ARCTURUS THERAPEUTICS

Building the Next Generation of RNA Medicines

Development of a self-transcribing and replicating (STARR™) mRNA vaccine candidate against SARS-CoV-2

September 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; our efforts to develop a vaccine against COVID-19, the safety, efficacy or reliability of a 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: 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

Proprietary mRNA Technologies Driving Promising Therapeutic Programs

BUILDING INNOVATIVE RNA MEDICINES

Broad and Strong Intellectual Property Portfolio

- 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	

Value Drivers include Clinical Pipeline, Patents, mRNA & STARR™ and LUNAR® Delivery Platforms

Arcturus Partnered Programs

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

Arcturus Partnered Pipeline is Across Diverse Indications, Chemistry and Cell Types and Soon to Be in the Clinic

Arcturus Pipeline of mRNA Medicines

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Name	Indication	IND/CTA Estimated Timing	Clinical Stage	Route of Administration	Target Organ	Target Cells	Prevalence Worldwide
LUNAR-OTC (ARCT-810)	Ornithine Transcarbamylase (OTC) Deficiency	IND & CTA: Trials Allowed to Proceed	U.S. Phase 1b N.Z. Phase 1	Intravenous (i.v.)	Liver	Hepatocytes	> 10,000
LUNAR-COV19	ARCT-021 Vaccine	HSA Approved CTA: Allowed to Proceed	Singapore Phase 1/2 Clinical	Intramuscular (i.m.)	Muscle	Myocytes Dendritic Cells	Global
LUNAR-CF	Cystic Fibrosis	IND 2021	Preclinical	Inhaled Aerosol	Lung	Bronchial Epithelial Cells	> 70,000
LUNAR-CV	Rare Cardiovascular Disease	IND 2022	Preclinical	Intravenous (i.v.)	Liver	Hepatocytes	Undisclosed
LUNAR-MD	Rare Metabolic Disease	IND 2022	Preclinical	Intravenous (i.v.)	Liver	Hepatocytes	Undisclosed

- **LUNAR-OTC (ARCT-810): Phase 1b & Phase 1 Clinical Trials Allowed to Proceed Under IND & CTA, Respectively**
- **LUNAR-COV19: CTA Filing Target Summer 2020**
- **LUNAR-CF: IND Application Filing Target 2021**

Arcturus LUNAR-COV19 Vaccine is Differentiated

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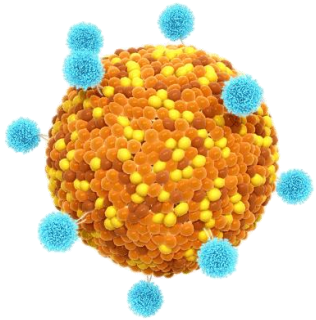

STARR™ mRNA & LUNAR® Delivery

Key Differences from other mRNA vaccines

- Self-replicating STARR™ mRNA Technology, not conventional mRNA
- Proprietary LUNAR® Nanoparticle Delivery Technology
- Novel, proprietary and integrated Manufacturing Processes for mRNA Drug Substance and Drug Product

The integration of all three capabilities that are proprietary to Arcturus and the iterative process required creates significant challenges for a self-replicating mRNA to be developed

Arcturus COVID-19 Vaccine has Significant Advantages

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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

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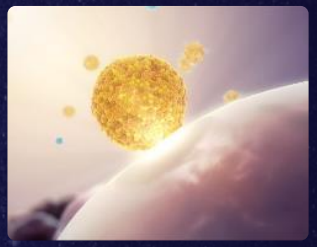
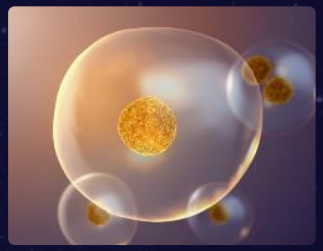
LUNAR Associates with Cell Membrane



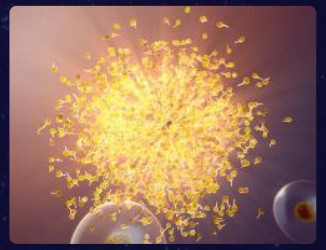
Enters Cell
Via Endocytosis

Lipid Particle in Endosome



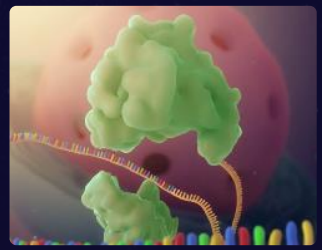
Increased Acidity as
Endosome Ages

pH-Mediated Disruption



Rapid Biodegradation
of Vehicle

RNA in Cytosol



RNA Processing
and Translation

Arcturus Developing LUNAR-COV 19 Vaccine with Duke-NUS

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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 by Duke-NUS

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

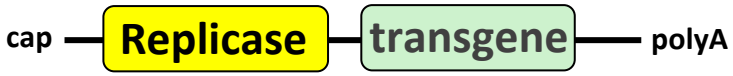
Data generated from the Duke-NUS system gives Arcturus the ability to more efficiently select the dose and streamline the vaccine development program

