

# ARCTURUS THERAPEUTICS

Building the Next Generation of RNA Medicines

M a y 2 0 1 9

# 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 success for 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 press 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, 2018, filed with the SEC on March 18, 2019 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.

# Investment Highlights

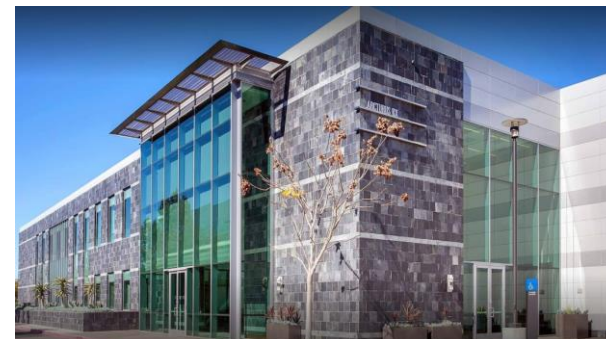
**Arcturus is an mRNA Medicines Drug Development Company Focused on Rare Diseases**

## **LUNAR® Delivery Platform Validated by Multiple Strategic Partners**

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

## **Broad and Strong Intellectual Property Portfolio**

- 152 Patents & Patent Applications
- LUNAR® Delivery Technology
- RNA Drug Substance & Drug Product Process Manufacturing



HQ: **San Diego**; Founded: **2013**; Nasdaq: **ARCT**  
Outstanding Shares: **10.8 M**; Employees: **80**;  
Insider Ownership: **24%**

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

# Key Value Drivers: mRNA Medicines & Platform



BUILDING INNOVATIVE  
RNA MEDICINES

## Arcturus LUNAR® Delivery Platform: Enabling Genetic Medicines



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

## Arcturus mRNA Medicines

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

*OTC Deficiency market potential \$500M annual sales*

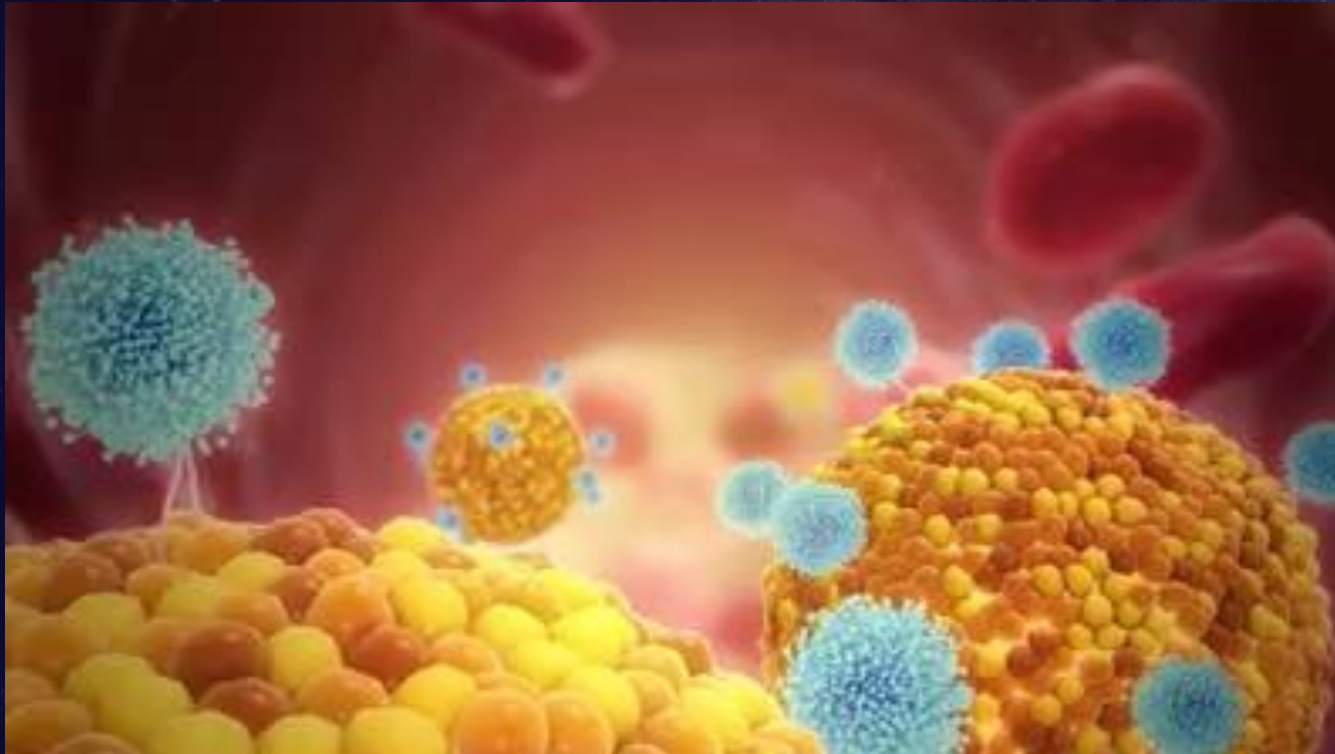
**LUNAR-CF** to treat Cystic Fibrosis (CF); Funded by the

