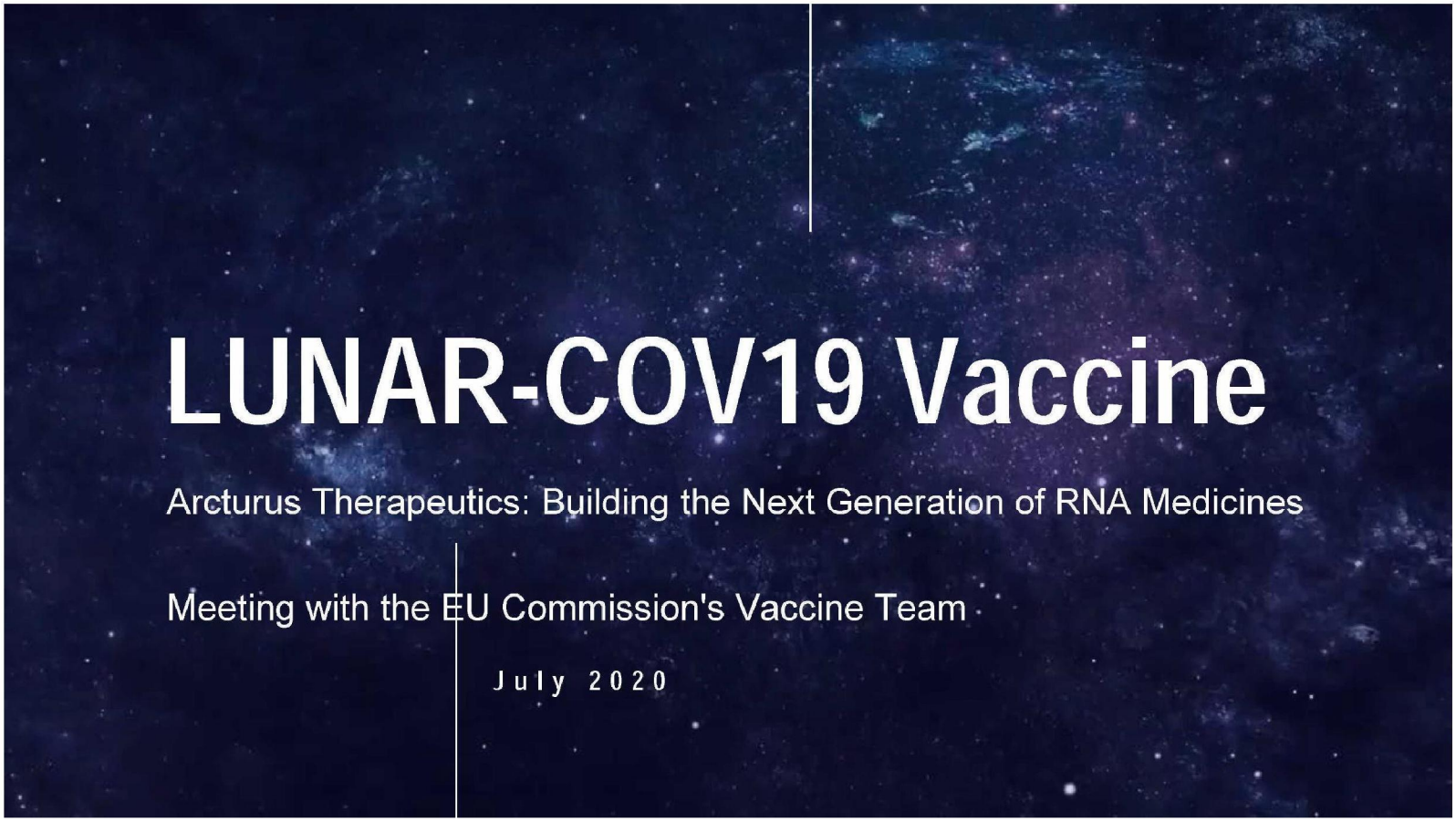
LUNAR-COV19 Vaccine
Arcturus Therapeutics: Building the Next Generation of RNA Medicines
Meeting with the EU Commission's Vaccine Team
July 2020

ARCTURUS THERAPEUTICS

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: 97
- 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

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Proprietary mRNA Technologies Driving Promising Therapeutic Programs

Broad and Strong Intellectual Property Portfolio

BUILDING INNOVATIVE RNA MEDICINES

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

Program	Indication
LUNAR-COV19 (ARCT-021)	COVID-19 Vaccine
LUNAR-OTC (ARCT-810)	Ornithine Transcarbamylase (OTC) Deficiency
LUNAR-CF	Cystic Fibrosis
LUNAR-CV	Rare Cardiovascular Disease
LUNAR-MD	Rare Metabolic Disease
ADDITIONAL EARLIER STAGE PROGRAMS	

