UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): May 10, 2021

ARCTURUS THERAPEUTICS HOLDINGS INC.

(Exact name of registrant as specified in its charter)

Delaware	**001-38942**	**32-0595345**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

10628 Science Center Drive, Suite 250
San Diego, California 92121
(Address of principal executive offices)

Registrant's telephone number, including area code: (858) 900-2660

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common stock, par value $0.001 per share	**ARCT**	**The Nasdaq Stock Market LLC**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 2.02. Results of Operations and Financial Conditions.

On May 10, 2021, Arcturus Therapeutics Holdings Inc. (the "Company" or "Arcturus") issued a press release, a copy of which is furnished herewith as Exhibit 99.1, announcing the Company's financial results for the quarter ended March 31, 2021 and providing a corporate update (the "Press Release").

The information contained in Item 2.02 of this Current Report on Form 8-K, including the Press Release, shall not be deemed "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liability of that section or Sections 11 and 12(a)(2) of the Securities Act of 1933, as amended. In addition, this information shall not be deemed incorporated by reference into any of the Company's filings with the Securities and Exchange Commission (the "SEC"), except as shall be expressly set forth by specific reference in any such filing.

Item 7.01. Regulation FD Disclosure.

The Company has made available a presentation about its business (the "Presentation"), a copy of which is furnished herewith as Exhibit 99.2 to this Current Report on Form 8-K and is hereby incorporated by reference.

The furnishing of the Presentation is not an admission as to the materiality of any information therein. The information contained in the Presentation is summary information that should be considered in the context of the Company's filings with the SEC and other public announcements the Company may make by press release or otherwise from time to time.

Cautionary Note Regarding Forward-Looking Statements

Certain statements in this Current Report on Form 8-K, the Press Release and the Presentation are "forward-looking statements" that involve substantial risks and uncertainties for purposes of the safe harbor provided by the Private Securities Litigation Reform Act of 1995. Any statements, other than statements of historical fact included in this Current Report on Form 8-K, the Press Release and the Presentation, including those regarding strategy, future operations, collaborations, the likelihood of success, and the efficacy or safety, of the Company's pipeline, including ARCT-021, ARCT-810 or ARCT-032, the potential administration regimen or dosage, or ability to administer multiple doses of, any of Company's drug candidates, the ability to enroll subjects in clinical trials, the Company's efforts to develop a vaccine against COVID-19 and therapeutic potential thereof based on the Company's mRNA therapeutics, the Company's manufacturing methods and technologies (including purification and lyophilization, and stability of manufactured product), the ability of the Company to scale up manufacturing of products or substances, the likelihood that a patent will issue from any patent application, its current cash position and expected cash burn and the impact of general business and economic conditions, are 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. Such statements are based on management's current expectations and involve 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, 2020, filed with the SEC on March 1, 2021 and in subsequent filings with, or submissions to, the SEC.

The statements made in this Current Report on Form 8-K, the Press Release and the Presentation speak only as of the date stated herein, and subsequent events and developments may cause the Company's expectations and beliefs to change. While the Company may elect to update these forward-looking statements publicly at some point in the future, the Company specifically disclaims any obligation to do so, whether as a result of new information, future events or otherwise, except as required by law. These forward-looking statements should not be relied upon as representing the Company's views as of any date after the date stated herein.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	**Description of Exhibit**
99.1	Press Release dated May 10, 2021
99.2	Presentation dated May 2021
104	Cover Page to this Current Report on Form 8-K in Inline XBRL

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: May 10, 2021

Arcturus Therapeutics Holdings Inc.

By: /s/ Joseph E. Payne
Name: Joseph E. Payne
Title: Chief Executive Officer

Arcturus Therapeutics Announces First Quarter 2021 Company Overview and Financial Results and Provides New Clinical Data

ARCT-021 Phase 2 interim data showed favorable safety profile and greater than 90% seroconversion after a single dose; data supports advancement into Phase 3

In negotiations with multiple regulatory authorities regarding ARCT-021 Phase 3 study program

Continued progress advancing mRNA therapeutic platform, including liver (ARCT-810) and lung (ARCT-032) targeted programs

Investor conference call at 4:30 p.m. ET today

San Diego, Calif, May 10, 2021 – Arcturus Therapeutics Holdings Inc. (the "Company", "Arcturus", Nasdaq: ARCT), a leading clinical-stage messenger RNA medicines company focused on the development of infectious disease vaccines and significant opportunities within liver and respiratory rare diseases, today announced its financial results for the first quarter ended March 31, 2021 and provided corporate updates.

"Arcturus has made continued progress advancing our clinical pipeline, highlighted by our development efforts for ARCT-021, a differentiated mRNA vaccine candidate targeting COVID-19. Based on promising data from our Phase 1/2 study, and the new interim safety and immunogenicity data from our Phase 2 study, we are looking forward to initiating ARCT-021 Phase 3 study as well as the continued advancement of our other pipeline programs," said Steve Hughes, M.D., Chief Medical Officer of Arcturus.

"Our Self-Transcribing and Replicating mRNA (STARR™) delivered with our LUNAR® delivery system potentially has important differences from currently authorized mRNA vaccines for emergency use. We believe that ARCT-021, as a single shot lyophilized self-amplifying mRNA vaccine, if approved, may represent a preferred vaccine option. We are very pleased with the recent successes in our mRNA drug product manufacturing efforts, and in the expansion of our global safety database – and the positive readthrough this provides to the Company's pipeline of mRNA therapeutics. We eagerly look forward to the next major development milestones for our vaccine, liver, and lung mRNA pipeline programs," said Joseph Payne, President & CEO of Arcturus.

Recent Corporate Highlights

ARCT-021, STARR™ mRNA Vaccine Candidate for SARS-CoV-2

Phase 2 study:

- Completed enrollment with 580 participants randomized and dosed
- Completed two interim analyses of the Phase 2 data which have been reviewed by the Data and Safety Monitoring Board (DSMB) with recommendation to proceed with no changes to protocol
- Data support initiation of Phase 3 study evaluating a single shot regimen of 5 microgram (µg)
- Interim immunogenicity data confirm high seroconversion rate (> 90%) at day 28 for IgG antibodies binding the full-length spike protein following a single 5 µg dose
- Phase 2 study is ongoing and the Company remains blinded to full trial data; data from additional endpoints are expected, including neutralizing antibody and T-cell data, during H2 2021

Phase 3 study:

- Single dose of 5 µg selected as the regimen for evaluation in Phase 3
- In negotiations with multiple regulatory authorities regarding Phase 3 study

Manufacturing:

- Completed GMP manufacturing and release of lyophilized ARCT-021 to support Phase 3
- Completed stockpiling of greater than 10 million doses of lyophilized ARCT-021
- Manufacturing capacity in place to support vaccine supply requirements under potential Emergency Use Authority (EUA)
- Lyophilized ARCT-021 stability predicted to be longer than 1 year at -20°C; stability studies at -20°C, 2-8°C and room temperature are ongoing

ARCT-810, mRNA Therapeutic Candidate for Ornithine Transcarbamylase (OTC) Deficiency

- Two additional sites in U.S. activated to support ongoing Phase 1b study
- 9-month (20 doses) chronic toxicology study completed in non-human primates with no adverse histological findings; doses exceeded maximum targeted clinical dose
- On track to file CTA this quarter for Phase 2 multiple dose study; ethics committee submission completed

ARCT-032, mRNA Therapeutic Candidate for Cystic Fibrosis

- CTA filing on track for Q4

Financial results for the quarter ended March 31, 2021

Revenues in conjunction with strategic alliances and collaborations: Arcturus' primary sources of revenues were from license fees and collaborative payments received from research and development arrangements with pharmaceutical and biotechnology partners. For the three months ended March 31, 2021, the Company reported revenue of $2.1 million, compared with $2.6 million in the three months ended March 31, 2020.

