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

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2021

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE TRANSITION PERIOD FROM TO**

Commission File Number 001-38942

ARCTURUS THERAPEUTICS HOLDINGS INC.

(Exact name of Registrant as specified in its Charter)

Delaware **(State or other jurisdiction of incorporation or organization)**	**32-0595345** **(I.R.S. Employer Identification No.)**
10628 Science Center Drive, Suite 250 **San Diego, California** **(Address of principal executive offices)**	**92121** **(Zip Code)**

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

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

Securities registered pursuant to Section 12(g) of the Act: **None**

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES ☒NO ☐

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. YES ☐ NO ☒

Indicate by check mark whether the Registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. YES ☒ NO ☐

Indicate by check mark whether the Registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the Registrant was required to submit such files). YES ☒ NO ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☒	Accelerated filer	☐
Non-accelerated filer	☐	Smaller reporting company	☐
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. ☐

Indicate by check mark whether the Registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. YES ☒ NO ☐

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES ☐ NO ☒

The aggregate market value of the common equity held by non-affiliates of the Registrant, based on the closing price of the common stock on The Nasdaq Stock Market on June 30, 2021 was $700.0 million.

As of February 23, 2022, the registrant had 26,375,002 shares of voting common stock outstanding.

Documents Incorporated by Reference: Certain portions of the registrant's definitive Proxy Statement for its 2022 Annual Meeting of Stockholders are incorporated by reference into Items 10, 11, 12, 13 and 14 of Part III of this Annual Report on Form 10-K.

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Special Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K, or this Annual Report, and the documents incorporated by reference herein may contain "forward-looking statements" within the meaning of the federal securities laws made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of various factors, including those set forth below under Part I, Item 1.A, "Risk Factors" in this Annual Report. Except as required by law, we assume no obligation to update these forward-looking statements, whether as a result of new information, future events or otherwise. These statements, which represent our current expectations or beliefs concerning various future events, may contain words such as "may," "will," "expect," "anticipate," "intend," "plan," "believe," "estimate" or other words indicating future results, though not all forward-looking statements necessarily contain these identifying words. Such statements may include, but are not limited to, statements concerning the following:

- the initiation, design, cost, timing, progress and results of, and our expected ability to undertake certain activities and accomplish certain goals with respect to, our research and development activities, preclinical studies and clinical trials;
- the potential safety, immunogenicity, efficacy or regulatory approval of any of our COVID-19 vaccine candidates as a booster or primary vaccination series;
- the potential effects and benefits of our technologies and product candidates on their own and in comparison to technologies, drugs or courses of treatment currently available or that may be developed by competitors.
- the likelihood that preclinical or clinical data will be predictive of future clinical results or efficacy or safety of a product candidate;
- the anticipated timing of enrollment, duration, milestones and announcements of results of clinical trials, and the submission of applications to conduct clinical trials;
- 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 or timing of any regulatory approval;
- the potential administration regimen or dosage, or ability to administer multiple doses of, any of our product candidates;
- our ability to obtain and maintain regulatory approval of our product candidates, and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;
- our plans to research, develop and commercialize our product candidates;
- our ability to successfully commercialize, and our expectations regarding future therapeutic and commercial potential with respect to, our product candidates;
- the rate and degree of market acceptance of our product candidates;
- the success of competing therapies that are or may become available;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets and address unmet medical needs;
- our ability to obtain and maintain intellectual property protection for our product candidates;
- interactions with regulatory authorities in the United States and foreign countries;
- our ability to attract and retain experienced and seasoned scientific and management professionals to lead the Company;
- the performance of our third-party suppliers and manufacturers, including our ability to scale-up manufacturing levels as necessary;

- our strategic alliance partners' election to pursue development and commercialization of any programs or product candidates that are subject to our collaboration and license agreements with such partners;
- our ability to attract collaborators with relevant development, regulatory and commercialization expertise;
- future activities to be undertaken by our strategic alliance partners, collaborators and other third parties;
- our ability to develop sales and marketing capabilities, whether alone or with potential future collaborators;
- our ability to avoid, settle or be victorious at costly litigation with shareholders, former executives or others, should these situations arise;
- our ability to obtain and deploy funding for our operations and to efficiently use our financial and other resources;
- our ability to continue as a going concern; and
- the accuracy of our estimates regarding future expenses, future revenues, capital requirements and need for additional financing.

Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results or performance to differ materially from those projected. These statements are only current predictions and are subject to known and unknown risks, uncertainties, and other factors that may cause our or our industry's actual results, levels of activity, performance or achievements to be materially different from those anticipated by the forward-looking statements. In addition, historic results of scientific research, preclinical and clinical trials do not guarantee that future research or trials will suggest the same conclusions, nor that historic results referred to herein will be interpreted the same in light of additional research, preclinical and clinical trial results. The forward-looking statements contained in this Annual Report are subject to risks and uncertainties, including those discussed in our other filings with the United States Securities and Exchange Commission, or the SEC. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance, or achievements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

References to Arcturus

In this Annual Report on Form 10-K, unless otherwise stated or the context otherwise indicates, references to the "Company," "Arcturus," "we," "our" and "us" mean Arcturus Therapeutics Holdings Inc. and its consolidated subsidiaries from and after the effective time of the Redomiciliation (as defined below) and, prior to that time, to our predecessor, Arcturus Therapeutics Ltd.

Trademarks and Tradenames

The Arcturus logo and other trademarks of Arcturus appearing in this Annual Report on Form 10-K are the property of Arcturus. All other trademarks, service marks and trade names in this Annual Report on Form 10-K are the property of their respective owners. Solely for convenience, trademarks and trade names referred to in this report may appear without the ® or ™ symbols.

Market Data and Forecasts

Unless otherwise indicated, information in this Annual Report on Form 10-K concerning economic conditions, our industry, and our markets, including our general expectations and competitive position, market

opportunity and market size, is based on a variety of sources, including information from independent industry analysts and publications, as well as our own estimates and research.

Our estimates are derived from industry and general publications, studies and surveys conducted by third-parties, as well as data from our own internal research. These publications, studies and surveys generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information, and we have not independently verified industry data from such third-party sources. While we believe our internal research is reliable and that our internal estimates are reasonable, such research has not been verified by any independent source and our internal estimates are based on our good faith beliefs as of the respective dates of such estimates. We are responsible for all of the disclosure in this Annual Report on Form 10-K.

PART I

Item 1. Business

Overview

We are a late-stage global clinical messenger RNA medicines company focused on the development of infectious disease vaccines and significant opportunities within liver and respiratory rare diseases. In addition to our messenger RNA ("mRNA") platform, our proprietary lipid nanoparticle ("LNP") delivery system, LUNAR®, has the potential to enable multiple nucleic acid medicines, and our proprietary self-amplifying mRNA technology (Self-Transcribing and Replicating RNA, or STARR™, technology) has the potential to provide longer-lasting RNA and sustained protein expression at lower dose levels.

We are leveraging our proprietary LUNAR platform and our nucleic acid technologies to develop and advance a pipeline of mRNA-based vaccines and therapeutics for infectious diseases and rare genetic disorders with significant unmet medical needs. We continue to expand this platform by adding new innovative delivery solutions that allow us to expand our discovery efforts. Our proprietary LUNAR technology is intended to address the major hurdles in RNA drug development, namely the effective and safe delivery of RNA therapeutics to disease-relevant target tissues. We believe the versatility of our platform to target multiple tissues, its compatibility with various nucleic acid therapeutics, and our expertise in developing scalable manufacturing processes can allow us to deliver on the next generation of nucleic acid medicines.

We were a preclinical company until June 2020, when we initiated our first Phase 1 study for our mRNA-based therapeutic candidate for ornithine transcarbamylase ("OTC"). With the launch of our COVID-19 vaccine program in March of 2020 and the subsequent initiation by our collaborator in September 2021 of the Phase 3 arm of the Phase 1/2/3 study for our COVID-19 vaccine in Vietnam, we progressed to a late-stage clinical company. In addition, we continued to progress our therapeutic pipeline and collaborations, and to expand and improve our platform technologies. We continue to focus our development efforts on our distinct, proprietary self-amplifying mRNA technology, which is a significant component of most of our product candidates, including our lead COVID 19 vaccine candidates. During 2021, we entered into a significant collaboration with Vinbiocare Biotechnology Joint Stock Company (Vinbiocare), a member company of the Vingroup Joint Stock Company (Vingroup) group of companies, whereby we provide technical expertise and support services to Vinbiocare to assist in the build out of a manufacturing facility in Vietnam. Together with Vinbiocare, we advanced ARCT-154, our investigational next generation, self-amplifying mRNA-based vaccine for COVID-19, into a Phase 1/2/3 study in Vietnam, which is being funded and sponsored by Vinbiocare. To date, over 18,000 subjects have been dosed in the Phase 1/2/3 study. With Vinbiocare, we have completed submission to the Ministry of Health in Vietnam with respect to an application for an Emergency Use Authorization for ARCT-154 (LUNAR-COV19). We are also continuing to engage with major health authorities to identify pathways to have our products approved for the COVID-19 booster market.