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Arcturus Partnered Programs

BUILDING INNOVATIVE RNA MEDICINES

Program	Partner	Indication	Arcturus Chemistry	Arcturus Delivery	Program Status
LUNAR-GSD3	ultragenyx pharmaceutical	Glycogen Storage Disease Type III	mRNA	LUNAR® Hepatocytes	Target IND 2020+
LUNAR-RARE	ultragenyx pharmaceutical	Undisclosed Rare Disease	mRNA	LUNAR® Hepatocytes	Preclinical
LUNAR-HBV	Johnson & Johnson	Hepatitis B	RNA	LUNAR® Hepatocytes	Preclinical
LUNAR-NASH	Takeda	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

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Arcturus Pipeline of mRNA Medicines

BUILDING INNOVATIVE RNA MEDICINES

Name	Indication	Route of Administration	Target Organ (Cell Type)	Prevalence Worldwide	Anticipated Milestones
LUNAR-COV19 (ARCT-021)	COVID-19 Vaccine	Intramuscular (i.m.)	Muscle (Myocytes, Dendritic Cells)	Global	Phase 1/2 Initiate Dosing Summer 2020
LUNAR-OTC (ARCT-810)	Ornithine Transcarbamylase (OTC) Deficiency	Intravenous (i.v.)	Liver (Hepatocytes)	> 10,000	Phase 1 Data Q4 2020
LUNAR-CF	Cystic Fibrosis	Inhaled Aerosol	Lung (Bronchial Epithelial Cells)	> 70,000	DC Selection 2020 IND 2021
LUNAR-CV	Rare Cardiovascular Disease	Intravenous (i.v.)	Liver (Hepatocytes)	Undisclosed	IND 2021
LUNAR-MD	Rare Metabolic Disease	Intravenous (i.v.)	Liver (Hepatocytes)	Undisclosed	IND 2022

Multiple mRNA Therapeutic Programs with Milestones in 2020

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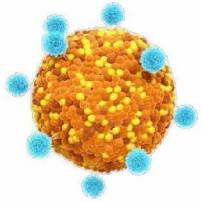
Arcturus Vaccine LUNAR-COV19 is Differentiated

BUILDING INNOVATIVE RNA MEDICINES



STARR™ mRNA & LUNAR® Delivery

Key Differences from other mRNA vaccines

Arcturus COVID-19 mRNA vaccine uses:

- Self-replicating mRNA, not conventional mRNA
- LUNAR® Nanoparticle Delivery
- Novel Manufacturing Processes for mRNA Drug Substance and Drug Product

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Arcturus COVID-19 Vaccine has Significant Advantages

BUILDING INNOVATIVE RNA MEDICINES

Potential Single Shot

- Small, single intramuscular injection, devoid of adjuvants
- Simpler logistics for vaccinating large populations
- Lyophilized formulation further simplifies distribution

Very Low Dose

- Reduced potential side effects, e.g. ISR's
- Means potentially more people vaccinated per manufactured batch

Utilizes STARR™ mRNA (self-transcribing and self-replicating 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 mRNA vaccine
- LUNAR® Delivery Technology is Non-Viral

Readily Manufactured

- Arcturus Proprietary Processes
- Proven; Scalable; High yields; High purities
- Capacity established in EU and US

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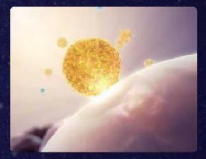
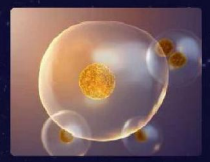
LUNAR® Delivery Technology

BUILDING INNOVATIVE
RNA MEDICINES



LUNAR Associates with Cell Membrane

Enters Cell Via Endocytosis

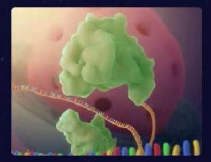


Lipid Particle in Endosome

Increased Acidity as Endosome Ages

pH-Mediated Disruption

Rapid Biodegradation of Vehicle



RNA in Cytosol

RNA Processing and Translation

ARCTURUS THERAPEUTICS

LUNAR® Delivery of mRNA; Safety in Primates

BUILDING INNOVATIVE RNA MEDICINES

Arcturus LUNAR® Delivery of mRNA in Primates at High Doses

- No adverse events observed at multiple i.v. doses of 1000 ug of LUNAR®-formulated mRNA

Arcturus LUNAR-OTC Program Illustrates Safety of LUNAR Delivery of mRNA

- Anticipated dosing for LUNAR-OTC is 20,000 ug, monthly; i.v.
- IND accepted in US; CTA approved in New Zealand

Arcturus COVID19 Vaccine Dose is Considerably Lower

- Anticipated dose is low (1-10 ug; intramuscular, i.m.)