STARR™ RNA Technology

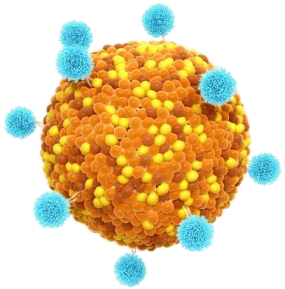
STARR™ Technology

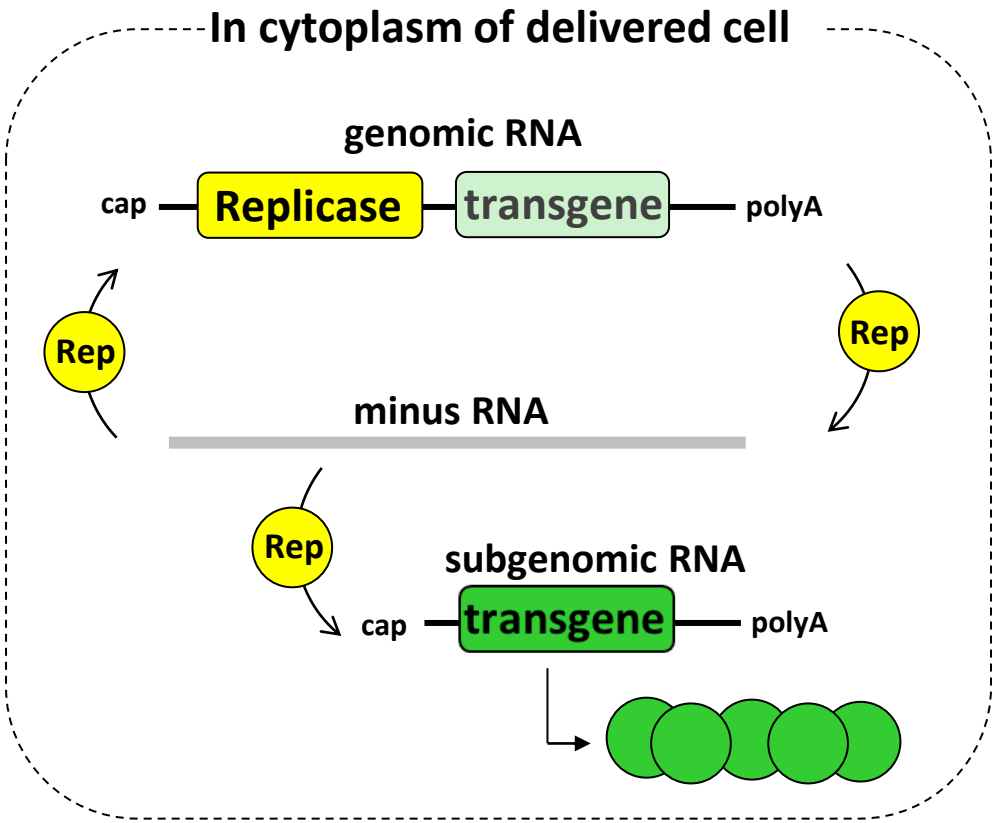
Cargo: Synthetic IVT

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

mRNA vs Replicon RNA

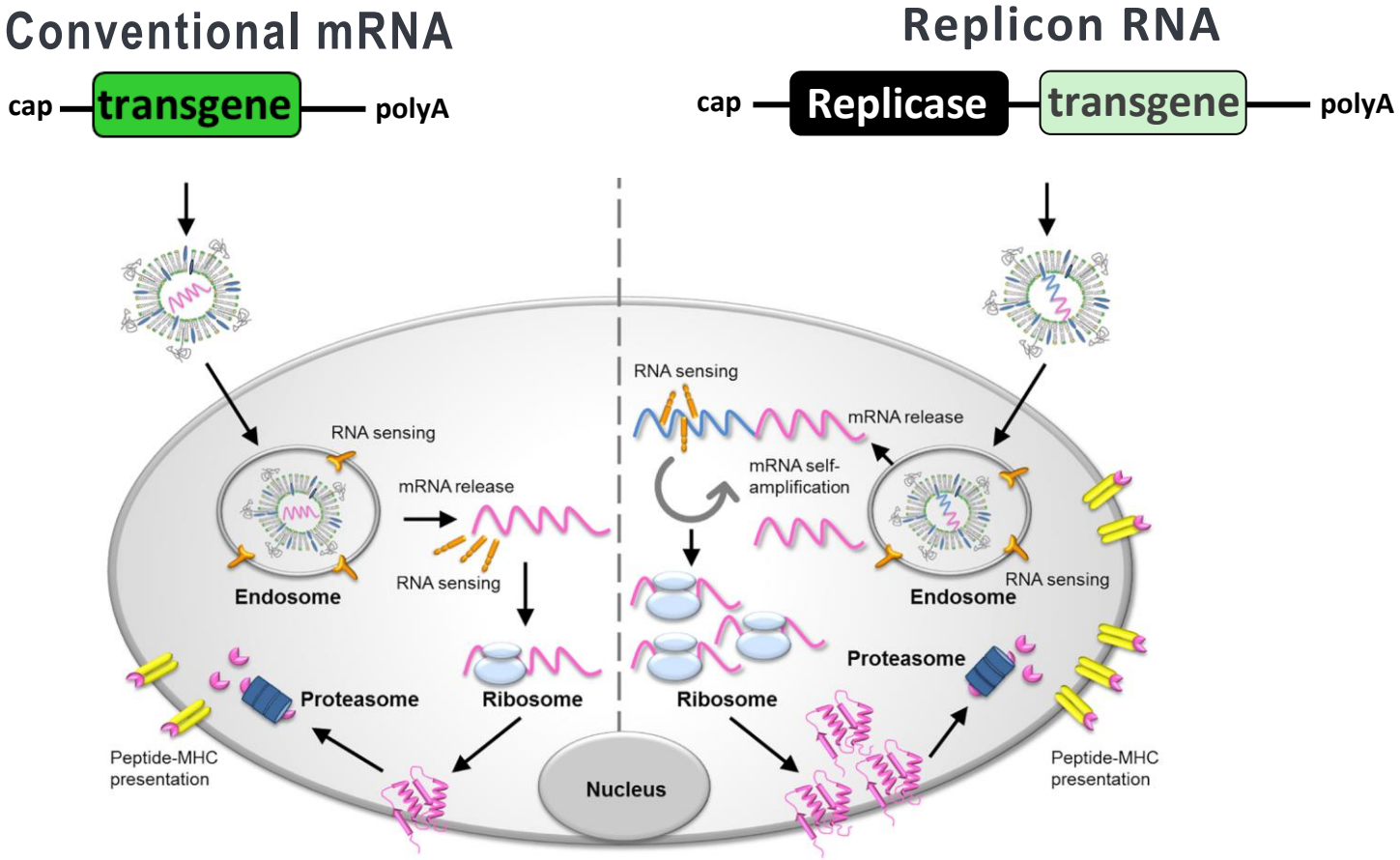


Figure modified from Maruggi, et al. (2019) Mol. Therapy 27:757

Different profiles of transgene expressions

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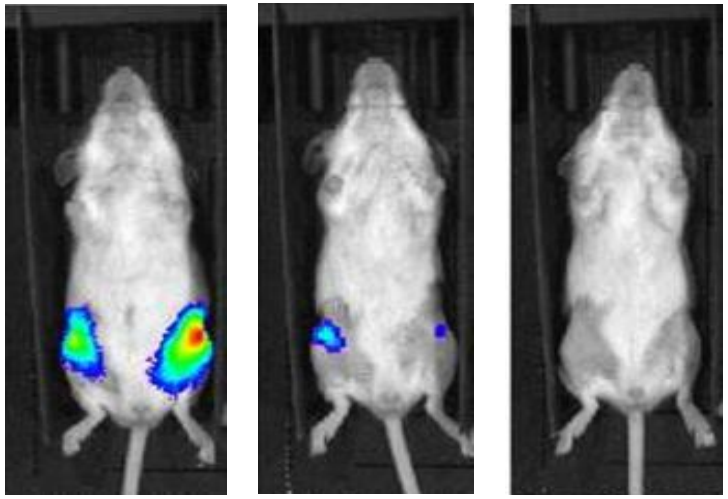
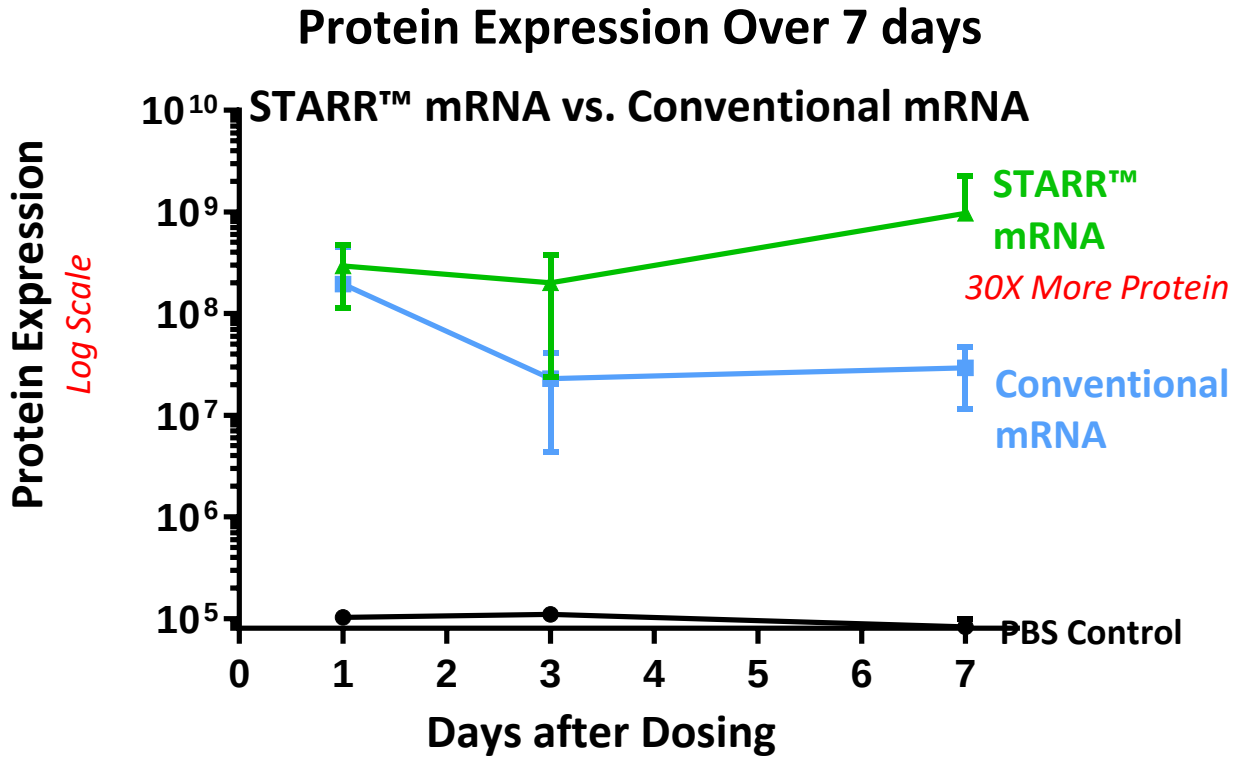
STARR™ mRNA Superior to Conventional mRNA

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

Immunogenicity Study Design

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-NUS independently conducted all immunogenicity Assays

