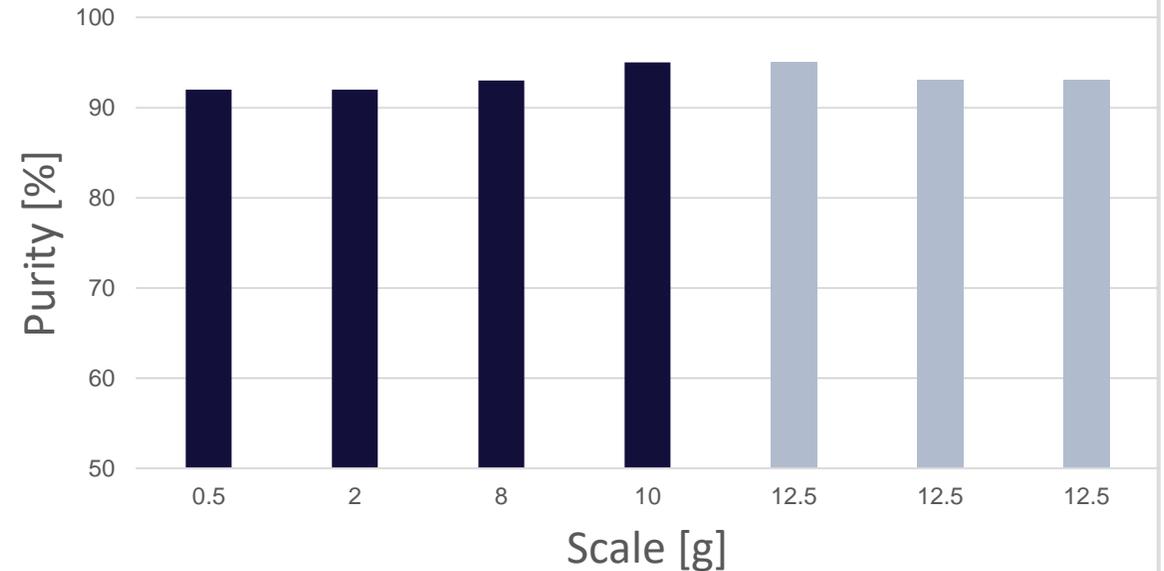
Drug Substance (mRNA) Manufacturing



RNA Yield



RNA Purity



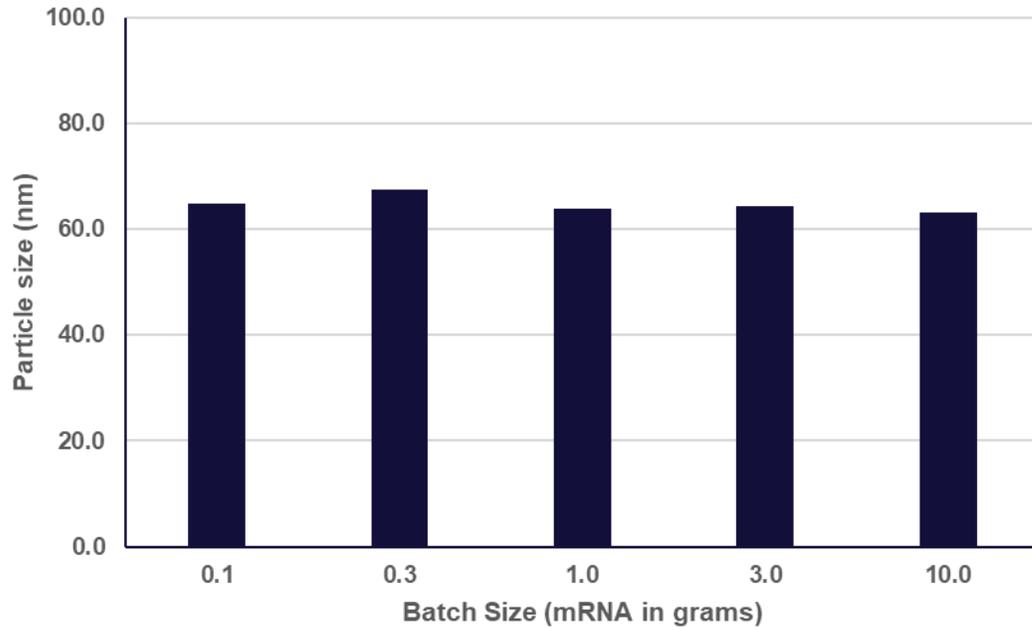
- Non-GMP Lots Produced at Arcturus
- GMP Lots Produced at CMO as part of recent GMP campaign

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

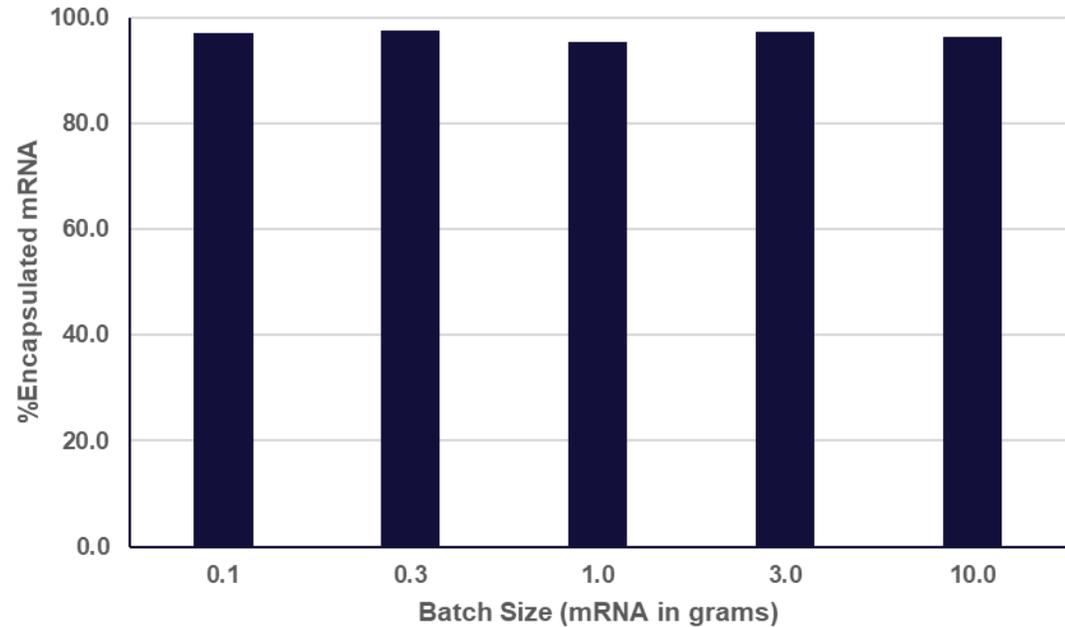
Drug Product (LUNAR[®] + mRNA) Manufacturing



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

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