Because dose of COVID-19 vaccine is low, and delivered with LUNAR®, safety profile is promising

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Arcturus Developing COVID-19 Vaccine with DukeNUS Medical School

BUILDING INNOVATIVE RNA MEDICINES

Arcturus Duke-NUS Partnership Initiated March 4, 2020

- Duke-NUS Medical School: an academic world leader in coronaviruses and infectious diseases
- 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 streamline the vaccine development program


STARR™ RNA Technology

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STARR™ Technology

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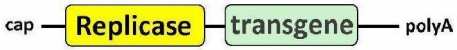
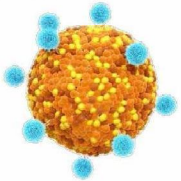
RNA MEDICINES

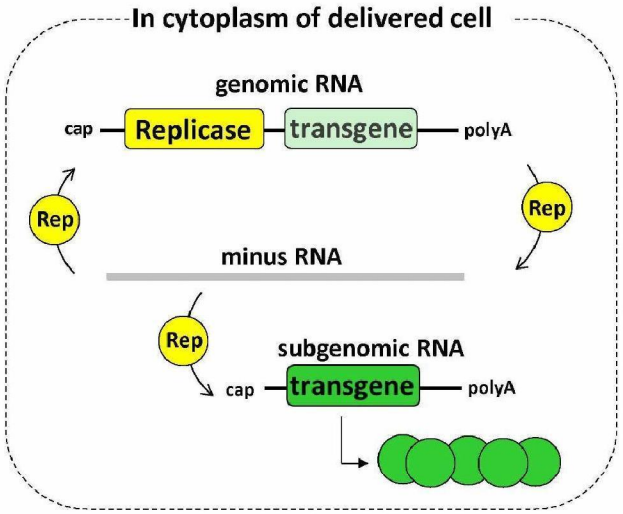
Cargo: Synthetic IVT

Self-Transcribing and Replicating RNA (STARR)



Delivery Vehicle: LUNAR®





STARR™ technology can be used to generate a protective immune response or drive therapeutic protein expression

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mRNA vs Replicon RNA

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RNA MEDICINES

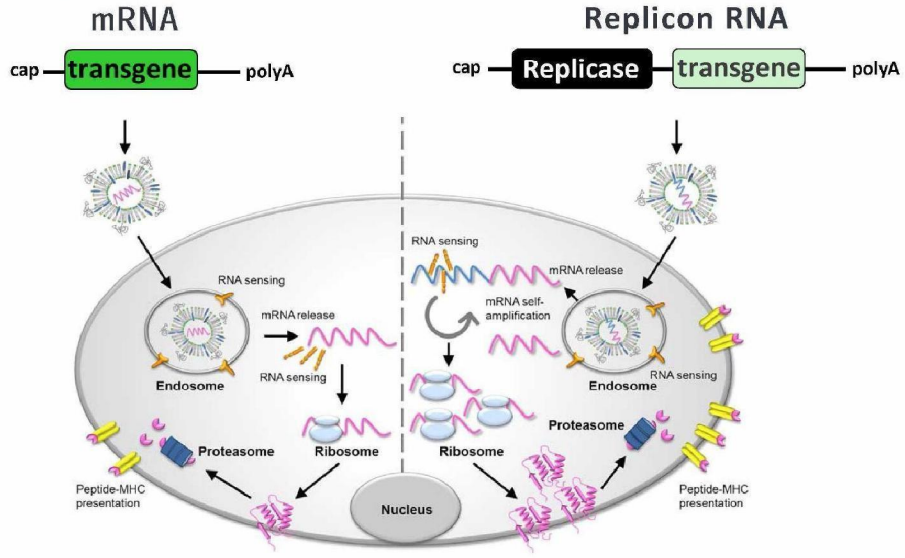

Figure modified from Maruggi, et al. (2019) 10.1016/j.ymthe.2019.02.012. Therapy 27:757

Different profiles of transgene expressions

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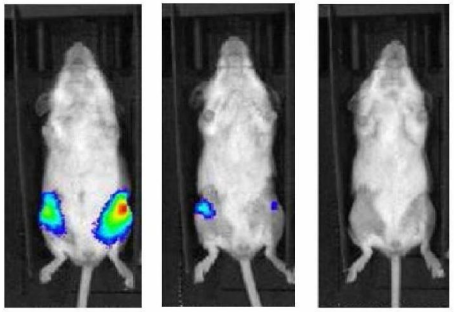
BUILDING INNOVATIVE RNA MEDICINES

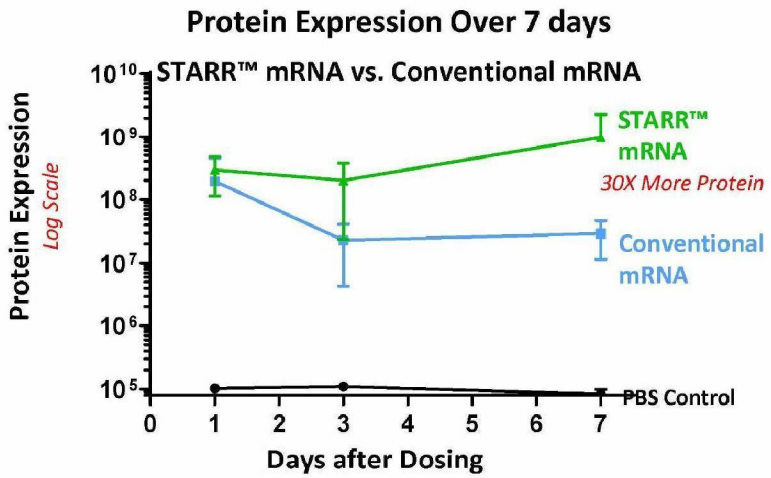
STARR™ mRNA Superior to Conventional mRNA