Operating expenses: Total operating expenses for the three months ended March 31, 2021 were $59.8 million compared with $12.1 million for the three months ended March 31, 2020 and $33.3 million for the three months ended December 31, 2020.

Research and development expenses increased by approximately $42.1 year over year and $25.8 million sequentially from the fourth quarter of 2020. The primary driver of the sequential increase was driven by higher clinical and manufacturing cost of $17.2 million for our ARCT-021 program. The remaining increase was primarily driven by higher personnel costs and related to the acquisition of an exclusive license from Alexion Pharmaceuticals for certain patent-pending inventions relating to nucleic acid purification technologies for approximately $5.0 million of Arcturus stock.

Net loss: For the three months ended March 31, 2021 Arcturus reported a net loss of approximately $56.3 million, or ($2.15) per basic and diluted share, compared with a net loss of $9.8 million, or ($0.67) per basic and diluted share in the three months ended March 31, 2020 and a net loss of $31.1 million, or ($1.25) per basic and diluted share in the three months ended December 31, 2020.

The Company's cash balance totaled $466.9 million as of March 31, 2021, compared to cash and cash equivalents of $463.0 million at December 31, 2020. Based on our current plans, the Company's cash position is expected to be sufficient to support operations for more than two years.

Monday, May 10th @ 4:30 p.m. ET

Domestic:	877-256-4295
International:	212-231-2927
Conference ID:	21993793
Webcast:	http://public.viavid.com/index.php?id=144682

About Arcturus Therapeutics

Founded in 2013 and based in San Diego, California, Arcturus Therapeutics Holdings Inc. (Nasdaq: ARCT) is a clinical-stage mRNA medicines and vaccines company with enabling technologies: (i) LUNAR® lipid-mediated delivery, (ii) STARR™ mRNA Technology and (iii) mRNA drug substance along with drug product manufacturing expertise. Arcturus' diverse pipeline of RNA therapeutic and vaccine candidates includes mRNA vaccine programs for SARS-CoV-2 (COVID-19) and Influenza, and other programs to potentially treat Ornithine Transcarbamylase (OTC) Deficiency, and Cystic Fibrosis along with partnered programs including Glycogen Storage Disease Type 3, Hepatitis B Virus, and non-alcoholic steatohepatitis (NASH). Arcturus' versatile RNA therapeutics platforms can be applied toward multiple types of nucleic acid medicines including messenger RNA, small interfering RNA, replicon RNA, antisense RNA, microRNA, DNA, and gene editing therapeutics. Arcturus' technologies are covered by its extensive patent portfolio (209 patents and patent applications, issued in the U.S., Europe, Japan, China and other countries). Arcturus' commitment to the development of novel RNA therapeutics has led to collaborations with Janssen Pharmaceuticals, Inc., part of the Janssen Pharmaceutical Companies of Johnson & Johnson, Ultragenyx Pharmaceutical, Inc., Takeda Pharmaceutical Company Limited, CureVac AG, Synthetic Genomics Inc., Duke-NUS Medical School, and the Cystic Fibrosis Foundation. For more information visit www.ArcturusRx.com. In addition, please connect with us on Twitter and LinkedIn.

Forward Looking Statements

This press release contains forward-looking statements that involve substantial risks and uncertainties for purposes of the safe harbor provided by the Private Securities Litigation Reform Act of 1995. Any statements, other than statements of historical fact included in this press release, are forward-looking statements, including those regarding strategy, future operations, collaborations, the planned initiation, design or completion of clinical trials, the likelihood that the Company will obtain clearance from regulatory authorities to proceed with planned clinical trials, the likelihood that preclinical or clinical data will be predictive of future clinical results, the likelihood that clinical data will be sufficient for regulatory approval or completed in time to submit an application for regulatory approval within a particular timeframe, the likelihood of success (including safety and efficacy) of the Company's pipeline, including ARCT-021, ARCT-810 or ARCT-032, the potential administration regimen or dosage, or ability to administer multiple doses of, any of Company's drug candidates, the ability to enroll subjects in clinical trials, the Company's efforts to develop a vaccine against COVID-19 and therapeutic potential thereof based on the Company's mRNA therapeutics, the Company's manufacturing methods and technologies (including purification and lyophilization, and stability of manufactured product), the ability of the Company to scale up manufacturing of products or substances, the likelihood that a patent will issue from any patent application, its current cash position and expected cash burn and the impact of general business and economic conditions. Actual results and performance could differ materially from those projected in any forward-looking statements as a result of many factors including, without limitation, the ability to enroll subjects in clinical trials as a result of the COVID-19 pandemic, the impact of commercialization of third-party COVID-19 vaccines on the design, and ability to conduct, clinical trials, the availability of manufacturing capacity and raw materials, unexpected clinical results, government regulations impacting the regulatory environment or intellectual property landscape, and general market conditions that may prevent such achievements or performance. 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. Such statements are based on management's current expectations and involve 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, 2020, and in subsequent filings with, or submissions to, the SEC. Except as otherwise required by law, Arcturus disclaims 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.