Anti-Spike Glycoprotein IgM Immune Response

10 Days Post Vaccination

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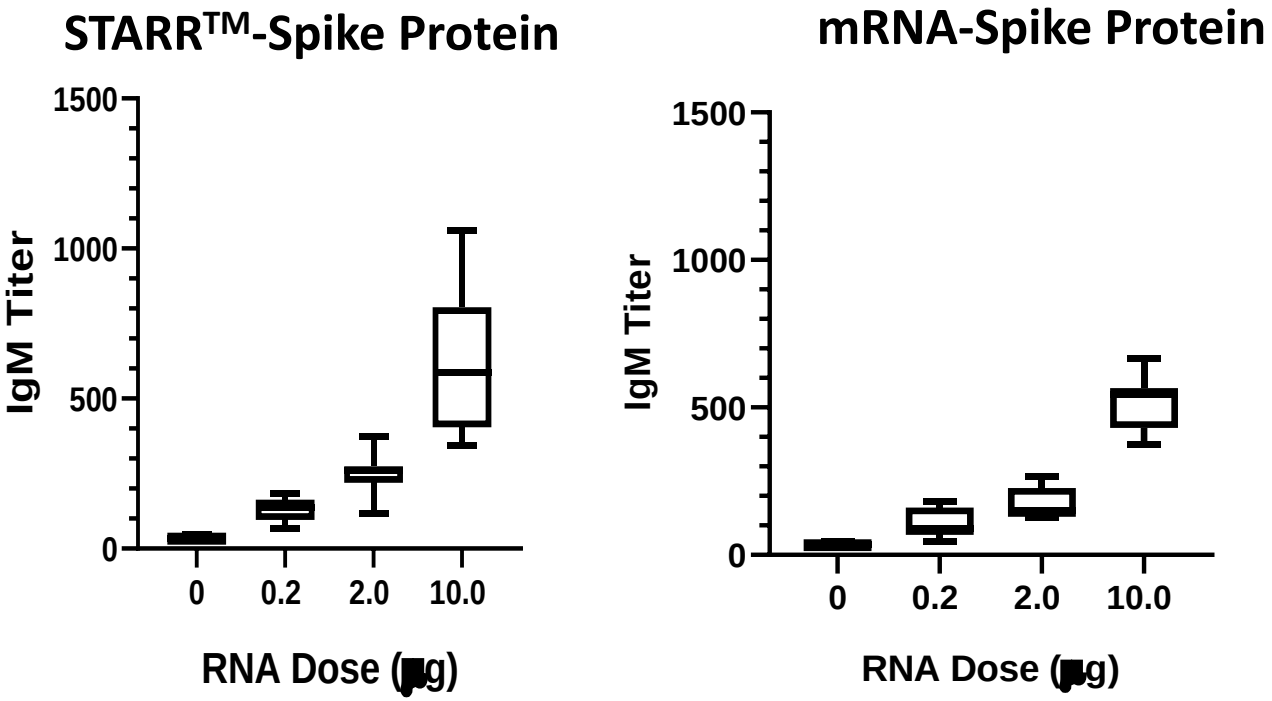
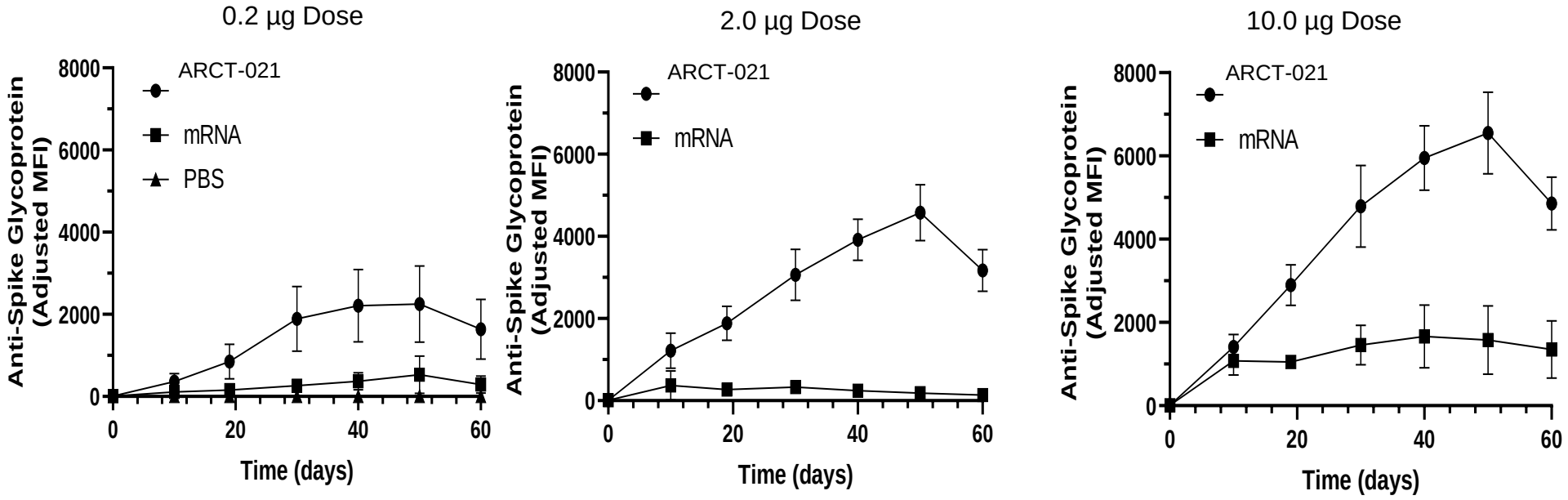


Summary of Anti-Spike Protein IgM Titer Results

- 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

Anti-Spike Glycoprotein IgG Antibody Titers

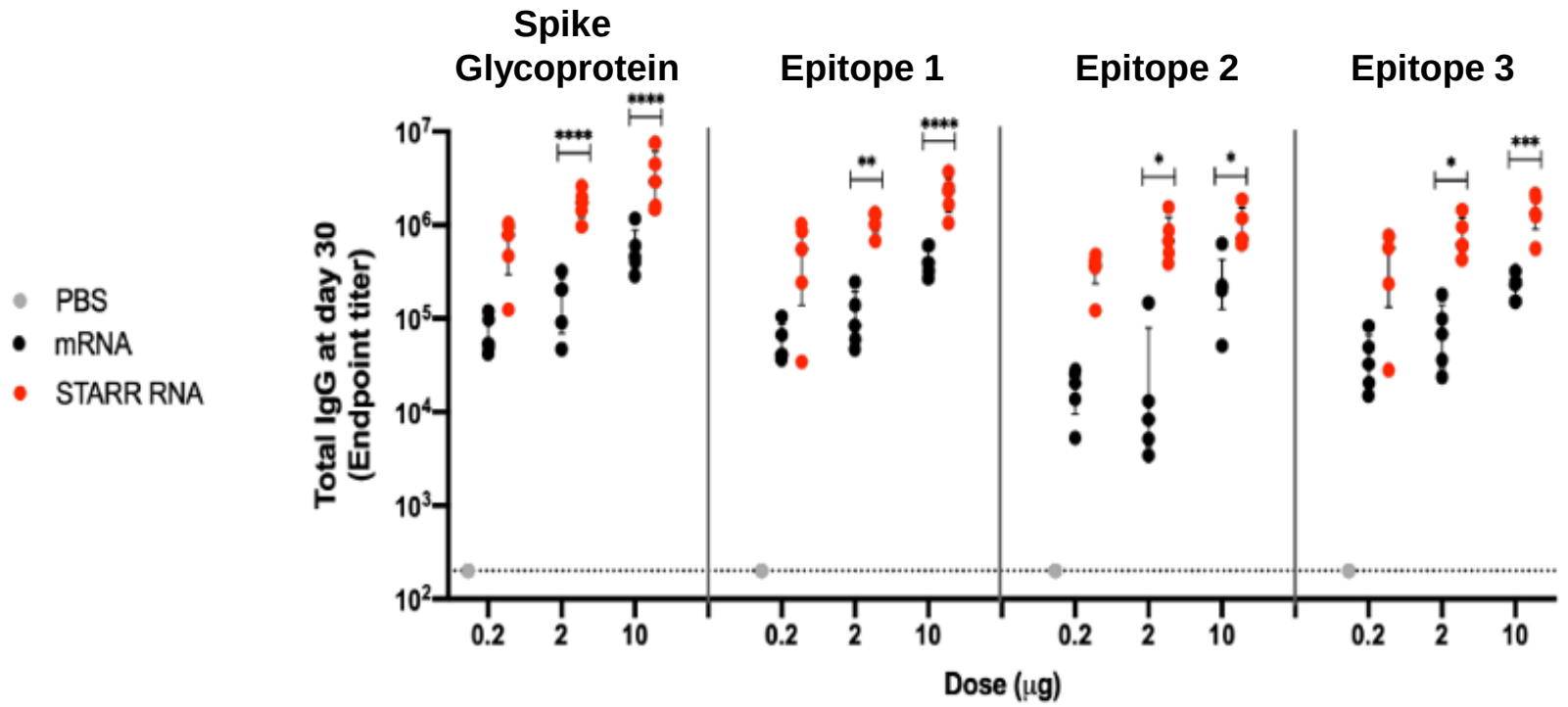


Summary of Results

- Higher anti-SARS-CoV-2 Spike Glycoprotein IgG elicited by STARR™ RNA compared to mRNA after single vaccination
- IgG produced by STARR™ vaccination continues to increase up to day 40 for the 0.2 µg and day 50 for the 2.0 µg and 10 µg RNA doses, whereas the IgG levels produced by the mRNA plateaued at day 10

STARR vs mRNA SARS-CoV-2 Vaccine

30 Day Endpoint Titer Epitope Mapping



- STARR-based vaccine produced 10-fold higher anti-full-length spike glycoprotein IgG compared to mRNA-based vaccine
- STARR-based vaccine IgG titers against epitopes 1, 2 and 3 representing different spike protein domains were at least 10-fold higher than mRNA-based vaccine IgG titers
- STARR-based vaccine IgG titers for 0.2 µg RNA dose were equivalent or greater than anti-spike glycoprotein IgG titers obtained with 10.0 µg mRNA vaccine indicating a 50 fold greater potency