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

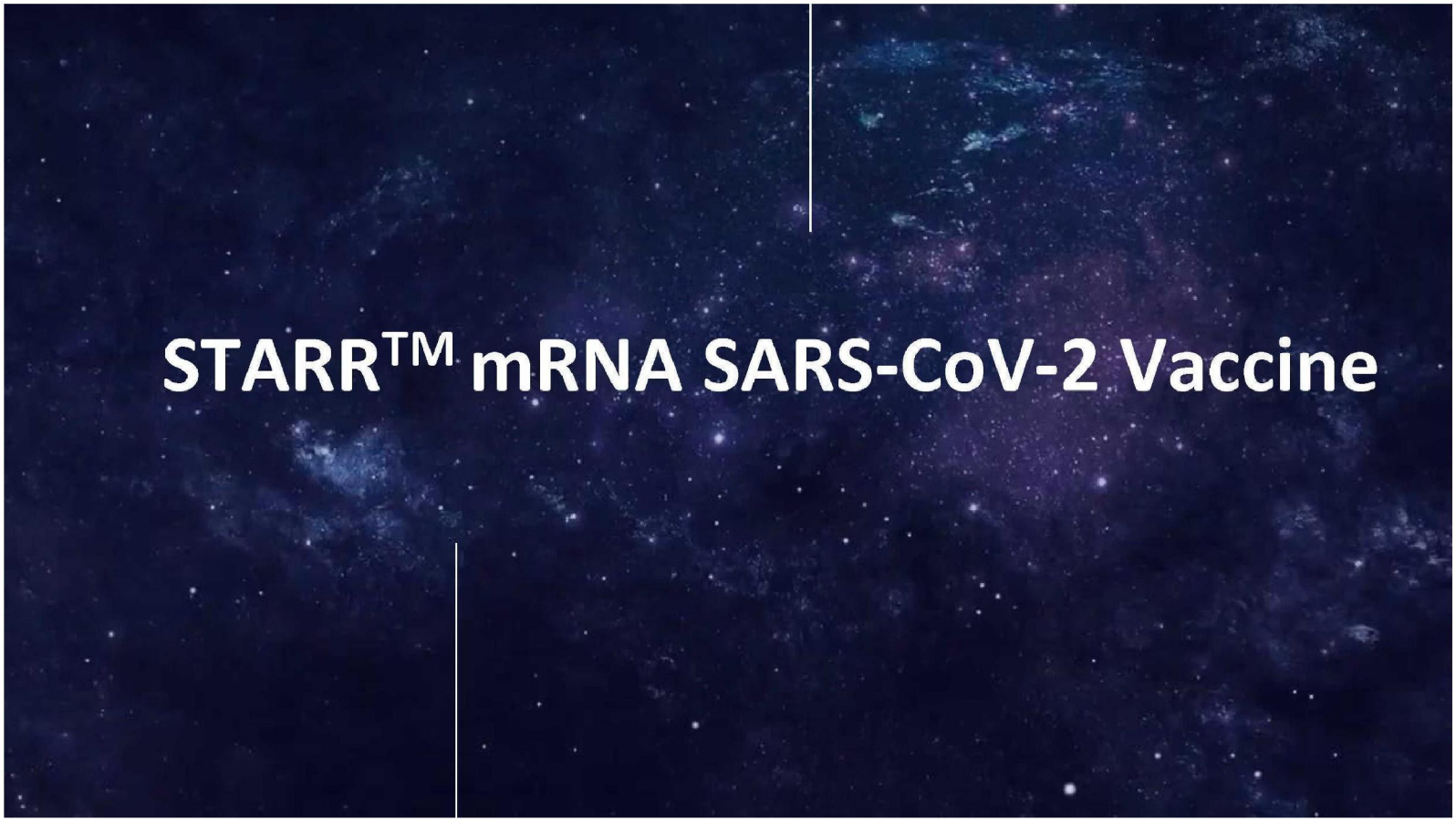


STARR™ Technology | Conventional mRNA | PBS Control



- BALB/c mice were administered a 2 mg dose of either STARR™ RNA or mRNA expressing luciferase in a 50 mL injection volume.
- Protein expression was measured on days 1, 3 and 7 after administration.