IR and Media Contacts

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Carlo Tanzi, Ph.D.
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ctanzi@kendallir.com

ARCTURUS THERAPEUTICS HOLDINGS INC. AND ITS SUBSIDIARIES

CONDENSED CONSOLIDATED BALANCE SHEETS

(in thousands, except par value information)

	March 31, 2021 (unaudited)	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 466,839	$ 462,895
Accounts receivable	2,007	2,125
Prepaid expenses and other current assets	1,150	2,769
Total current assets	469,996	467,789
Property and equipment, net	3,427	3,378
Operating lease right-of-use asset, net	6,690	5,182
Equity-method investment	1,248	—
Non-current restricted cash	107	107
Total assets	$ 481,468	$ 476,456
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 5,597	$ 10,774
Accrued liabilities	29,800	20,639
Deferred revenue	17,936	18,108
Total current liabilities	53,333	49,521
Deferred revenue, net of current portion	11,313	12,512
Long-term debt, net of current portion	58,147	13,845
Operating lease liability, net of current portion	5,710	4,025
Other long-term liabilities	358	—
Total liabilities	$ 128,861	$ 79,903
Stockholders' equity		
Common stock: $0.001 par value; 60,000 shares authorized; 26,319 issued and outstanding at March 31, 2021 and 26,192 issued and outstanding at December 31, 2020	26	26
Additional paid-in capital	552,743	540,343
Accumulated deficit	(200,162)	(143,816)
Total stockholders' equity	352,607	396,553
Total liabilities and stockholders' equity	$ 481,468	$ 476,456

ARCTURUS THERAPEUTICS HOLDINGS INC. AND ITS SUBSIDIARIES

CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(unaudited)

(in thousands except per share data)

	Three Months Ended		
	March 31,		December 31,
	2021	2020	2020
Collaboration revenue	$ 2,127	$ 2,646	$ 2,238
Operating expenses:			
Research and development, net	50,050	7,917	24,286
General and administrative	9,743	4,191	9,034
Total operating expenses	59,793	12,108	33,320
Loss from operations	(57,666)	(9,462)	(31,082)
Gain (loss) from equity-method investment	1,248	(163)	—
Gain from foreign currency	430	—	16
Finance expense, net	(358)	(152)	(38)
Net loss	$ (56,346)	$ (9,777)	$ (31,104)
Net loss per share, basic and diluted	$ (2.15)	$ (0.67)	$ (1.25)
Weighted-average shares outstanding, basic and diluted	26,243	14,521	24,886
Comprehensive loss:			
Net loss	$ (56,346)	$ (9,777)	$ (31,104)
Comprehensive loss	$ (56,346)	$ (9,777)	$ (31,104)

ARCTURUS THERAPEUTICS

Building the Next Generation of RNA Medicines

May 2021

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 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.

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' most recent Annual Report on Form 10-K with the SEC and in other filings that Arcturus makes with 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 a Clinical-Stage mRNA Vaccines and Medicines Company

Publicly Traded (Nasdaq: ARCT)

- Headquarters: San Diego, CA
- Number of Employees: 140
- 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 · Recipharm

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
- 209 Patents & Patent Applications

Program	Indication
LUNAR-COV19	COVID-19 Vaccine
LUNAR-FLU	Flu Vaccine
LUNAR-OTC	Ornithine Transcarbamylase (OTC) Deficiency
LUNAR-CF	Cystic Fibrosis

ADDITIONAL EARLIER STAGE PROGRAMS

Arcturus Pipeline of mRNA Medicines

Franchise	Product Name	Indication	Route of Administration	Cell Target	Prevalence Worldwide	Stage	Anticipated Milestones
VACCINES	**LUNAR-COV19** (ARCT-021)	COVID-19	Intramuscular	Myocytes & Dendritic Cells	Global	Phase 2	Phase 3 CTA Q2 EUA H2 2021
	LUNAR-FLU	Influenza	Intramuscular	Myocytes & Dendritic Cells	Global	Preclinical	IND/CTA H1 2022
HEPATIC	**LUNAR-OTC** (ARCT-810)	Ornithine Transcarbamylase Deficiency	Intravenous	Periportal Hepatocytes	> 10,000	Phase 1b	Phase 2 Multiple Dose Study CTA Q2 2021
RESPIRATORY	**LUNAR-CF** (ARCT-032)	Cystic Fibrosis	Inhaled	Bronchial Epithelial Cells	> 70,000	Preclinical	CTA Q4 2021

EUA = Emergency Use Authorization; CTA = Clinical Trial Application; IND = Investigational New Drug Application

Multiple mRNA Therapeutic and Vaccine Programs in Clinical Development with Milestones

Partnerships Maximize Platform

Program	Partner	Indication
LUNAR-HBV	Johnson & Johnson	Hepatitis B Virus (HBV)
LUNAR-NASH	Takeda	Nonalcoholic Steatohepatitis (NASH)
LUNAR-GSD3	ultragenyx pharmaceutical	Glycogen Storage Disease Type III
LUNAR-RARE	ultragenyx pharmaceutical	Undisclosed Rare Disease
LUNAR-RPL	Undisclosed Large Pharma	Vaccines
LUNAR-AH	Undisclosed Animal Health Pharma	Vaccines

Greater than $1 Billion in Potential Milestones & Royalties

LUNAR® Delivery Technology

Biodegradable, highly optimized for each cell type

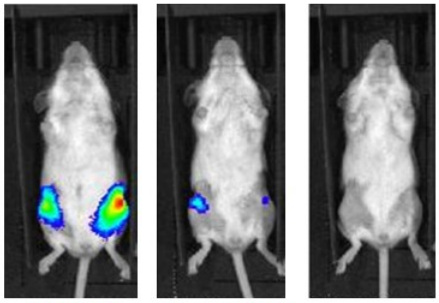
BUILDING INNOVATIVE RNA MEDICINES

BUILDING INNOVATIVE RNA MEDICINES

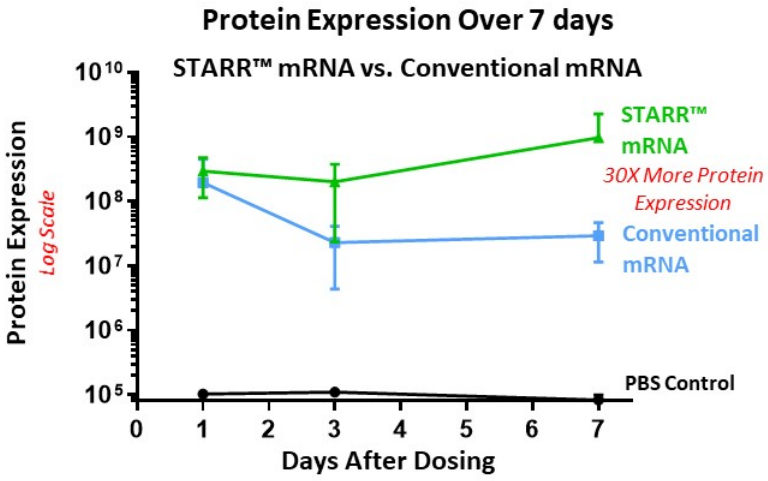
STARR™ mRNA Expression Superior to Conventional mRNA

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



Single dose of STARR™ mRNA technology with LUNAR® delivery provided enhanced protein expression *in vivo* (mouse)