Day 30 and Day 60 Mouse Neutralizing Antibody Titers

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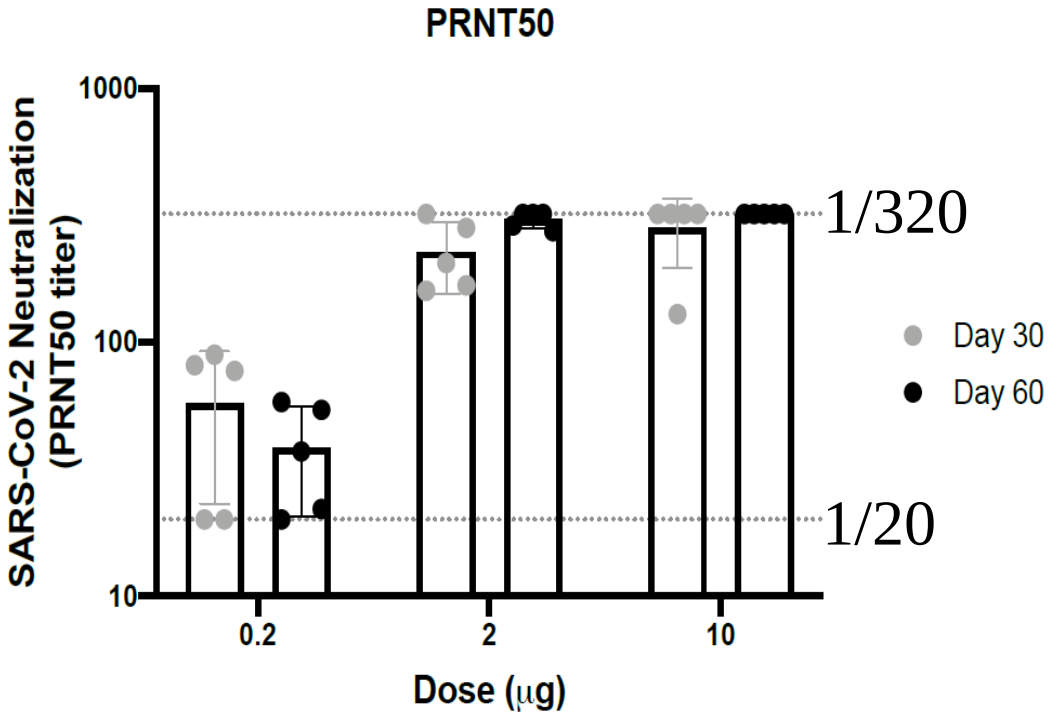

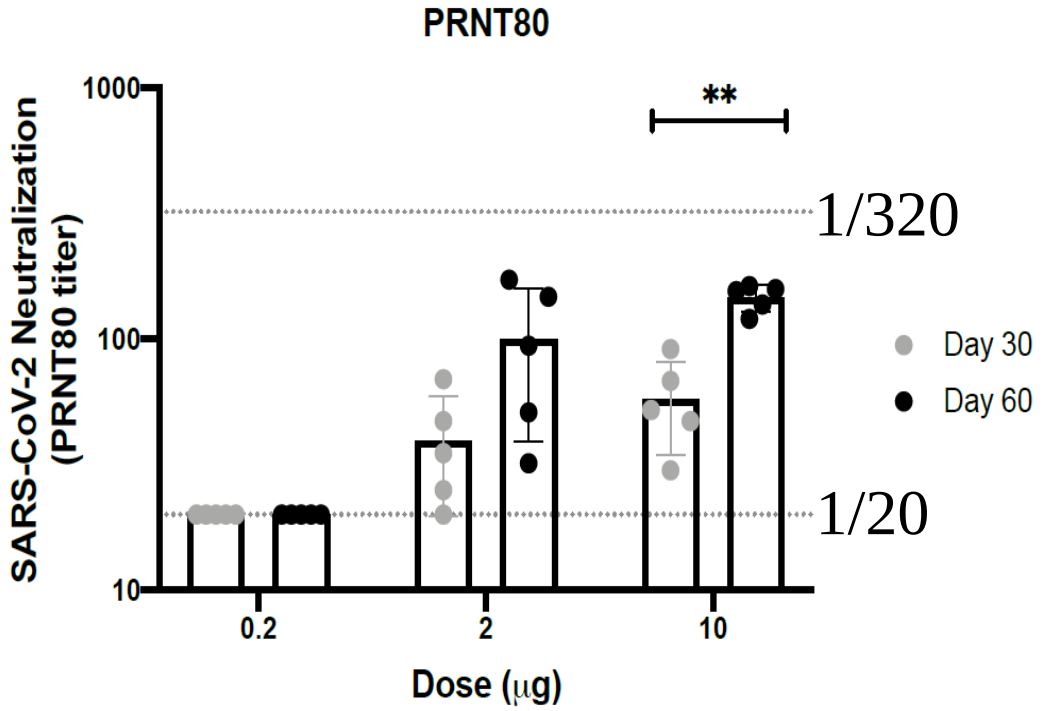

- 0.2 µg RNA dose showed 80% seroconversion by day 30 and 100% seroconvernsion by day 60 post vaccination
- 2.0 µg and 10 µg RNA doses yielded 100% seroconversion by day 30 and maintained 100% seroconversion by day 60 post vaccination
- PRNT 80 neutralizing antibody increased ~2-fold from day 30 to day 60 for the 2.0 µg and 10 µg RNA doses

Arcturus Vaccine elicits a Balanced Cell Mediated Immune Response

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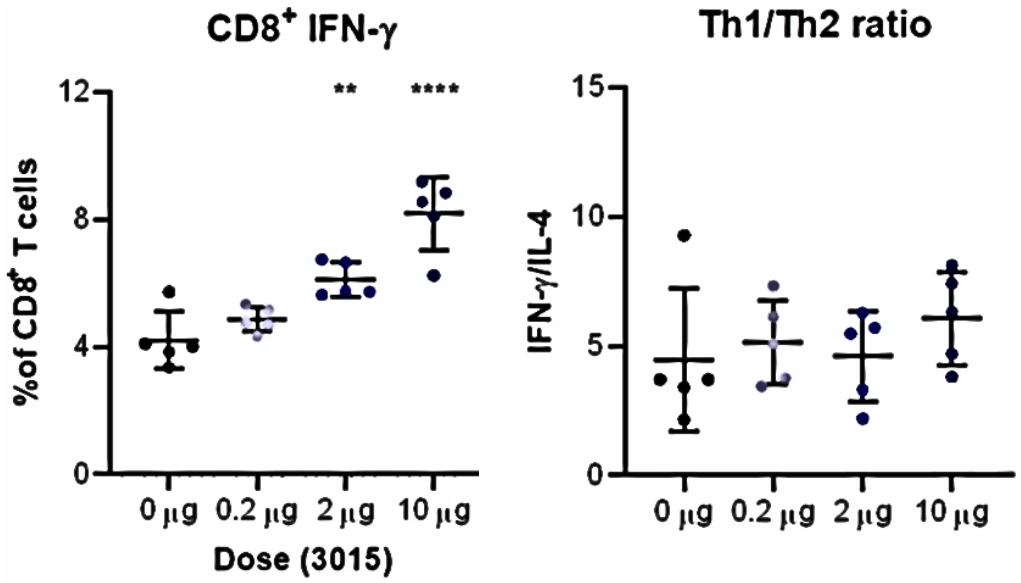