*Class I CF market potential \$900M annual sales*

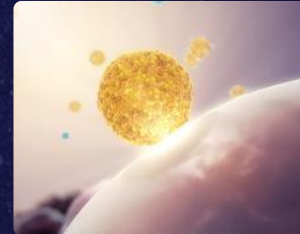




# LUNAR<sup>®</sup> Mechanism of Delivery



**LUNAR Associates  
with Cell Membrane**



Enters Cell  
Via Endocytosis

**Lipid Particle in  
Endosome**



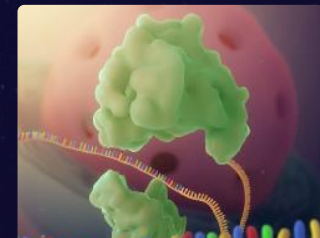
Increased Acidity as  
Endosome Ages

**pH-Mediated  
Disruption**



Rapid Biodegradation  
of Vehicle






**RNA  
in Cytosol**



RNA Processing  
and Translation



# Arcturus Platform: Enabling Genetic Medicines

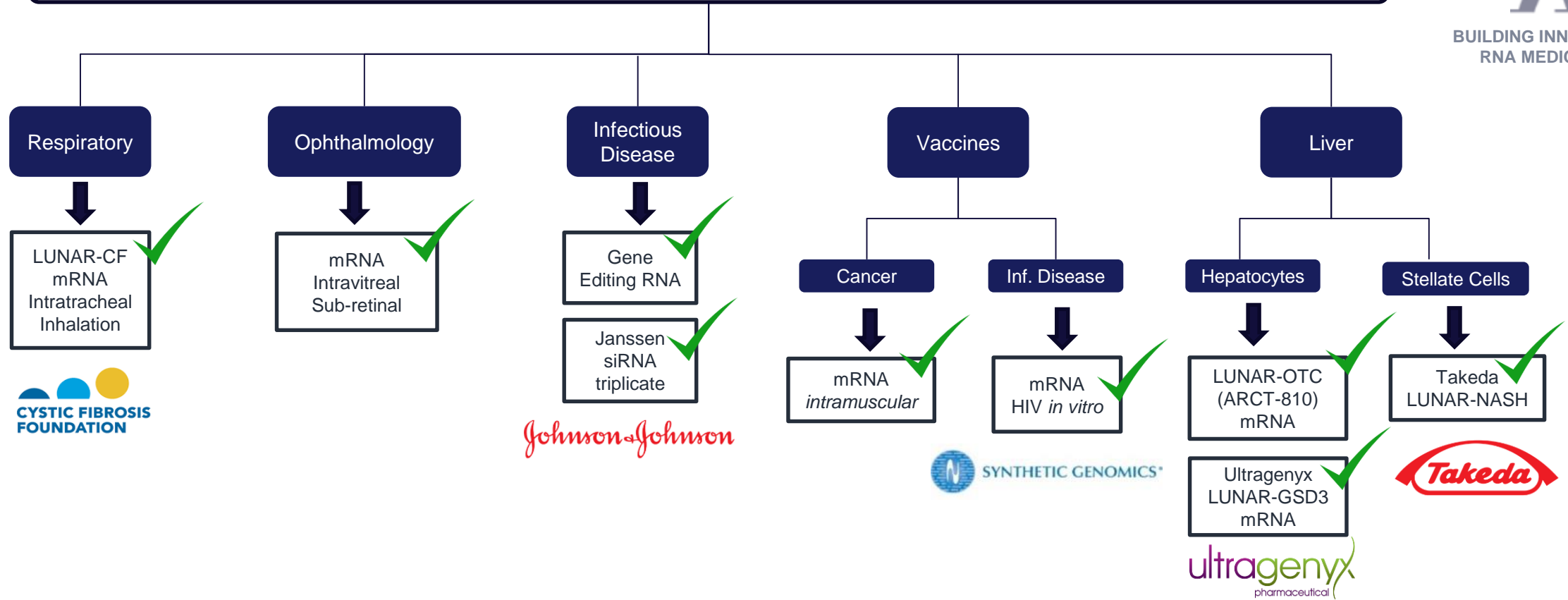
Name	Partner	Year of Initiation	Indication	Arcturus Chemistry	Arcturus Delivery	mRNA Process
LUNAR-HBV		2015	Hepatitis B	RNA	LUNAR® Hepatocytes	ARCT
LUNAR-NASH		2017	NASH	RNA	LUNAR® Stellate Cells	ARCT
LUNAR-GSD3		2016	Glycogen Storage Disease Type III	mRNA	LUNAR® Hepatocytes	ARCT
LUNAR-RARE		2016	Rare Disease	mRNA	LUNAR® Hepatocytes	ARCT
LUNAR-RPL		2017	Vaccines	SGI's Replicon RNA	LUNAR® Intramuscular	SGI