We expect to receive in the near term significant data from studies of our COVID-19 vaccine and regulatory guidance which will determine our course of action with respect to the development and commercialization of our vaccine candidate. Commercialization of ARCT-154 will require significant additional funds. We are considering additional partnering opportunities to assist in these efforts. We cannot be certain that we will identify a partner or enter into an acceptable arrangement. We will continue to evaluate our business opportunities in a surgical manner to maximize our ability to develop approved products while making most efficient use of our available resources.

In addition to progressing our self-amplifying mRNA-based vaccine candidates for COVID-19, we continued to advance our pipeline and collaborations, and to expand and improve our platform technologies.

As part of our vaccine franchise we are evaluating in preclinical studies the efficacy and safety of a seasonal influenza vaccine (our LUNAR-FLU mRNA vaccine candidate) and plan to select a STARR candidate in 2022.

Our rare disease programs have also continued to advance. In our ornithine transcarbamylase (OTC) deficiency program, with the overall gradual return to near-normal for clinical trials in the COVID-19 era, sites are finding more opportunities to screen potential participants for the Phase 1b study of ARCT-810 (LUNAR-OTC) and health authorities in the UK, Spain and Belgium have approved a Phase 2 multiple-dose study of ARCT-810 in OTC-deficient patients. We anticipate completion of dosing of the first cohort of the Phase 1b study by the first half of 2022. We anticipate screening to commence in our Phase 2 study in the second quarter of 2022 and to receive interim data in the second half of 2022. For the cystic fibrosis program, results from a series of nonclinical and preclinical studies have led us to an optimized formulation and nebulizer system that is being advanced into the

clinic. We expect to file an application for a First-in-Human study for ARCT-032 (LUNAR-CF), our mRNA therapeutic candidate for cystic fibrosis, in the third quarter of 2022.

We also continue to make significant progress with our manufacturing processes and operations. We have, with our manufacturing partners, manufactured current good manufacturing practice ("CGMP") batches yielding significant quantities of clinical trial materials for ARCT-810 (LUNAR-OTC) and ARCT-021, ARCT-154, and ARCT-165 (our LUNAR-COV19 vaccine candidates). We continue to make progress towards completion of a manufacturing facility in Hanoi, Vietnam, with our collaboration partner Vinbiocare, capable of producing 200 million doses per year, and technology transfer for commercial manufacturing is in process.

The Company was founded in 2013 as Arcturus Therapeutics, Inc., and we have maintained our principal executive offices in San Diego, California since that time. In November 2017, Alcobra Ltd., an Israeli limited company, merged with our company, changed its name to Arcturus Therapeutics Ltd. ("Arcturus Israel"), and commenced trading on Nasdaq under the symbol "ARCT." On June 17, 2019, we redomiciled to the United States (the "Redomiciliation") and changed our name to Arcturus Therapeutics Holdings Inc.

Nucleic Acid Medicines and an Introduction to Arcturus' Platform Technologies

Nucleic Acid Medicines

Nucleic acid medicines have the potential to treat diseases caused by genetic mutations, including diseases that cannot be treated by conventional drugs, such as small molecules and biologics. Some of these medicines function by providing the means for producing a deficient yet vital protein in vivo. Within a cell, DNA carries the blueprint, in the form of genes, from which all proteins necessary for life are encoded. Each gene's code is transcribed into a nucleic acid molecule called mRNA, which informs the cell's own machinery how to organize amino acid building blocks to make one or more proteins needed for normal biological function.

Nucleic acid therapeutics represent a significant advancement in targeted medicines and several of this class of therapeutics are being developed by public and private companies. The general objectives of these therapies include:

- to increase the amount of a functioning target protein by introducing a functional gene or mRNA that encodes for a protein that replaces a malfunctioning protein (mRNA therapy, CRISPR, gene therapy, replicon);
- to restore a functional protein by correcting its encoding mRNA sequence;
- to reduce the amount of a target protein in a patient by binding to and destroying the associated target mRNA (antisense and small interfering RNA ("siRNA")); and
- to introduce proteins from viruses or malfunctioning proteins in certain cancers to train the immune system to recognize and clear these proteins (nucleic acid vaccines).

Brief Introduction to our LUNAR® and STARR™ Technology Platforms

LUNAR®

A key challenge for nucleic acid medicines is the safe and effective delivery of the nucleic acid molecule. We have developed a novel lipid-mediated delivery system called LUNAR. LUNAR is a multi-component drug delivery system that incorporates a mixture of novel biodegradable lipids. Lipids are molecules that contain hydrocarbons and make up the building blocks of the structure and function of living cells. Examples of lipids include fats, oils, waxes, certain hormones and most of the cell membrane that is not made up of protein. LUNAR is designed to address technical challenges facing the delivery of nucleic acid medicines into cells. We continue to expand our library of proprietary lipids, with over 250 to date. Our preclinical studies have shown that formulations can be customized for the indication and target cell type of interest, and we have also demonstrated that our formulation process is scalable and reproducible. Our LUNAR platform is described in more detail below.