STARR™ protein expression increased ~10 fold whereas mRNA decreased ~100 fold over 7-day period


STARR™ mRNA SARS-CoV-2 Vaccine

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Immunogenicity Study Design

BUILDING INNOVATIVE RNA MEDICINES

Type of Construct	Antigen	Dose (µg)	Dosing Schedule	Bleed Dates (Day)	# of mice/ group	Assays
STARR™	Full Length Spike (1278 AA)	0.2, 2.0, 10.0	Day 0 ~~Day 28~~[c]	10, 20, 30, 40, 50, 60	5	Neutralizing Ab Titer[a] Total Anti-S IgM[b] Total Anti-S IgG[b]
mRNA	Full Length Spike (1278 AA)	0.2, 2.0, 10.0	Day 0 ~~Day 28~~[c]	10, 20, 30, 40, 50, 60	5	Neutralizing Ab Titer[a] Total Anti-S IgM[b] Total Anti-S IgG[b]
Negative Control	PBS		Day 0 ~~Day 28~~[c]	10, 20, 30, 40, 50, 60	5	Neutralizing Ab Titer[a] Total Anti-S IgM[b] Total Anti-S IgG[b]

[a] Neutralization assay conducted on Vero-E6 cells with a SARS-CoV-2 Singapore Clinical Isolate. Serum diluted 1:10 and neutralization criteria was no CPE after 4-day incubation at 37°C

[b] Spike specific IgM and IgG responses will be assayed by Luminex Binding Assay

[c] Boost at day 28 as was not given due to steadily increasing Ab levels

Dr. Eng Eong Ooi's Lab at Duke-National University of Singapore (DUKE-NUS) independently conducted all immunogenicity Assays

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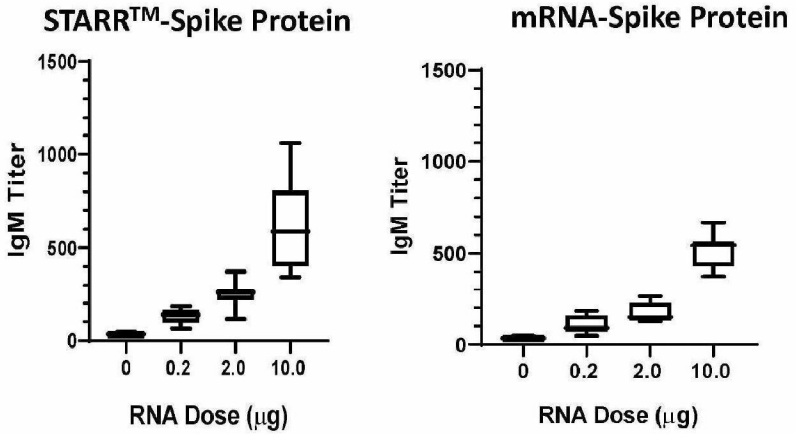
Anti-Spike Glycoprotein IgM Immune Response

10 Days Post Vaccination

BUILDING INNOVATIVE RNA MEDICINES



Summary of Anti-Spike Protein IgM Titer Results

- Increase in IgM titers with increasing RNA dose for both STARR™ and mRNA Spike protein post immunization
- Higher IgM titers observed for STARR™-Spike compared to mRNA-Spike at equivalent RNA doses

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Anti-Spike Glycoprotein IgG Antibody Titers

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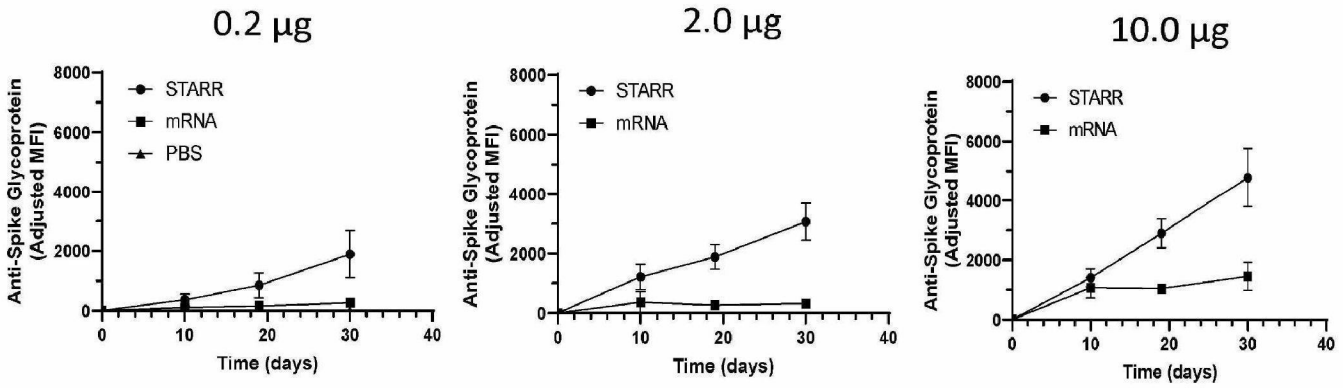
RNA MEDICINES