- Greater than \$1 Billion in Potential Milestones & Royalties
- Enabling Different Types of RNA – Messenger RNA, Gene Editing RNA, Replicon RNA
- Multiple Cell Types Targeted



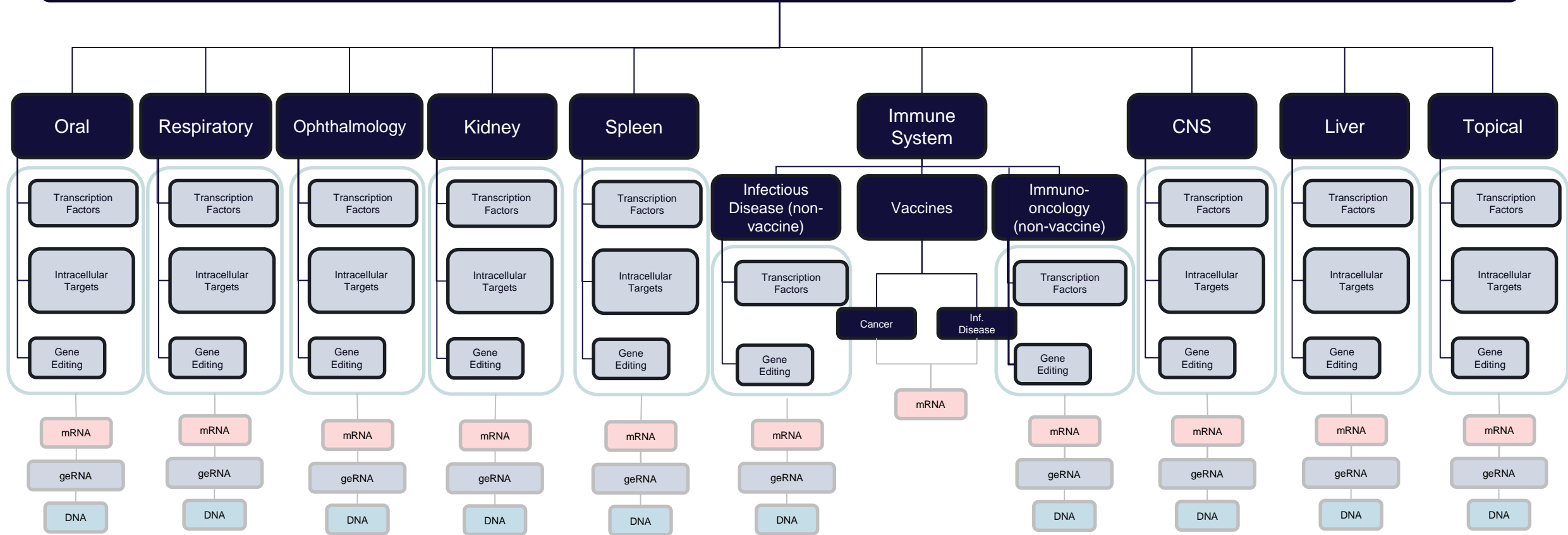
BUILDING INNOVATIVE  
RNA MEDICINES

# LUNAR® Platform Substantial Preclinical Proof-of-Concept Demonstrated



LUNAR® Platform Preclinical Proof-of-Concept Demonstrated in Hepatocytes, Liver Stellate Cells, Bronchial Epithelial Cells (Lung), Subretinal / intravitreal (Eye), Infectious Diseases, Cancer Vaccines

# Target Opportunities for LUNAR® Delivery Platform Exceed \$100 Billion in Potential Value



BUILDING INNOVATIVE  
RNA MEDICINES



# Arcturus Pipeline of mRNA Medicines



BUILDING INNOVATIVE  
RNA MEDICINES

Name	Indication	IND Date	Route of Administration	Target Organ	Target Cells	Prevalence Worldwide
<b>LUNAR-OTC (ARCT-810)</b>	Ornithine Transcarbamylase (OTC) Deficiency	Q4 2019	Intravenous (i.v.)	Liver	Hepatocytes	> 10,000
<b>LUNAR-CF</b>	Cystic Fibrosis	H1 2020	Nebulized Aerosol to Lung	Lung	Bronchial Epithelial Cells	> 70,000
<b>LUNAR-2020</b>	Rare Liver Disease	2021	i.v.	Liver	Hepatocytes	
<b>LUNAR-2020</b>	Rare Lung Disease	2021	Nebulized	Lung	Bronchial Epithelial Cells	

- Arcturus programs focus on messenger RNA (mRNA) drug products for rare diseases
- LUNAR-OTC (ARCT-810, intravenous mRNA medicine): Investigational New Drug (IND) Filing Target Q4 2019
- LUNAR-CF is funded by the Cystic Fibrosis (CF) Foundation – IND Target H1 2020
- If resources are available, we can progress more candidates into the clinic in 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 spikes of ammonia.
- OTC Deficiency patients are typically referred for liver transplant.