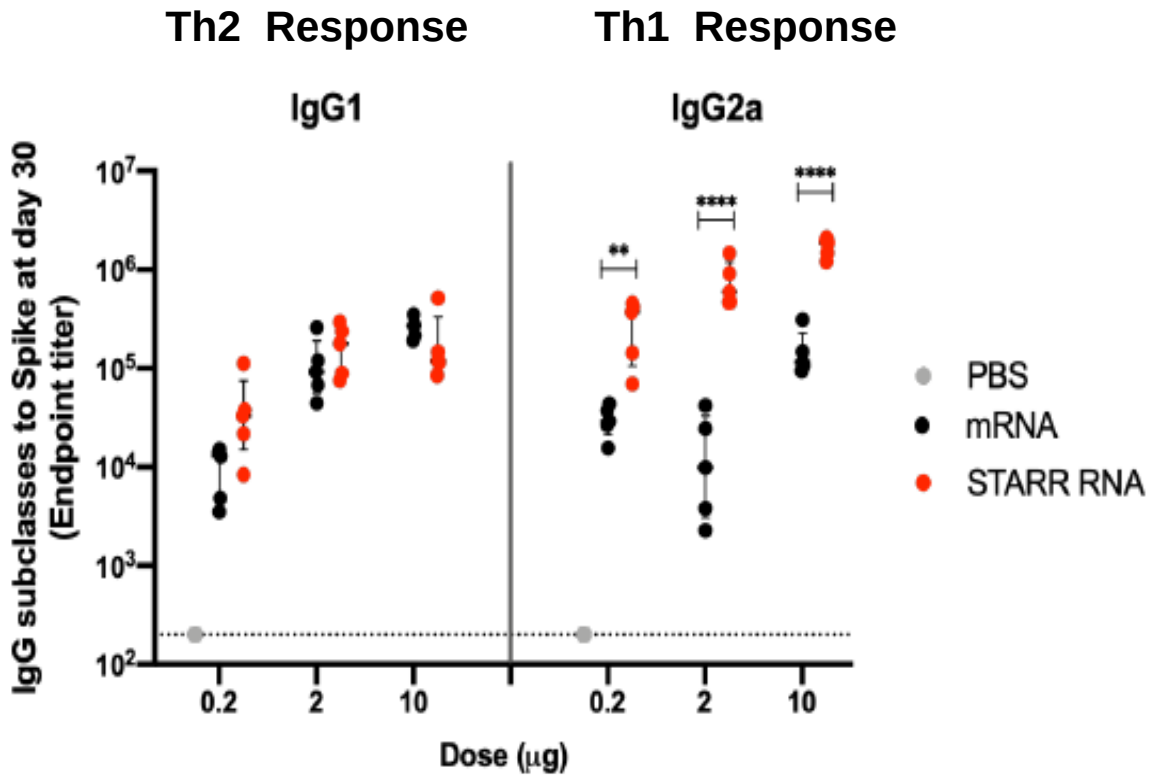
RNA Dose (μg)	% IFN-g + CD8+ T Cells	CD4+ Th1/Th2 (IFN-g/IL4)
0.0	4.0	4.6
0.2	4.5	5.3
2.0	6.0	5.0
10.0	8.0	6.0

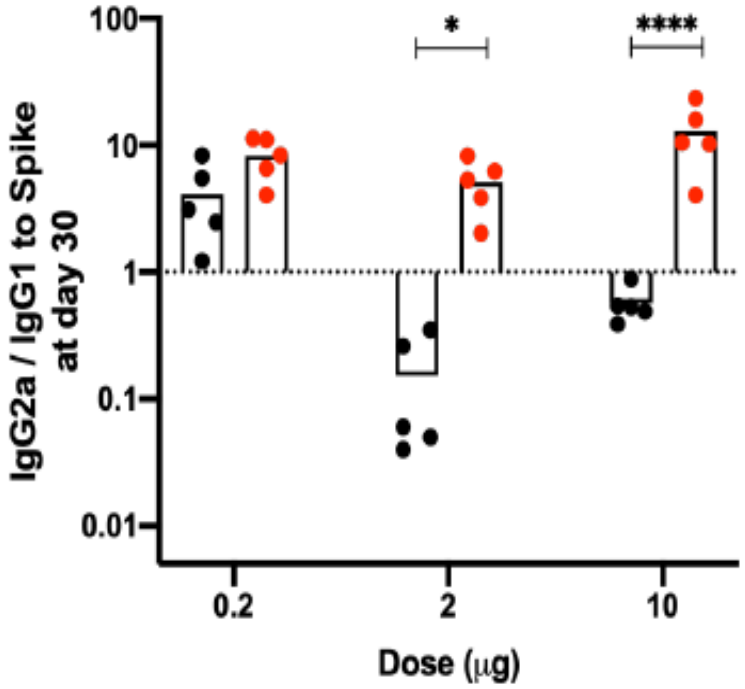
Results Summary

- 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

STARR vs mRNA SARS-CoV-2 Vaccine

Th1 response vs. Th2 Response in Balb/c Mice

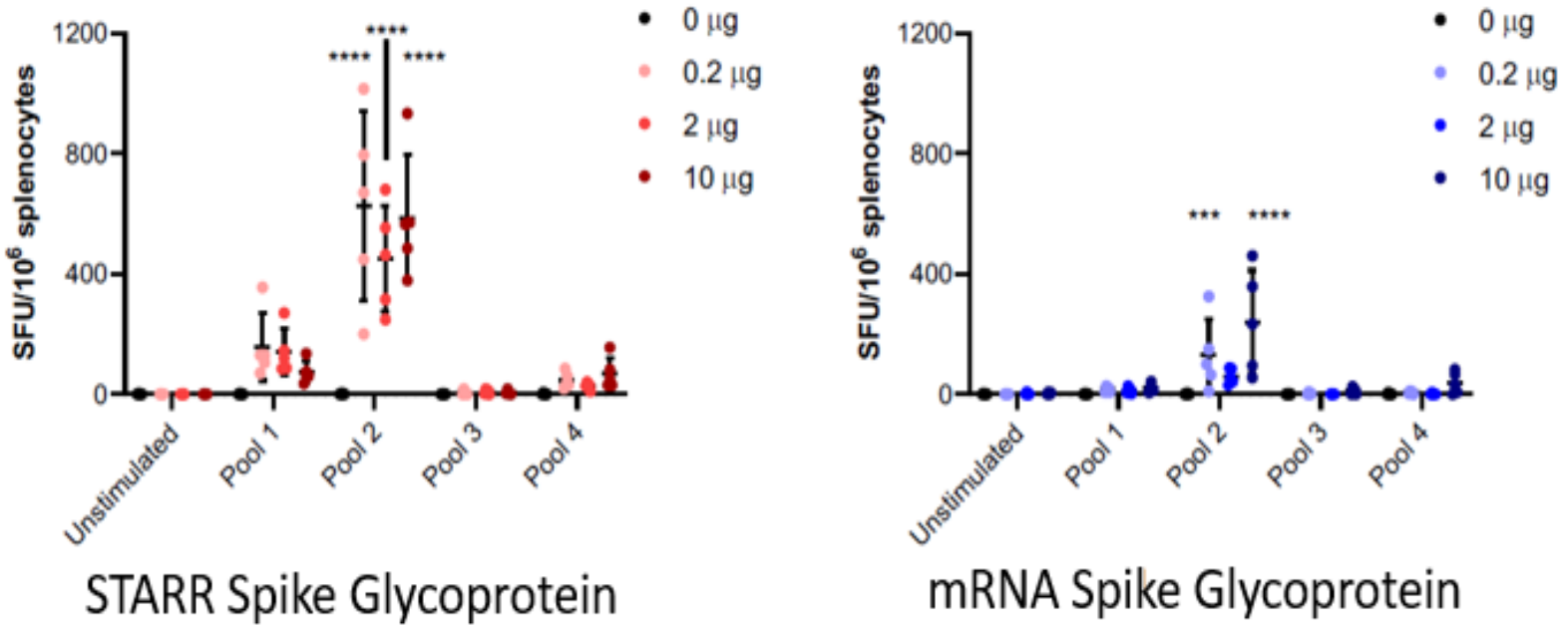




- STARR and mRNA-based vaccines have a Th1 response at the 0.2 µg RNA Dose (IgG2a/IgG1 >1)
- 2.0 µg and 10 µg RNA doses show STARR based vaccine maintain a Th1 response whereas mRNA-based vaccine has a Th2 response (IgG2a/IgG1 <1)

STARR vs mRNA SARS-CoV-2 Vaccine

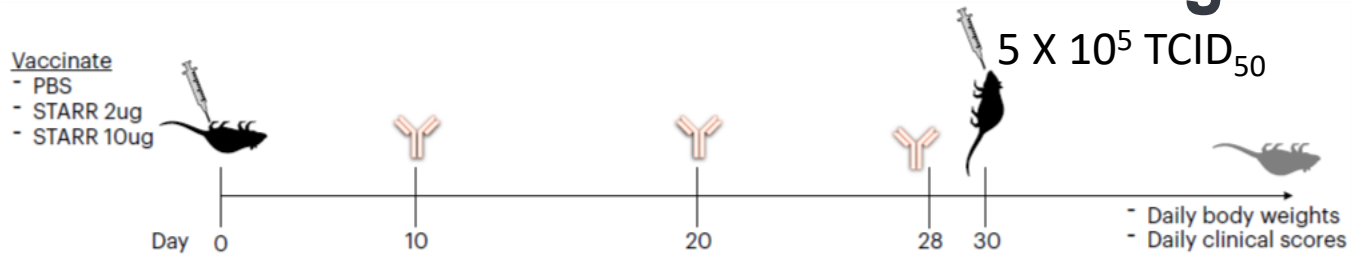
Spike Glycoprotein Specific T Cell Immune Response