Summary of Results

- Anti-spike glycoprotein IgG titers increases from Day 0 to Day 30 with STARR™
- Higher anti-SARS-CoV-2 Spike Glycoprotein IgG elicited by STARR™ compared to mRNA
- IgG continues to increase produced with STARR™ whereas a plateau is reached with mRNA
- Dose dependent increase in IgG titers

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Viral Neutralization Assay Results

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	% Seroconversion					
RNA Dose/ Construct	**0.2 µg**		**2.0 µg**		**10.0 µg**	
	D10	**D19**	**D10**	**D19**	**D10**	**D19**
STARR™	40%	60%	80%	100%	100%	100%
mRNA	20%	20%	20%	0%	40%	80%

Seroconversion Criteria

No observed CPE 4 days after coincubation

of Vero cells with virus and 1/10 dilution of serum

STARR™ expressed spike protein gene yielded superior inhibition of SARS-CoV-2 infection compared to spike protein gene expressed by mRNA at all RNA vaccination doses

LUNAR-COV19 Positive Preclinical Data

Arcturus COVID-19 vaccine to begin human dosing this Summer

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RNA MEDICINES

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

*One microgram (µg) is 1 billionth of a kilogram (i.e. 1 Kg STARR™ mRNA contains 500 million doses at 2 µg /dose).

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

Day 30 Mouse Neutralizing Antibody Titers

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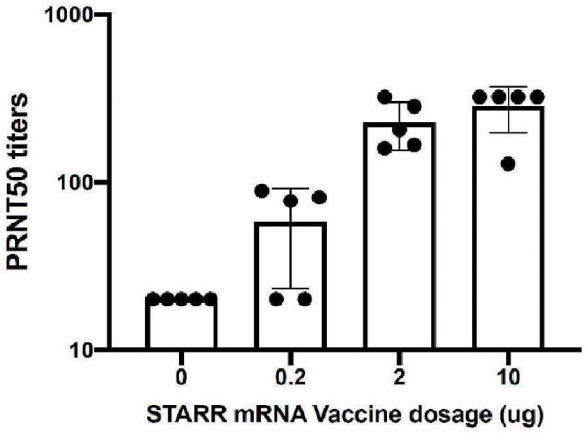
RNA MEDICINES



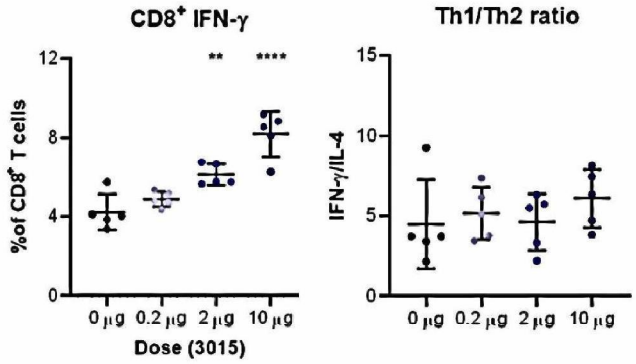
RNA Dose (µg)	% Seroconversion	Neutralizing Antibody Titers (Geometric Mean)
0.2	80%	57.7±2.0
2.0	100 %	217.9±1.4
10.0	100 %	≥ 320

Neutralizing Antibody Titer Results Summary

- 80% of mice vaccinated with a single dose of 0.2 µg had neutralizing antibody titers at ≥ 20
- 100% of mice vaccinated with 2 µg and 10 µg had neutralizing antibody titers ≥ 217

Arcturus Vaccine elicits a Balanced Cell Mediated Immune Response

BUILDING INNOVATIVE RNA MEDICINES



RNA Dose (µg)	% IFN-g + CD8+ T Cells	CD4+ Th1/Th2 (IFN-g/IL4)
0.0	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-g positive CD8+ T-cells
- Th1 biased CD4+ response and lack of change in Th1/Th2 ratio with increased RNA dose indicate balanced cell mediated immune response

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LUNAR-COV19 Data Summary

BUILDING INNOVATIVE RNA MEDICINES

- Very low dose: Strong neutralizing antibody response with just a single dose of 0.2 – 10 μg STARR™ RNA
- Strong humoral response continuous increase in neutralizing antibodies beyond Day 30
- Strong T-cell response: dose response increase in IFN-g positive $CD8^+$ T-cells
- Potential single shot simplifies vaccination campaigns
- Safety: balanced cellular immune response – low probability of immune pathology and Vaccine Induced Enhancement
- Superior immunogenic profile of STARR™ compared to conventional mRNA
- Adjuvant-free, Preservative-free, Antibiotic-free reduces public concerns