## **LUNAR-OTC Aims to Restore Enzyme Function**

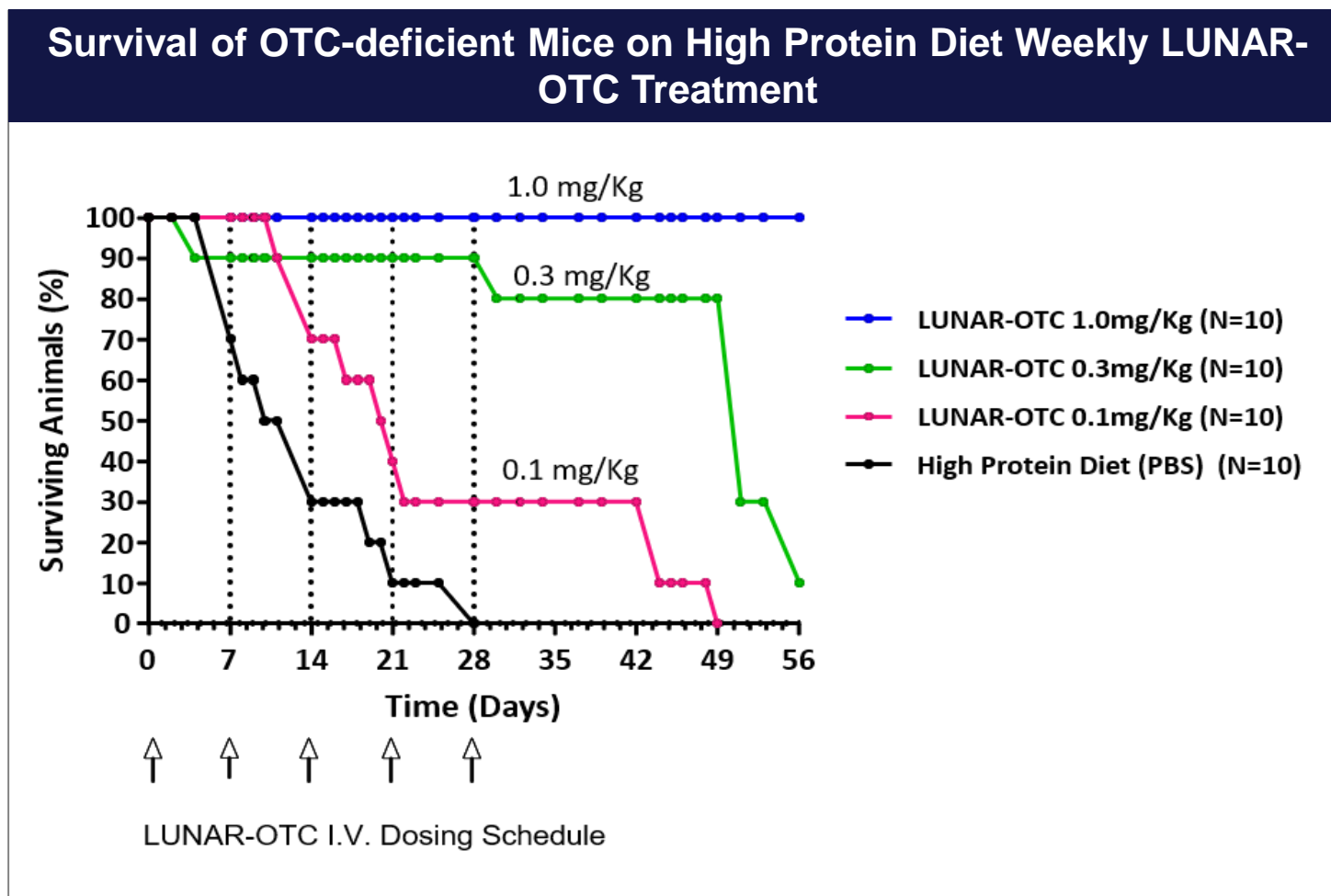
- Expression of OTC enzyme in liver has potential to restore normal urea cycle activity to detoxify ammonia, preventing neurological damage and removing need for liver transplantation