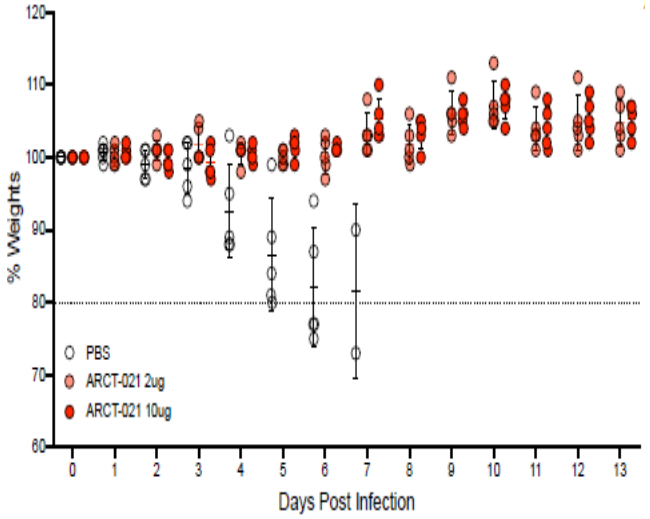


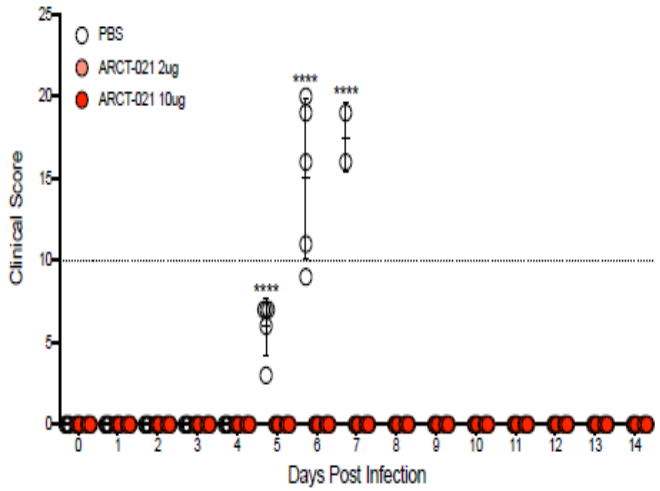
ELISPOT Results

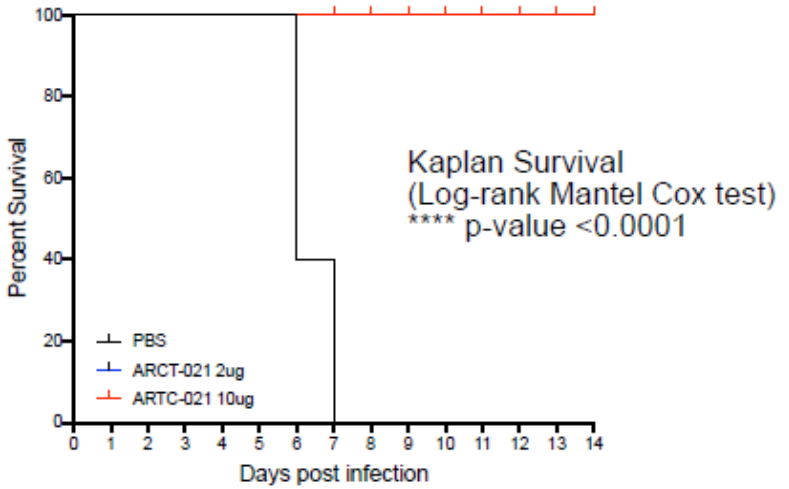
- STARR based vaccine produced higher number of spike glycoprotein specific T cells than mRNA-based vaccine
- The highest response was observed for Pool 2 and to a lesser extent to Pool 1

Single Vaccination of ARCT-021 Completely Protects Transgenic Mice from Viral Lethal Challenge





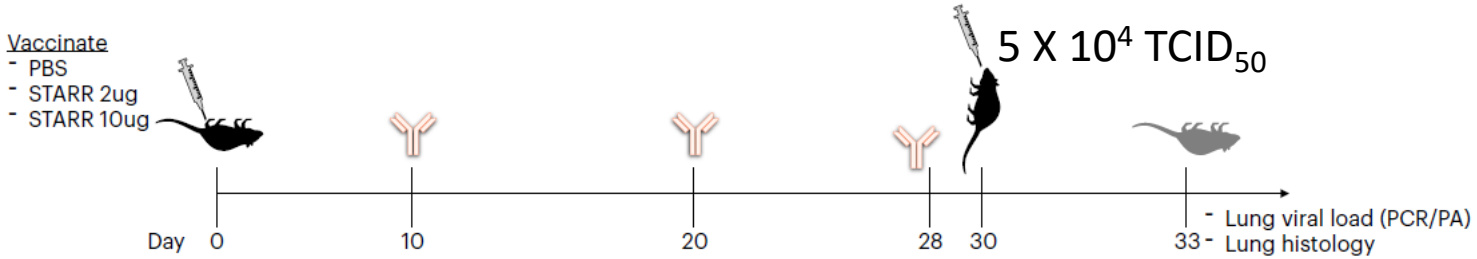




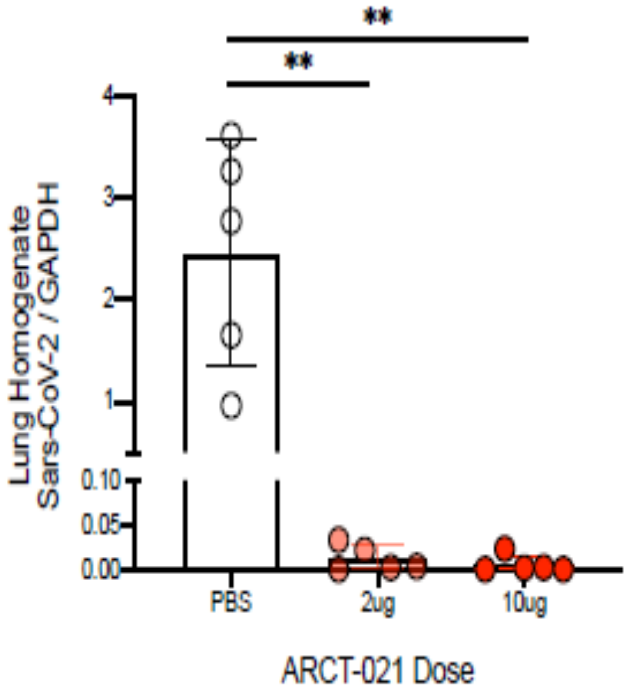
SARS-CoV-2 Virus Challenge Results

- Transgenic mice vaccinated with a single dose of either 2 µg or 10 µg RNA dose of ARCT-021 were completely protected from SARS-CoV-2 infection for 14 days post viral lethal challenge and showed no sign of infection based on body weight, clinical scores and behavior

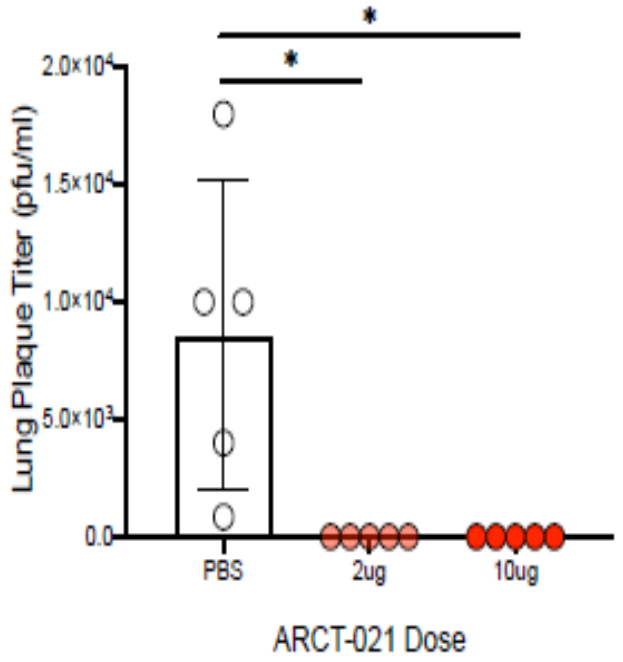
No Viral Infection Detected in Transgenic Mouse Lungs Vaccinated with ARCT-021



Lung Virus Copy Number



Lung Infectious Virus



No RT-PCR detectable viral RNA and no infectious virus detected in transgenic mouse lungs 5 days post sublethal viral challenge

LUNAR-COV19 Data Summary

- **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 60
- **Strong T-cell response:** dose response increase in IFN-g positive $CD8^+$ T-cells
- **Complete protection** against viral lethal challenge 30 days post single vaccination
- No indication of Vaccine Associated Immune Enhance Respiratory Disease (VAERD) in vaccinated transgenic mice following lethal and sublethal virus challenge
- **Balanced cellular immune response** – minimizes potential for enhanced respiratory disease (ERD) and lower dose may yield lower local and systemic reactogenic events suggesting a promising safety profile
- **Superior** immunogenic profile of STARR™ compared to conventional mRNA
- **No virus material, adjuvants, preservatives or antibiotics:** reduces public concerns