Arcturus LUNAR-COV19 is a most promising COVID-19 vaccine


Drug Substance / Drug Product
CMC

ARCTURUS THERAPEUTICS

INTERNAL RNA DEVELOPMENT PLATFORMS

Drug Substance: mRNA Design

BUILDING INNOVATIVE RNA MEDICINES

Arcturus' proprietary mRNA optimization platform

Optimized conditions

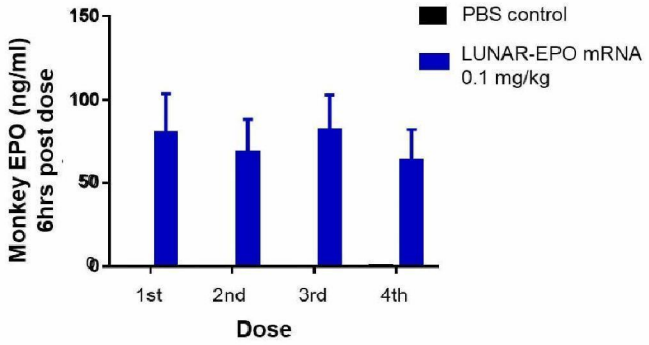
- mRNA sequence
- Chemistry
- Process optimization

→

- 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 THERAPEUTICS

Drug Substance (mRNA) Manufacturing

BUILDING INNOVATIVE RNA MEDICINES

DNA Template Production → IVT and Capping Reaction → Purification Process → Buffer Exchange & Concentration

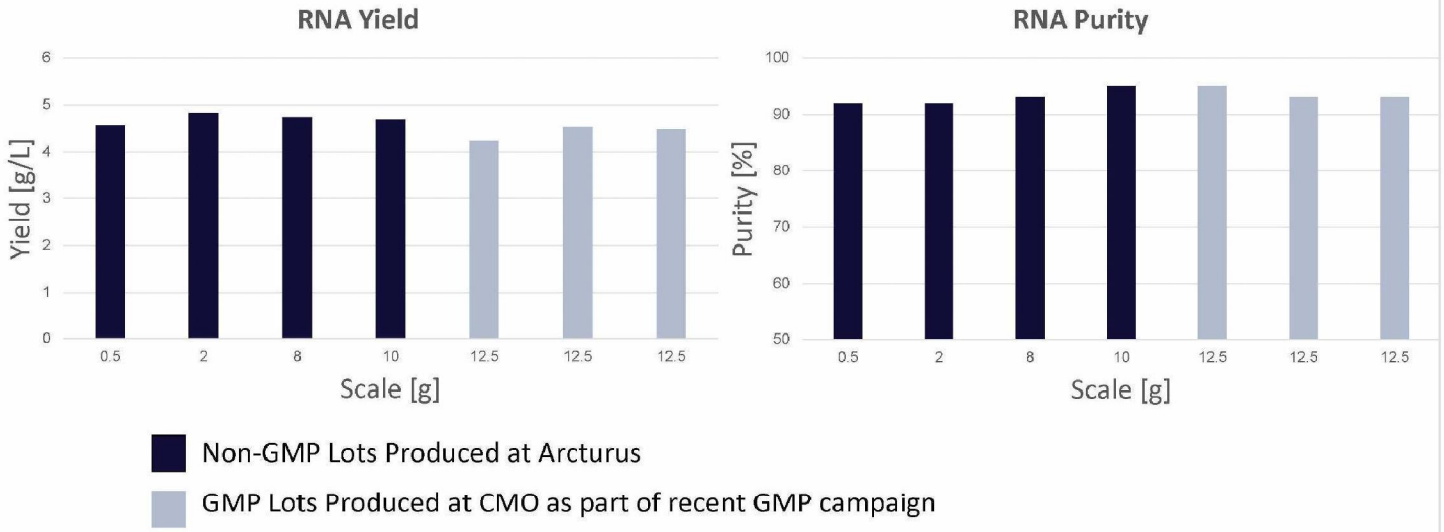
Features	Benefits
Optimized IVT Method	Reduced Cost; Higher Purity
Improved Capping Reaction	Reduced Cost of Goods
Proprietary Purification Process	Higher Purity in a Shorter Time
Efficient	Entire Process Less Than One Week
Scalable to > 1Kg	Access Large Patient Populations
Adaptable	Can Utilize a Variety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