# LUNAR-OTC

Disease Normalization Following Single and Repeat Dosing in OTC Mouse Model



BUILDING INNOVATIVE  
RNA MEDICINES



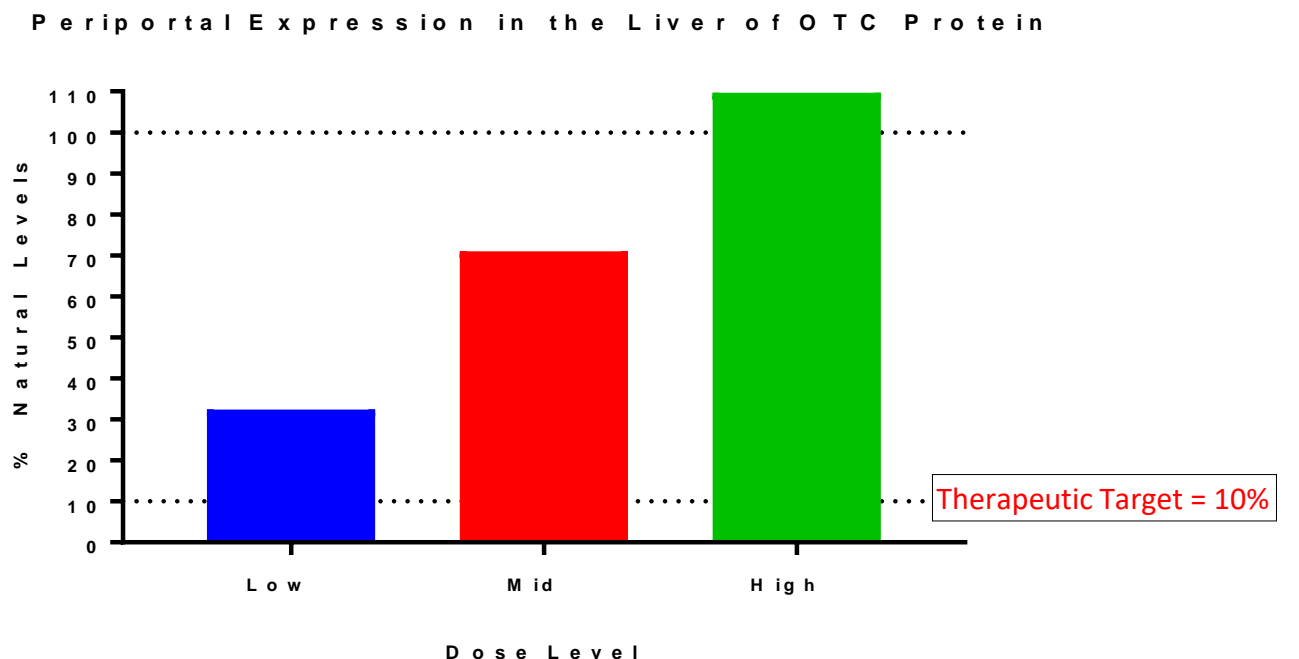
# LUNAR-OTC

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



BUILDING INNOVATIVE  
RNA MEDICINES

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

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

# Arcturus Safety Profile



BUILDING INNOVATIVE  
RNA MEDICINES

## 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
- Over \$3 Million invested to date

## 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 RNA
- ✓ @ 3 mg/kg x eight (8) weekly doses of non-coding RNA (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
- Well tolerated in mouse @ 7 mg/kg single dose

## IND-enabling toxicology studies at higher doses will provide Maximum Tolerated Dose (MTD)



# 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



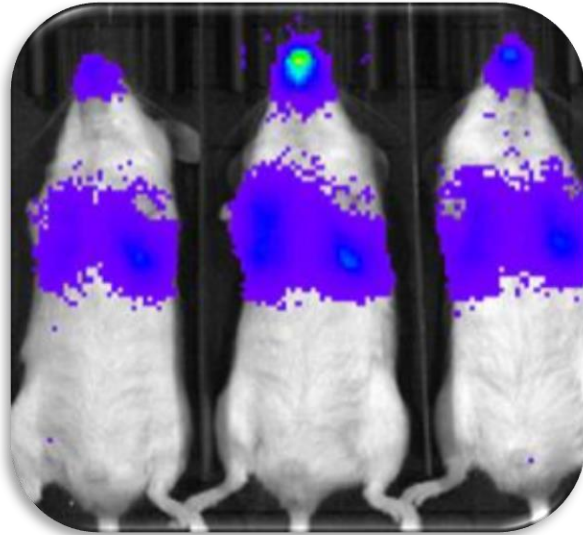
## **LUNAR-CF Aims to Restore CFTR Function**

- 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<sup>®</sup> Targeting Lung