LUNAR-COV19 (ARCT-021)
COVID-19 Vaccine Candidate

Arcturus COVID-19 Vaccine Candidate has Significant Advantages

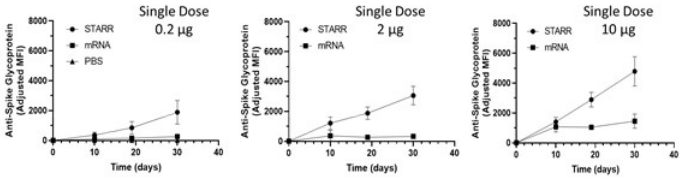
BUILDING INNOVATIVE RNA MEDICINES

- Duke-NUS Partnership DukeNUS Medical School
- mRNA Vaccine: No Adjuvants, No Viral Vector Used, Readily Updatable as New Variants Arise
- Self-amplifying (STARR™) mRNA and LUNAR® Non-viral Delivery Technology 
- Promising Clinical Data Demonstrate Humoral and Cellular Immunogenicity, and Tolerability Data
- Potential Single-Shot: Simpler Logistics for Vaccinating Large Populations
- Very Low Dose: Enables Rapid Global Scale-up
- Readily Manufactured: Arcturus Processes + Strategic Partnerships Catalent Recipharm
- Lyophilized Formulation: No need to be stored at ultra-cold temps, improved supply chain & distribution benefits

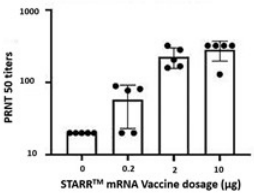
Preclinical Data: Robust Immune Response

Humoral Immunity

STARR™ induces more robust titers compared to conventional mRNA



Neutralizing antibody titers and high seroconversion at low doses

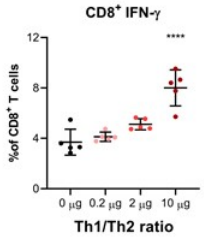


Single Dose (µg)	Seroconversion	Neutralizing Antibody Titers (Geometric Mean)
0.2	80 %	58
2	100 %	218
10	100 %	≥ 320

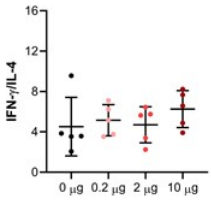
Cellular Immunity

7 Days Post Single Dose

Adaptive Cellular Response (CD8+ cells)



Balanced Th1/Th2 Immune Response (CD4+ cells)

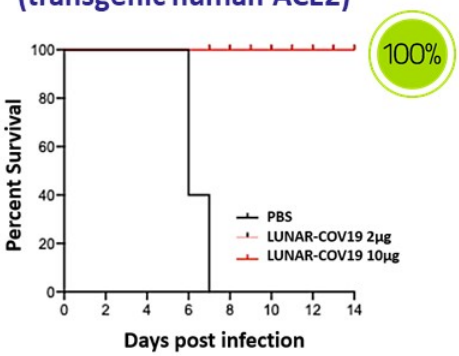


- Single administration with a very low dose of Arcturus COVID vaccine results in potent immune reaction
- STARR™ mRNA generates neutralizing antibodies (anti-SARS-CoV-2 Spike Glycoprotein IgG) and a cellular T-cell mediated immune response at a much lower dose level compared to conventional mRNA

ARCT-021 Significantly Effective in Challenge Models

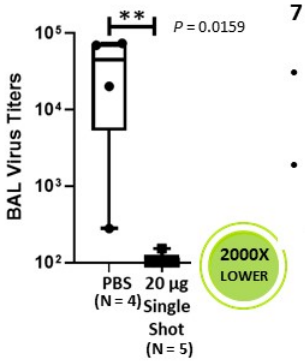
BUILDING INNOVATIVE RNA MEDICINES

Mouse Model (transgenic human ACE2)



ARCT-021 significantly effective in a virus challenge study in the human ACE2 transgenic mouse model; single dose provided complete protection from SARS-CoV-2 infection and death, compared to control mice which experienced 100% mortality

Primate Model (macaque)



7 Days After SARS-CoV-2 Virus Challenge

- Lung viral titers exceeded 13,100 (median) in non-vaccinated primates (PBS)
- Lung viral titers = 6.5 (median); more than 2000X lower in primates administered a single shot of ARCT-021

Single administration of ARCT-021 significantly effective in primate model (macaque); vaccinated macaques show substantial (3.30 log lower) reductions in median lung viral titers

ARCT-021 Clinical Trial and Manufacturing Update

Phase 1/2 Clinical Trial

- Completed dosing all subjects (n=106), including older adults
- At interim analysis, observed high seroconversion rates for IgG binding antibodies, and Th1 dominant CD4+ immune responses, neutralizing antibodies (PRNT50) Geometric Mean Titer (GMT) levels in the range of titers observed in convalescent serum
- Favorable safety and tolerability observations; no subjects have withdrawn from dosing

Phase 2 Clinical Trial Ongoing

- More than 500 participants dosed across USA and Singapore
- Two dose levels being evaluated: 5 µg and 7.5 µg

Phase 3 Clinical Trial; EUA

- Expect to commence Phase 3 clinical trial Q2 2021; targeting Emergency Use Authorization H2 2021
- Lyophilized (freeze-dried) version of ARCT-021 vaccine product on track to be evaluated in Phase 3 clinical trial

Manufacturing

- With our global manufacturing partners, we are on track to manufacture finished doses of lyophilized ARCT-021 in Q1 2021 for stockpiling purposes, and have laid the foundation to produce hundreds of millions of doses of lyophilized ARCT-021 over the next 18 months

Lyophilization Process Advantage Over Conventional Frozen Liquid

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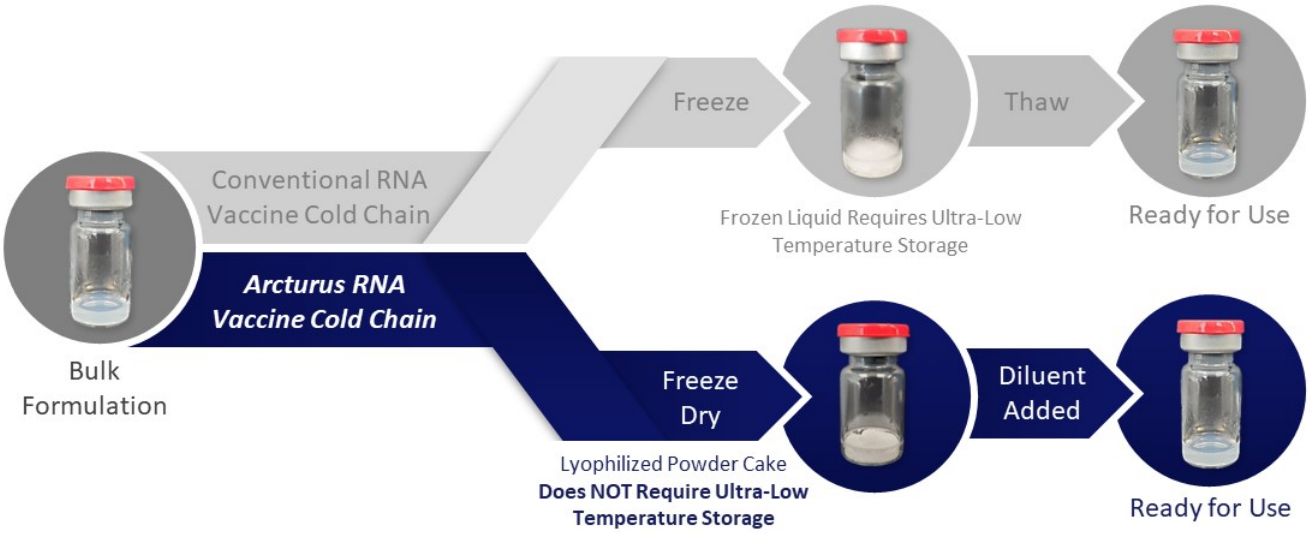