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

ARCTURUS THERAPEUTICS

Drug Substance (mRNA) Manufacturing

BUILDING INNOVATIVE
RNA MEDICINES



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

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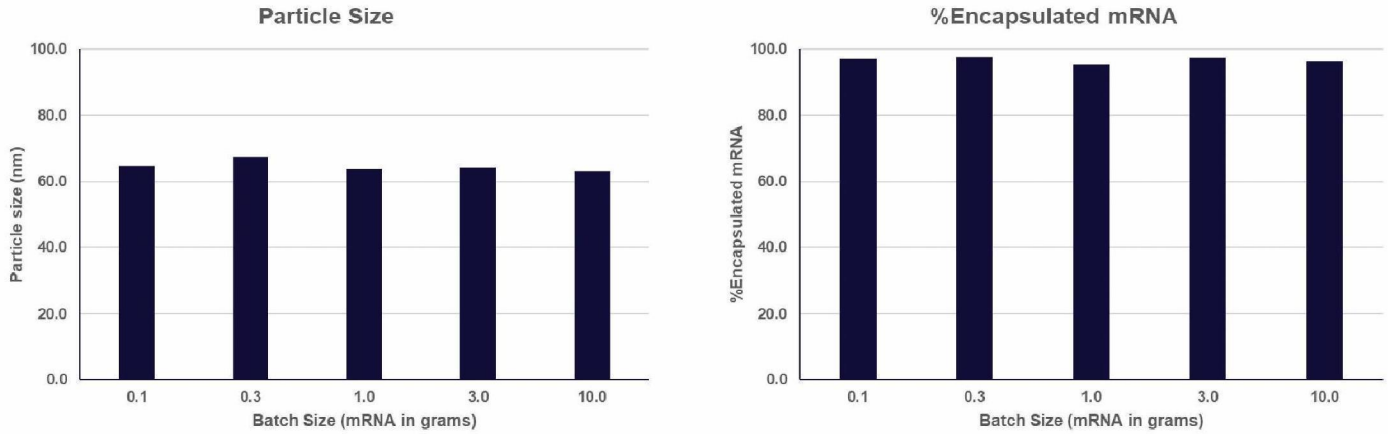
Drug Product (LUNAR® + mRNA) Manufacturing

BUILDING INNOVATIVE
RNA MEDICINES



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

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cGMP Manufacturing LUNAR-COV19 Summary

BUILDING INNOVATIVE RNA MEDICINES

- We plan to manufacture 30g of LUNAR-COV19 drug product this year
- The anticipated vaccine human dose is between 1 μg - 10 μg of RNA
- Bulk drug product and fill/finish to be completed in Austria and Germany. Drug mRNA substance manufactured in the U.S. at Catalent
- Additional manufacturing capacity ex-US not yet announced
- Our Phase 2/3 and commercial product will be a lyophilized vaccine packaged in vials
- We are committed to producing tens of millions of doses in 2020 and hundreds of millions of doses in 2021 and beyond

Hundreds of millions of dose capacity in 2021 and beyond


LUNAR-COV19 Clinical Plans

ARCTURUS THERAPEUTICS

LUNAR-COV19 Clinical Plan

BUILDING INNOVATIVE RNA MEDICINES

Phase 1/2 Clinical Trial to begin in Summer 2020

Shipment of GMP Manufactured LUNAR-COV19 Vaccine

Human Dosing to Initiate this Summer

- Phase 1/2 clinical trial at single site: Duke-NUS Medical School in Singapore

Primary Goal: Identify optimal dose

Primary Endpoints: Safety and tolerability

Secondary Endpoints: Measures of immunogenicity and virus neutralization

Also evaluating T-cell responses (CD8+ and TH1/TH2 and epitope mapping)

Study Design:

- 108 healthy volunteer adults
- 3 dose levels
- Elderly as well as younger adults

Trial design allows us to potentially rapidly select dose to take forward to large registrational studies

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LUNAR-OTC (ARCT-810) Clinical Plan

BUILDING INNOVATIVE RNA MEDICINES

Phase 1 Clinical Trial to begin based on COVID-19 restrictions being lifted

Two Single Dose Studies to Initiate in 2020

- Phase 1b clinical trial in up to 12 stable OTC-deficient patients – IND allowed to proceed in the U.S.
- Phase 1 clinical trial in up to 30 healthy volunteers – Clinical Trial Application (CTA) approved in New Zealand

Primary Goal: Identify safest doses to take forward into multiple dose clinical trials

Primary Endpoints: Safety and tolerability

Exploratory Endpoints: Biomarkers include ureagenesis, plasma ammonia levels and OTC enzyme activity, urine orotic acid levels

Study Design*

- Single ascending dose (SAD) studies; randomized, placebo controlled and blinded
- Healthy volunteer study – up to 5 dose levels
- Patient study – up to 3 dose levels
- All doses are within the anticipated range for therapeutic biological effect

*** Doses are > thousand-fold higher than anticipated effective LUNAR-COV19 vaccine dose (1 to 10 µg)**

ARCTURUS THERAPEUTICS

Arcturus COVID-19 Vaccine Opportunity Overview

BUILDING INNOVATIVE RNA MEDICINES

Vaccines are Needed ASAP

- The pandemic has impacted the global economy
- Significant health risks when removing COVID-19 'stay-at-home' restrictions

Availability of Vaccines is Limited

- Extraordinarily high demand, > 5 billion people
- Manufacturing large amounts is very difficult
- Countries are now securing rights and access for their citizens
- First batches of vaccines are already accounted for, eliminating initial access to supply (i.e. U.S. (BARDA) aligned with Moderna, J&J; UK with AstraZeneca, etc.)

Secure Rights and Access to Vaccine(s)

- Singapore has secured rights to the first batch of doses of Arcturus COVID-19 vaccine
- Ongoing discussions with governments globally
- Rights to Arcturus COVID-19 vaccine is secured upon execution of an agreement

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ARCTURUS therapeutics