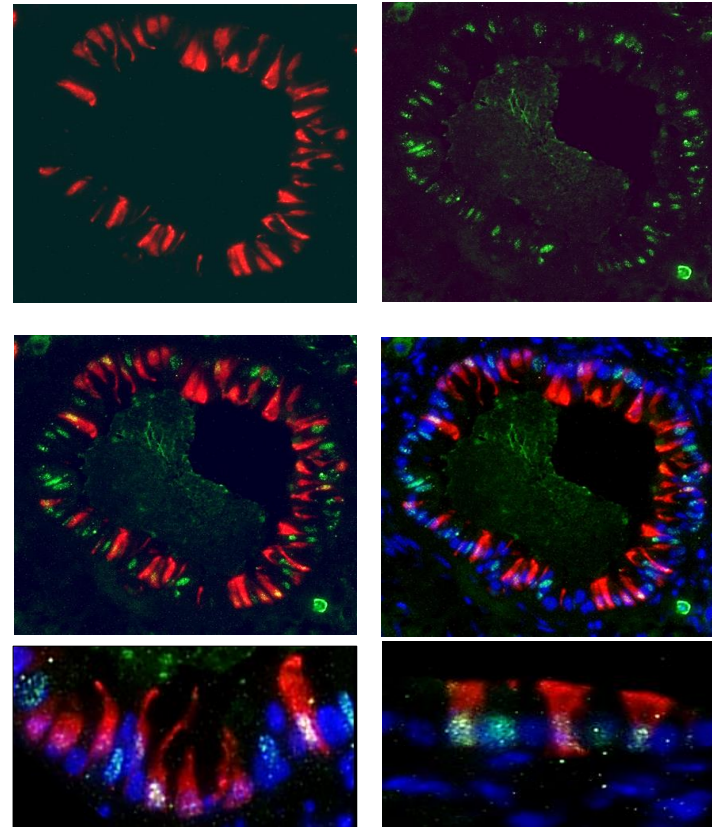
## Nebulization



LUNAR-Luc mRNA

## LUNAR<sup>®</sup> Delivery into Bronchial Epithelial Cells (BECs)

TdTomato/FoxJ1/Dapi



Functional Delivery of LUNAR<sup>®</sup>-mRNA into Lung Epithelial Cells

# Drug Substance: mRNA Design

BUILDING INNOVATIVE  
RNA MEDICINES

## Arcturus' proprietary mRNA optimization platform

### Optimized conditions

- mRNA sequence
- Chemistry
- Process optimization

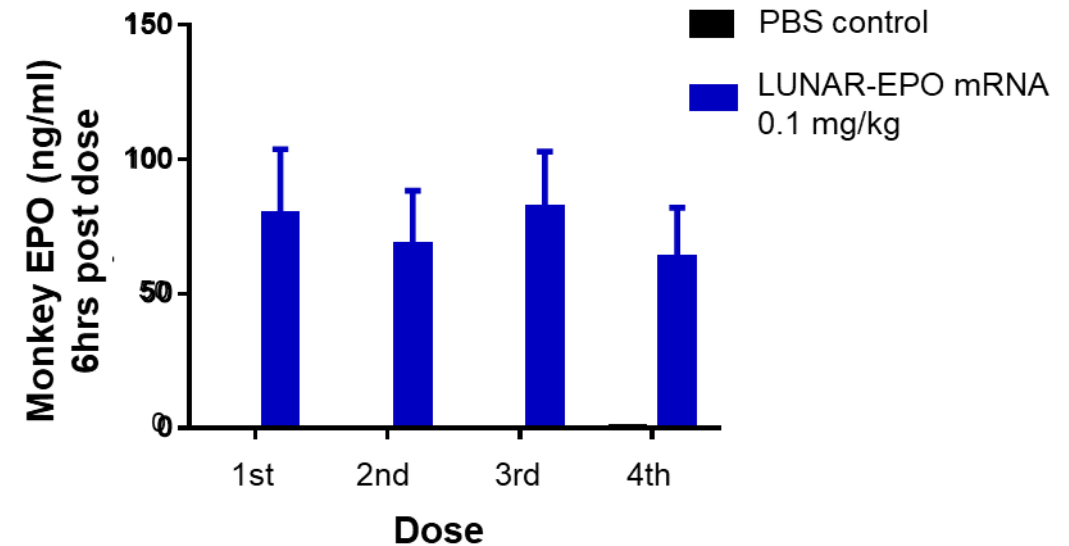


- Improved protein expression and duration
- Improved functional activity



## Sustained hEPO activity in NHPs upon repeat dosing

### Weekly Dosing in Non-Human Primates



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

# Arcturus mRNA Manufacturing



BUILDING INNOVATIVE  
RNA MEDICINES



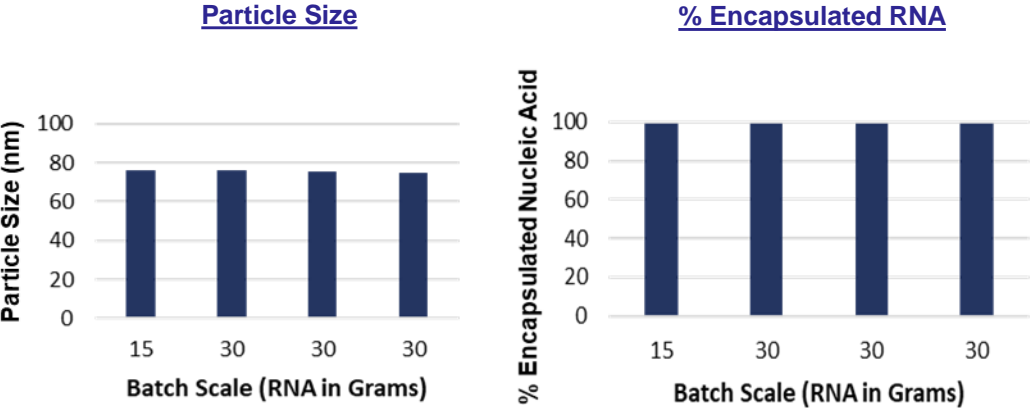
Features	Benefits
Optimized IVT Method	Reduced Cost; Higher Purity
Improved Capping Reaction	Reduced Cost of Goods
Proprietary Purification Process	Higher Purity in a Shorter Time
Efficient	Entire Process Less Than One Week
Scalable to > 1Kg	Access Large Patient Populations
Adaptable	Can Utilize a Variety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