- **Lyophilized version of ARCT-021 maintains key quality attributes of the frozen liquid equivalent**
- **Collecting stability data at -20°C, 2-8°C, and Room Temperature**
- **Simpler handling: No dry ice at point of care, lower risk of degradation from uncontrolled temperature fluctuation**

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

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

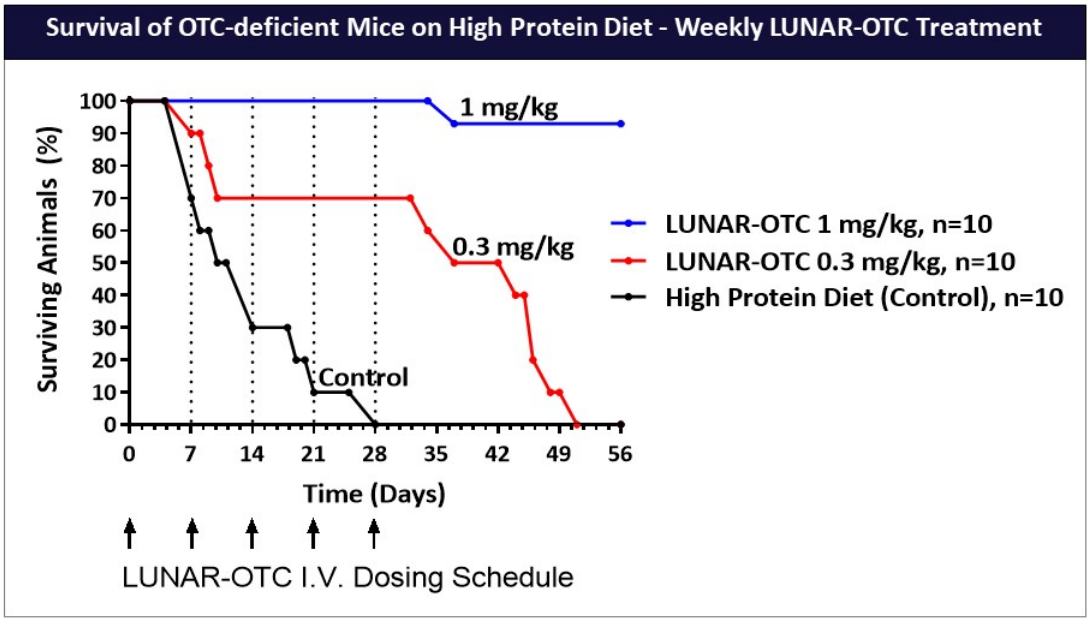
- Present standard of care involves a strict diet (low protein, high fluid intake) plus ammonia scavengers (sodium phenylbutyrate)
- Present standard of care does not effectively prevent life-threatening spikes of ammonia
- Severe OTC Deficiency patients are typically referred for liver transplant, currently 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

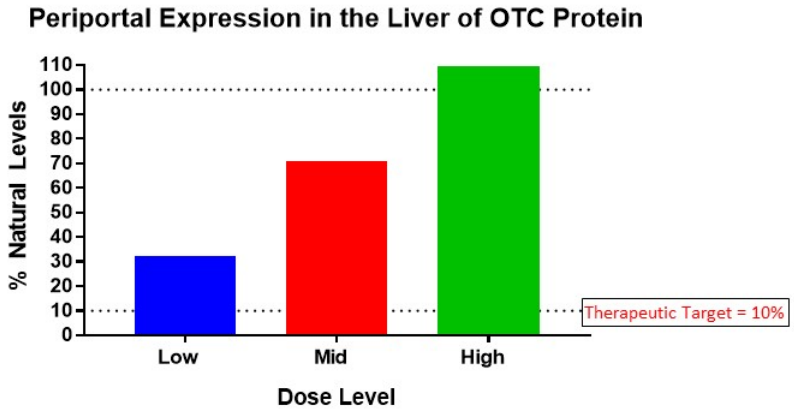
Disease Normalization Following Single and Repeat Dosing in OTC Mouse Model



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



*Li, L. et al. PGC-1α 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)

ARCT-810 Clinical Update

Phase 1 Clinical Trial Completed

- Double blind, randomized 2:1 active to placebo, dose-escalation trial in healthy adult volunteers
- All Adverse Events (AEs) mild or moderate
- Favorable PK profile: No LUNAR® lipids detectable after 48 hours following drug administration
- No steroid premedication
- Completed dose escalation of all cohorts (0.1, 0.2, 0.3, and 0.4 mg/kg)

Phase 1b Clinical Trial in OTC-Deficient Patients Ongoing

- Commenced patient enrollment
- First subject has been dosed
- Up to 12 patients; up to 3 dose levels
- All doses within anticipated range for therapeutic biological effect

Primary Goal: Identify safest doses to take forward into multiple dose clinical trials
Primary Endpoints: Safety and tolerability
Secondary Endpoints: Pharmacokinetics
Exploratory Endpoints: Biomarkers include ureagenesis, plasma ammonia levels and plasma OTC enzyme activity, and urine orotic acid levels

Next Milestone: CTA submission in Q2 2021 for Phase 2 Multiple Dose Study in OTC Deficient Patients

LUNAR-CF (ARCT-032)
Cystic Fibrosis

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

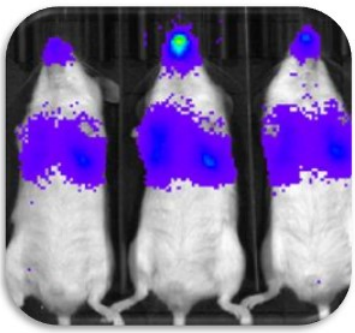
- No CFTR functional corrector is approved for treatment of all patients
- Present standard of care does not effectively prevent long-term effects of mucus accumulation. CF patients with late-stage loss of respiratory function require lung transplant