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

Drug Substance / Drug Product CMC

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Drug Substance: mRNA Design

Arcturus' proprietary mRNA optimization platform

Optimized conditions

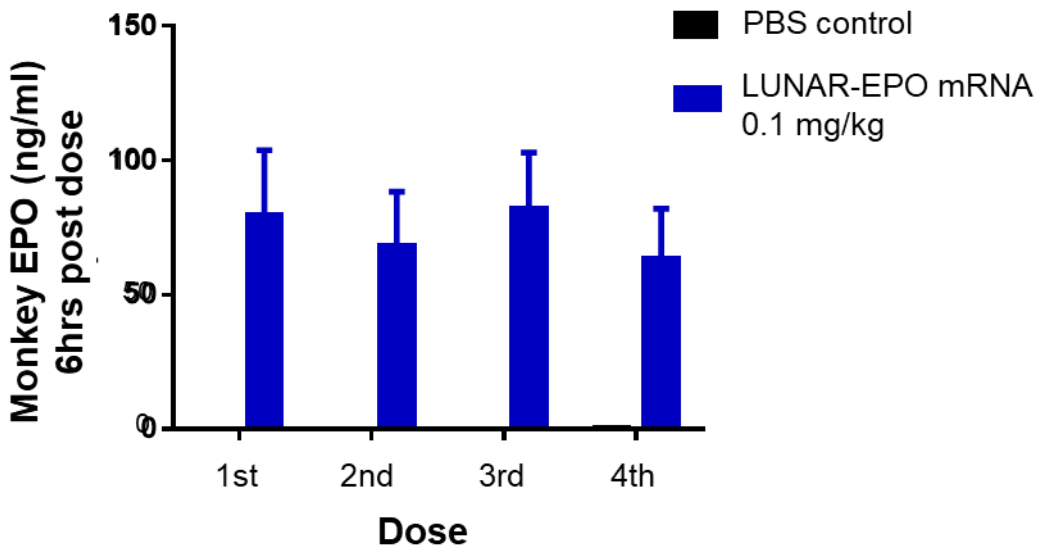
- mRNA sequence
- Chemistry
- Process optimization

→

- 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

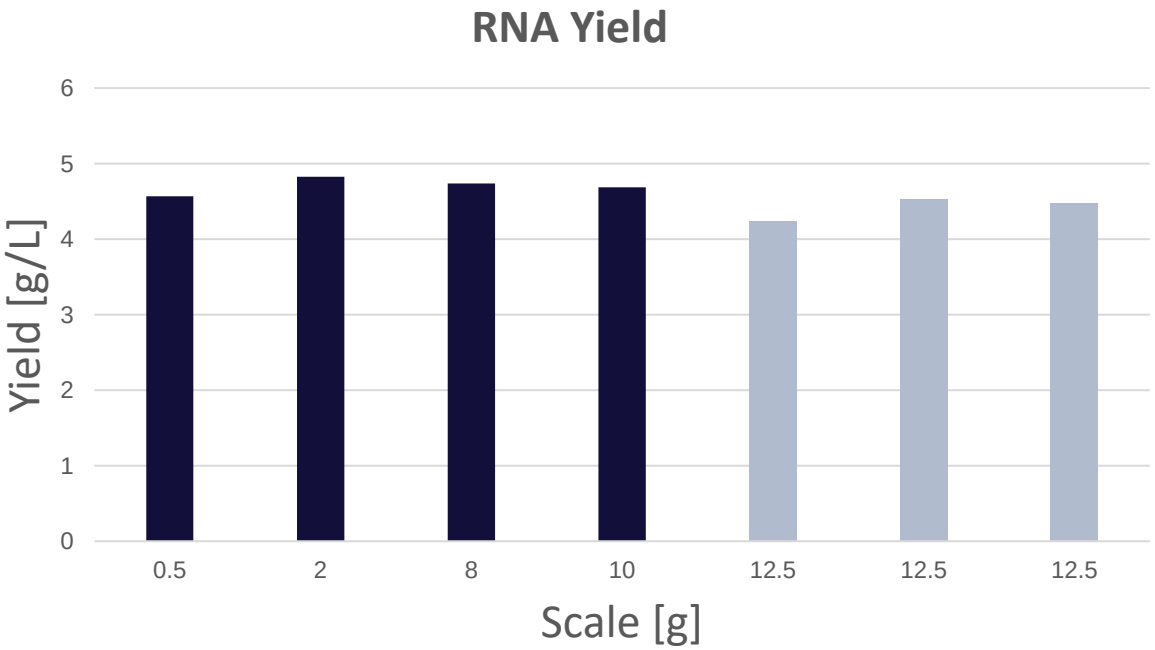
Drug Substance (mRNA) Manufacturing

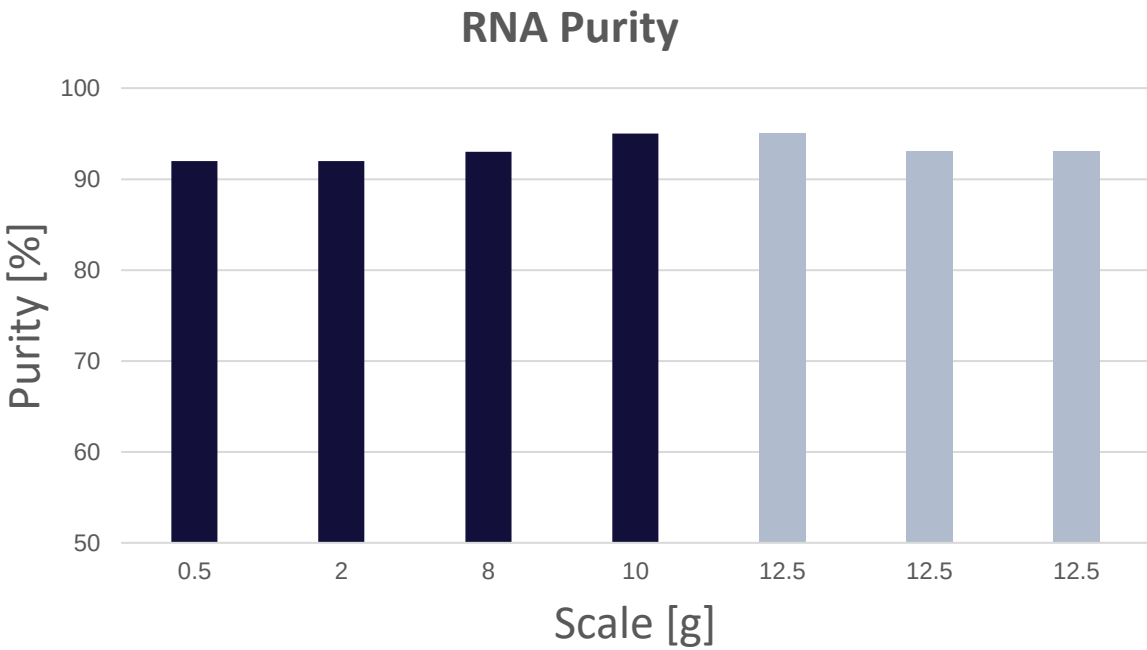
Features	Benefits
Optimized IVT Method	Reduced Cost; Higher Purity
Improved Capping Reaction	Reduced Cost of Goods
Proprietary Purification Process	Higher Purity in a Shorter Time
Efficient	Entire Process Less Than One Week
Scalable to > 1Kg	Access Large Patient Populations
Adaptable	Can Utilize a Variety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