**Arcturus’ Internal mRNA Production: Up to 30 g in Less Than One Week**

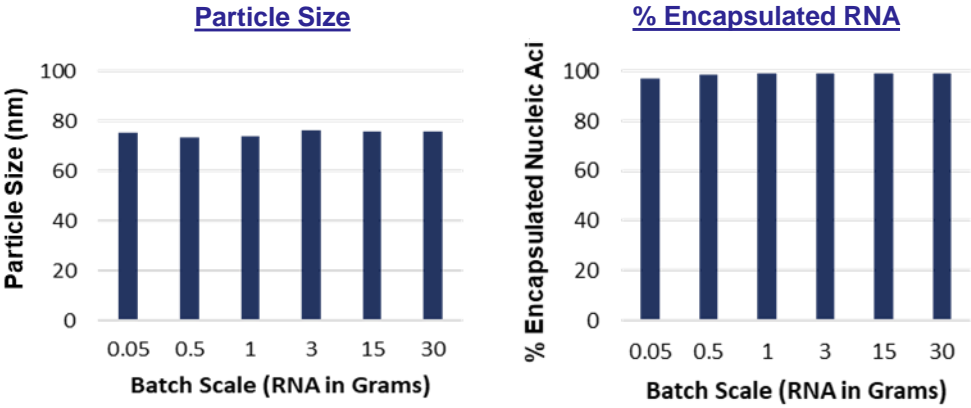


# Drug Product: LUNAR<sup>®</sup> Formulation & Production

## LUNAR<sup>®</sup> Reproducibility



## LUNAR<sup>®</sup> Scalability



LUNAR<sup>®</sup> Has Been Successfully Scaled From Milligram to Multigram Batch Sizes



ARCTURUS THERAPEUTICS

# Board of Directors



BUILDING INNOVATIVE  
RNA MEDICINES



**Dr. Peter Farrell**

*Chairman of the Board*



**Andrew Sassine, MBA**

*Director of the Board*



**James Barlow, MA**

*Director of the Board*



**Dr. Magda Marquet**

*Director of the Board*



**Joseph E. Payne, MSc**

*Director of the Board,  
Founder, President & CEO*



**ResMed**

Founder and Chairman



Former Portfolio Manager



Former Chief Accounting Officer



Chairman and Co-Founder



ARCTURUS THERAPEUTICS

# Management Team



BUILDING INNOVATIVE  
RNA MEDICINES



**Joseph E. Payne, MSc**  
*Founder, President & CEO*



**Dr. Pad Chivukula**  
*Founder, CSO & COO*



**Andrew Sassine, MBA**  
*CFO*



**Kevin Skol, MBA**  
*Sr. VP of Business  
Development & Alliance  
Management*



**Dr. Suezanne Parker**  
*VP of Translational Biology*