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

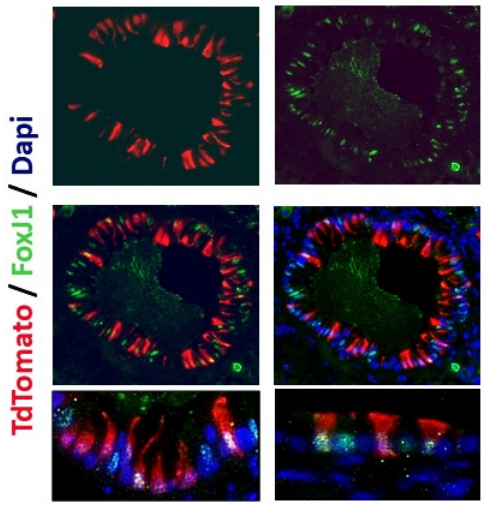
Delivery of LUNAR®-mRNA to Rodent Airways

Nebulization: Upper/Lower Airways



LUNAR® + Luciferase mRNA

LUNAR® Targets Mice Epithelial Airways (TdTomato), Including Ciliated Cells (TdTomato/FoxJ1)



Efficient delivery of LUNAR®-mRNA formulations in rodent airways

LUNAR®, an aerosolized delivery platform for lung

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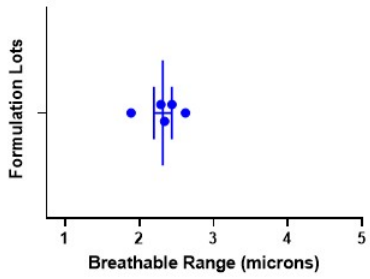
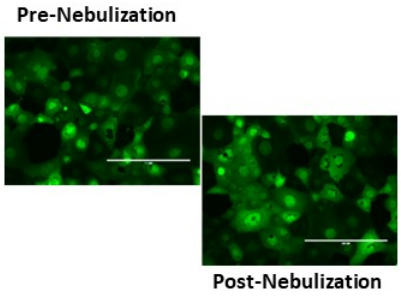
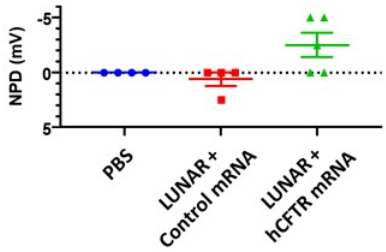
Aerosolized LUNAR® Particles are Breathable



Aerosolized LUNAR® -mRNA (EGFP) maintains activity



LUNAR®-mRNA (hCFTR) is biologically active *in vivo* (NPD, Mouse)



Aerosolized LUNAR® droplets are in the optimal breathable range (1-5 microns)
Aerosolized LUNAR® maintains activity as measured by EGFP protein expression & Nasal Potential Difference (NPD)

Delivery of LUNAR®-mRNA into Epithelial Airways in Ferret

EGFP conversion in tracheal epithelial airways observed in the ROSA26TG Ferret model

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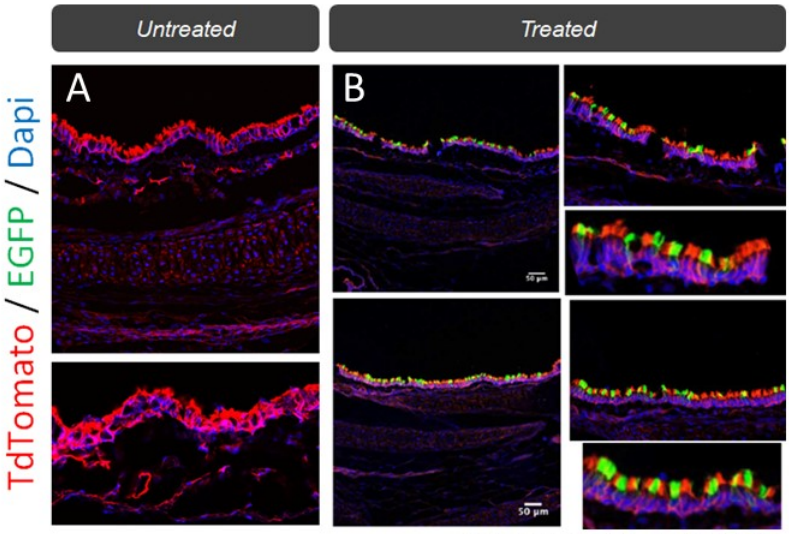
- Ferrets are an excellent species for modeling certain human lung diseases*
- Novel LUNAR® formulations of CRE mRNA were tested in a transgenic ROSA26TG ferret model
- Activation of EGFP expression indicates that LUNAR® targets epithelial airways
- Anticipated next steps: CTA Q4 2021



In collaboration with John Engelhardt

LUNAR® effectively delivered mRNA to the tracheal epithelial airways in a Ferret model

*Yu, M., Sun, X., Tyler, S.R. *et al.* Highly Efficient Transgenesis in Ferrets. *Sci Rep* **9**, 1971 (2019)

Moving Forward

Anticipated Near-Term Milestones and Cash Position

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ARCT-021 (LUNAR-COV19)	
Phase 3 Initiation	**Q2 2021**
Emergency Use Authorization (EUA)	**H2 2021**

ARCT-810 (LUNAR-OTC)	
Phase 2 Multiple Dose Study Clinical Trial Application	**Q2 2021**

ARCT-032 (LUNAR-CF)	
Clinical Trial Application (CTA)	**Q4 2021**

Cash Position
$463.0 Million as of December 31, 2020

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Management Team

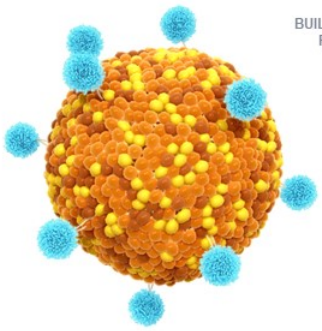
Joseph E. Payne, MSc
President & CEO

Pad Chivukula, Ph.D.
CSO & COO

Andrew Sassine, MBA
CFO

Steve Hughes, M.D.
Chief Medical Officer

Lance Kurata, J.D.
Chief Legal Officer



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Director of the Board

James Barlow, MA
Director of the Board

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Director of the Board

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Director of the Board, CFO

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DukeNUS Medical School

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University of Virginia School of Medicine

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UC San Diego

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VLP Therapeutics

Michael Hodges, M.D., BSc.

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amplyx

Drew Weissman, M.D., Ph.D.