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

Drug Substance (mRNA) Manufacturing

BUILDING INNOVATIVE
RNA MEDICINES





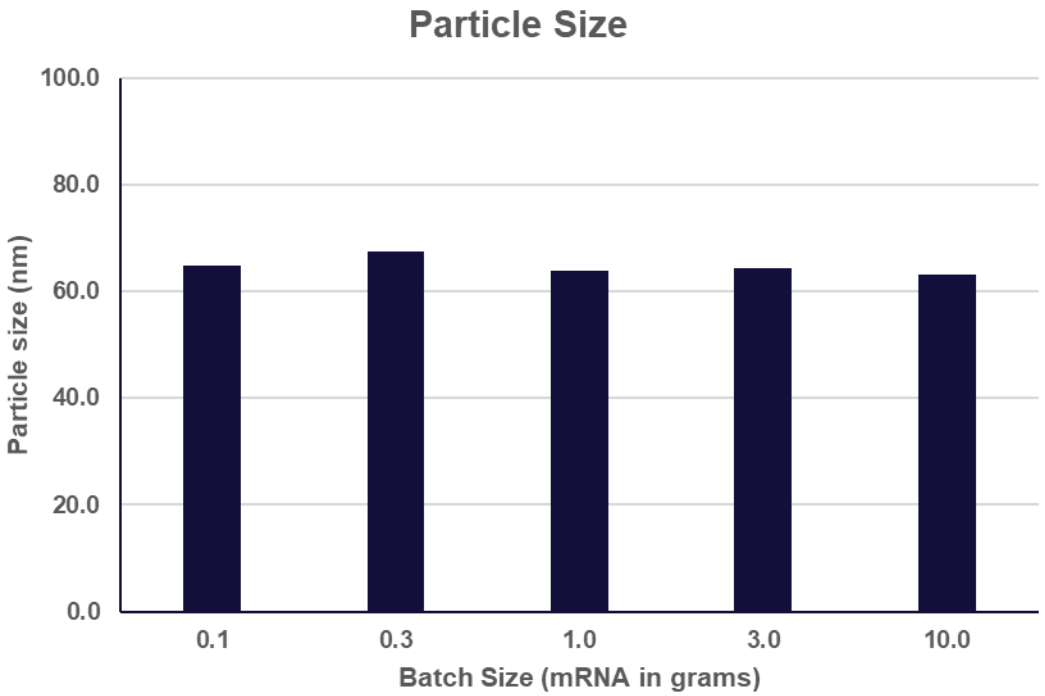
Non-GMP Lots Produced at Arcturus

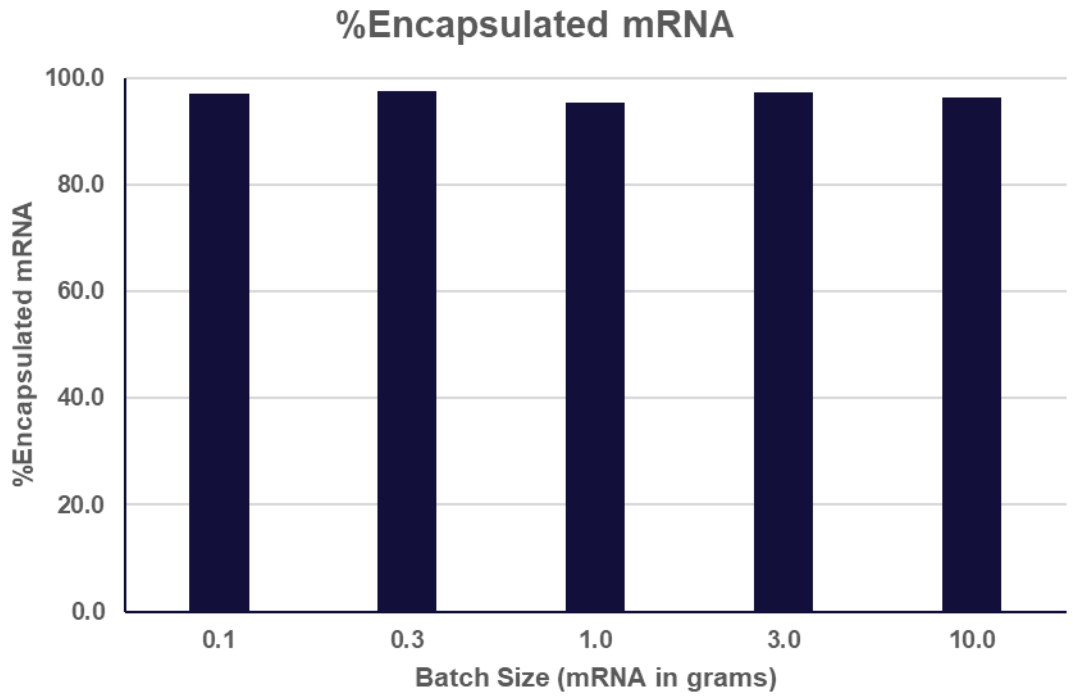
GMP Lots Produced at CMO as part of recent GMP campaign

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

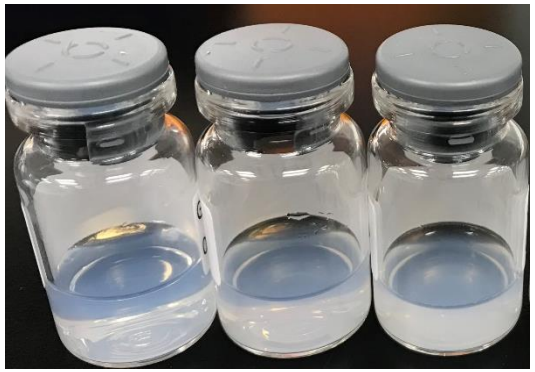




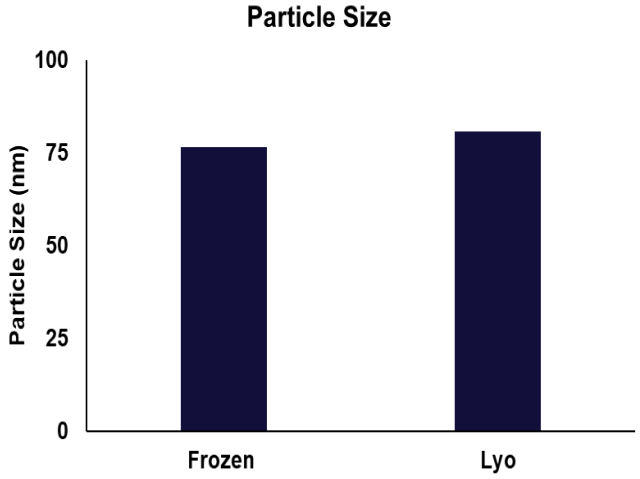
- **Manufacturing of Drug Product Demonstrated up to Multigram Scale with Yields ≥ 85%**
- **GMP Batch of LUNAR®-OTC (ARCT-810) Drug Product Manufactured and Released**

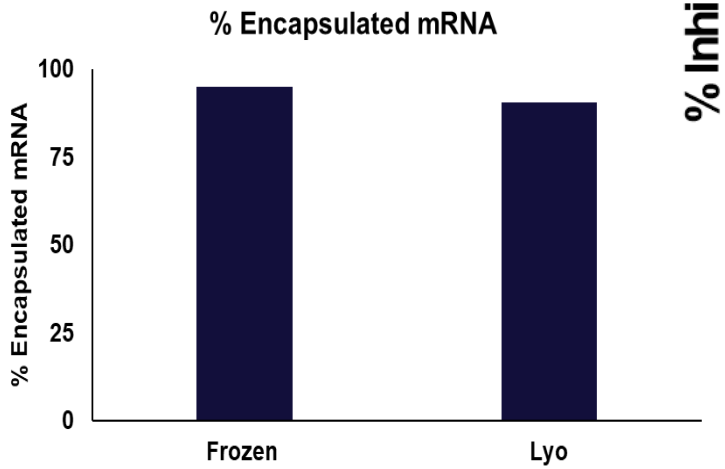
Lyophilized ARCT-021

Lyophilized

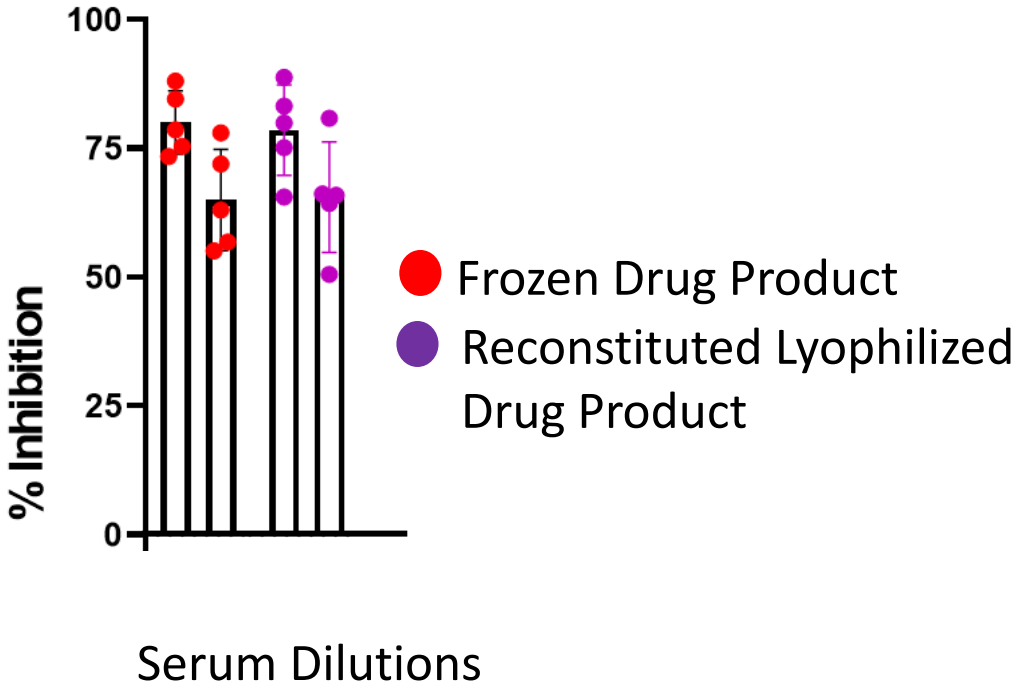


Reconstituted





Inhibition of Receptor Binding Domain



- Lyophilized ARCT-021 maintains key physicochemical properties
- Lyophilized formulation yielded equivalent mouse neutralizing antibody titers based on inhibition of ACE2 receptor binding assay (surrogate neutralizing antibody titer assay)

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

ARCTURUS therapeutics