Professor of Medicine at the Perelman School of Medicine

Perelman School of Medicine University of Pennsylvania

Appendix

LUNAR-COV19 Preclinical Seroconversion Data

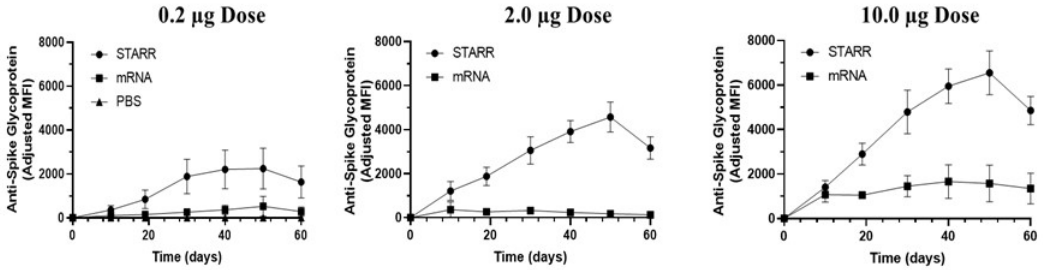
Seroconversion Rate (% of Animals) – STARR™ mRNA vs. Conventional mRNA

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

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

Preclinical Data: Anti-Spike Protein Levels Continue to Increase Up to 50 Days

Single Administration of LUNAR-COV19



- **Higher titers** (anti-SARS-CoV-2 Spike Glycoprotein IgG) elicited by STARR™ mRNA
- **Titers continue to increase up to 50 days** with STARR™ mRNA; plateau reached with conventional mRNA
- Dose dependent increase in IgG titers; Luminex bead assay, 1/2000 serum dilution

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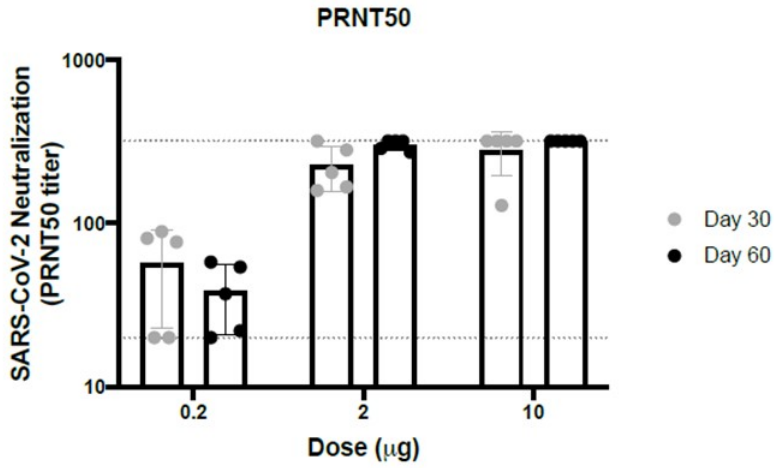
Preclinical Data: Neutralizing Antibodies Continue to Increase for 60 Days

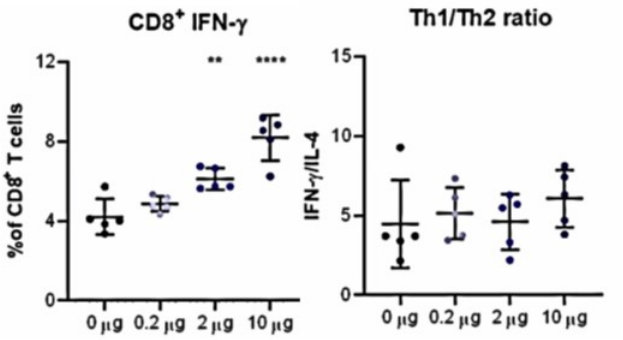
Single Administration (small dose, 2μg) of LUNAR-COV19



Virus neutralization assay: Serum dilutions are incubated with SARS-CoV-2 virus, then added to cells. The cells die forming plaques, which are counted. The serum dilution that reduces the number of plaques by 50% is recorded (PRNT50). Maximum serum dilution tested was 1/320

After single dose (2 μg) of LUNAR-COV19, neutralizing antibodies continue to increase for 60 days (>300 titer)

Preclinical Data: Arcturus Vaccine elicits a Balanced Cell Mediated Immune Response



RNA Dose (µg)	% IFN-γ+ CD8+ T Cells	CD4+ Th1/Th2 (IFN-γ/IL4)
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-γ positive CD8+ T-cells
- Th1 biased CD4+ response and stable Th1/Th2 ratio with increased RNA dose indicate balanced cell mediated immune response

Arcturus Safety Profile

External Validation

- Multiple strategic partnerships over many years confirms the positive potential 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)

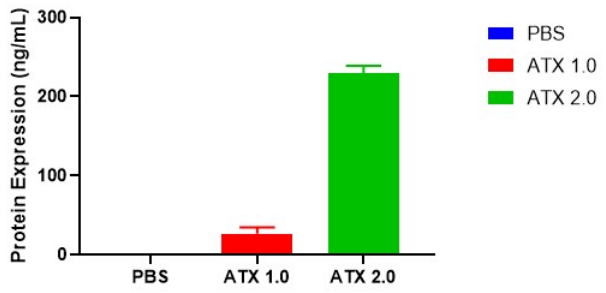
- ✓ **@ 15 mg/kg single dose of non-coding siRNA**
- ✓ **@ 3 mg/kg x eight (8) weekly doses of non-coding siRNA (total of 24 mg/kg over 2 months)**

Arcturus mRNA chemistry shows promising efficacy and tolerability data

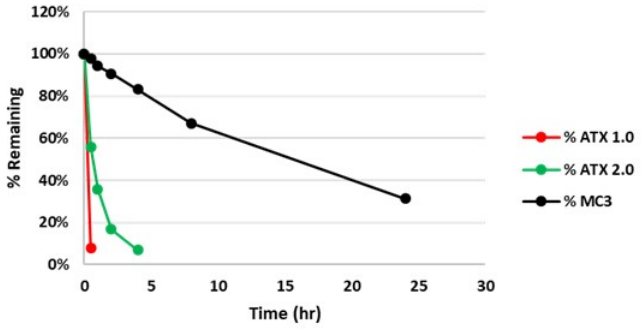
- Efficacy of OTC mRNA in mouse model @ 0.1 – 1 mg/kg

ATX Lipids are Effective and Biodegradable

Protein Expression (*in vivo*)



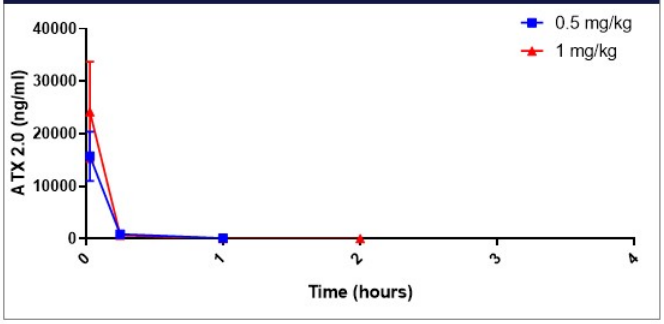
Esterase Catalyzed Degradation (*in vitro*)



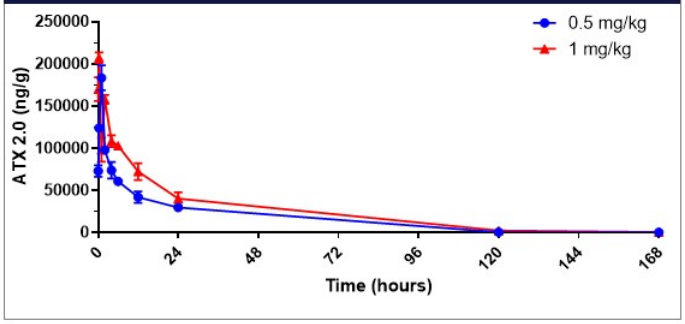
Next Generation ATX Lipids Retain Degradability & Improve Delivery Efficiency

ATX 2.0 Lipid is Biodegradable and Clears *in vivo*

Plasma



Liver



- **ATX Lipid (the major component in LUNAR® technology) is degraded *in vivo***
- **ATX 2.0 Lipid half-life in the liver is approximately 20 hours**

Key Existing Country Relationships

Singapore

Research Partnership with Duke-NUS Medical School

Financial Support from the Economic Development Board of Singapore

- $10 M Grant for Research and Preclinical Work
- $6.7 M Grant for Phase 1/2 Clinical Trial
- Executed Manufacturing Support Agreement for $46.6 Million Non-Recourse Loan
- Up to $175 Million in vaccine purchases

Israel

Supply Agreement with Israel Ministry of Health

- Announced August 18, 2020
- Up to $225 Million in vaccine purchases (with MOH election for 500,000 Initial Reserve Doses)
- $12.5 M Initial Reserve Payment was paid in Oct 2020

Drug Substance: mRNA Design

Arcturus' proprietary mRNA optimization platform

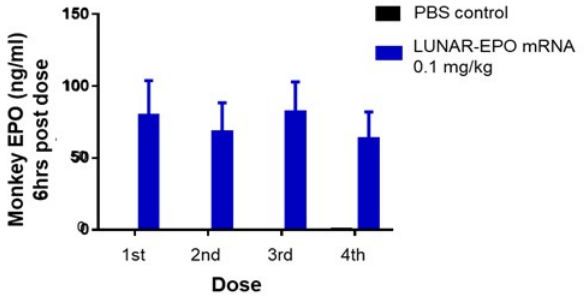
Optimize
mRNA sequence
Chemistry
Process

⇨

Improve
Protein Expression
Duration
Functional Activity

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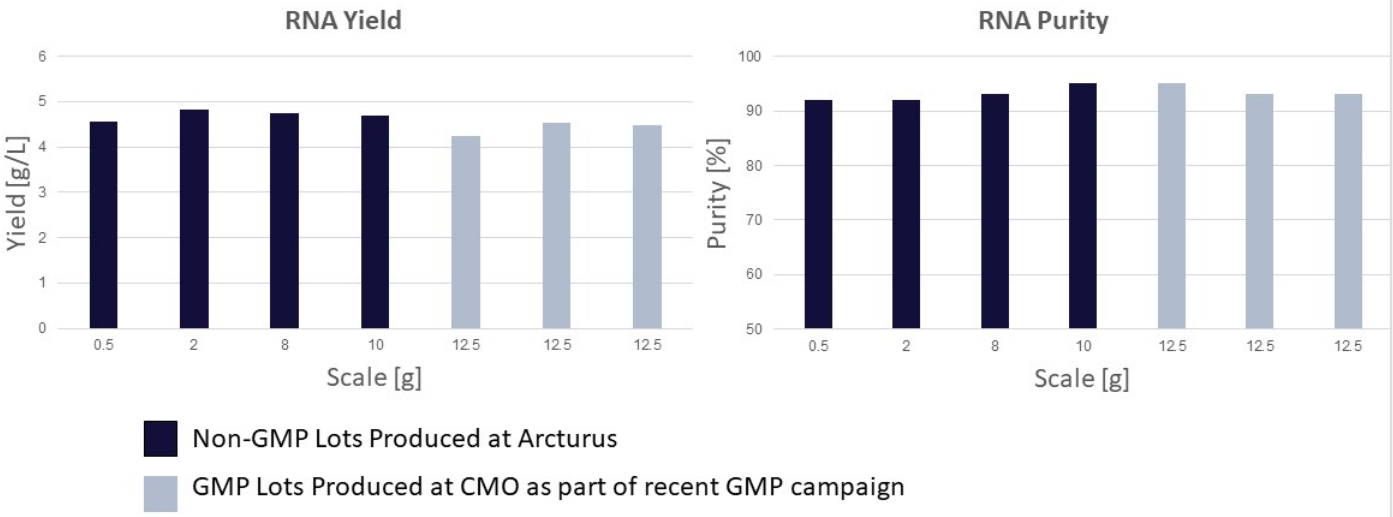
DNA Template Production → IVT and Capping Reaction → Purification Process → Buffer Exchange & Concentration

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

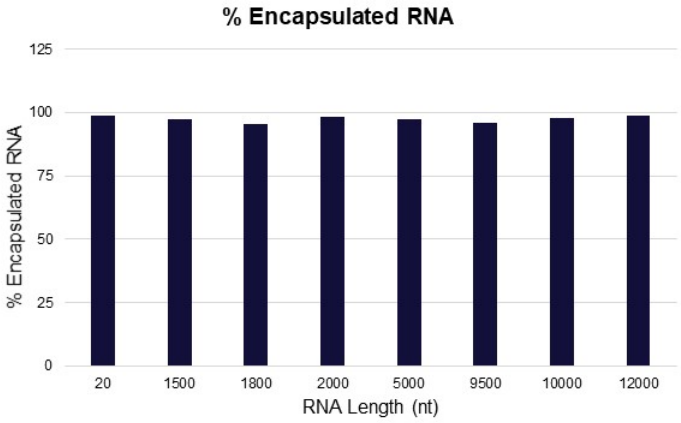
Drug Substance (mRNA) Manufacturing

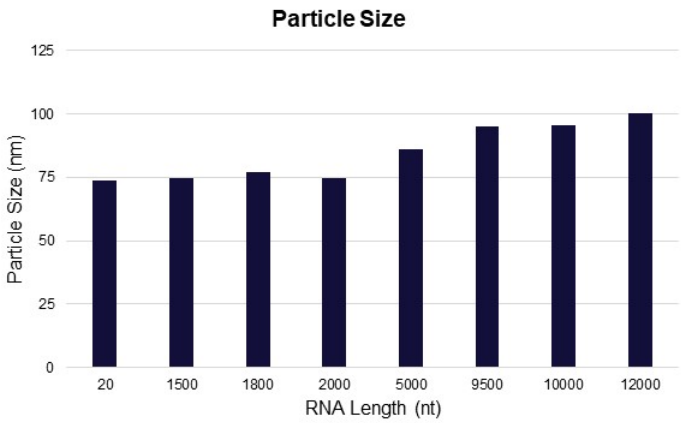


Three 12.5 g lots produced in recent GMP campaign are of equivalent quality and yield

LUNAR® Versatility

Compatible with RNA of Various size





LUNAR® Formulations Successfully Encapsulate RNA of Varying Sizes and Chemistries