STARR™

Our STARR technology is our proprietary self-amplifying mRNA (or saRNA) technology platform. When combined with a delivery system, such as our lipid-mediated delivery system LUNAR, the STARR technology has the potential to generate a protective immune response or drive therapeutic protein expression to prevent against or treat a variety of diseases. Self-amplifying RNA-based prophylactic vaccines developed with STARR may trigger

rapid and prolonged antigen expression within host cells affording patients protective immunity against infectious pathogens. We believe the combination of LUNAR and STARR technology may result in lower dose requirements (accompanied by fewer side effects) due to superior immune response and sustained protein expression compared to non-self-amplifying RNA-based vaccines and will likely enable us to produce greater volumes of vaccine doses more quickly. With the full enrollment of the pivotal Phase 1/2/3 study in Vietnam of ARCT-154, our next generation, self-amplifying mRNA-based vaccine for COVID-19, we are a global leader in the clinical development of self-amplifying RNA-based vaccines. Our STARR platform is described in more detail below.

Arcturus' Target ID and Discovery Paradigm

Our Development Programs

Arcturus' Internal Programs Pipeline

Franchise	Candidate	Indication	Prevalence	Route of Administration	Cell Target	Stage	Anticipated Milestones
Vaccines	LUNAR-COV19 (ARCT-154)	COVID-19 (Targeting VOCs)	Global	Intramuscular	Myocytes & Dendritic Cells	EUA Submitted	EUA Approval in Vietnam Q1 2022
	LUNAR-COV19 (ARCT-021)	COVID-19	Global	Intramuscular	Myocytes & Dendritic Cells	Phase 2	Phase 3 Initiation by Global Entity
	LUNAR-FLU	Influenza	Global	Intramuscular	Myocytes & Dendritic Cells	Preclinical	STARR™ Candidate Selection 2022
Hepatic	LUNAR-OTC (ARCT-810)	Ornithine Transcarbamylase Deficiency	> 10,000	Intravenous	Periportal Hepatocytes	Phase 2	Interim Data H2 2022
Respiratory	LUNAR-CF (ARCT-032)	Cystic Fibrosis	85,000-100,000	Inhaled	Bronchial Epithelial Cells	Preclinical	CTA Filing Q3 2022

Vaccines to Prevent Infectious Disease

According to the National Foundation for Infectious Diseases, over 50,000 people die each year due to vaccine-preventable diseases in the United States alone. According to the Centers for Disease Control and Prevention, influenza and pneumonia cases alone approach this number of deaths each year. With the SARS-CoV-2 pandemic, more than 900,000 individuals in the US have died of COVID. Outbreaks of new infectious diseases, and the rise of variants to existing viruses, create demand for new and novel approaches to producing vaccines in a more cost effective and quicker manner.

The current pandemic has highlighted the efficacy, safety, and rapidity in which nucleic acid medicines can be used to vaccinate vulnerable populations. In 2020, we initiated the development of our first self-amplifying mRNA vaccine candidate, ARCT-021, to protect against COVID-19. We commenced a Phase 1/2 trial in 2020 and two Phase 2 trials in 2021, and we have completed dosing of ARCT-021 in the trials. In 2021, we began development of two next generation vaccine candidates designed to elicit an improved neutralizing antibody response to circulating strains of SARS-CoV-2. We have completed enrollment for the trial of one of these vaccines, ARCT-154, in a Phase 1/2/3 trial in Vietnam. We have also expanded our vaccine program to include seasonal influenza and plan to submit an application in 2023 to initiate a Phase 1 human clinical trial.

Our internal vaccine programs include our LUNAR-COV19 and LUNAR-FLU as further described below. The recent coronavirus pandemic has proven that mRNA vaccines can be highly efficacious and nimble, allowing for adjustments in antigenic sequences in record time.

COVID-19

Coronaviruses are a family of viruses that can lead to respiratory illness, including Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV). Coronaviruses are transmitted

between animals and people and can evolve into strains not previously identified in humans. On January 7, 2020, a novel coronavirus was identified as the cause of pneumonia cases in Wuhan City, Hubei Province of China. On February 11, 2020, the World Health Organization announced the official name for the disease caused by SARS-CoV-2 virus (2019 novel coronavirus outbreak) as coronavirus disease 2019, commonly abbreviated as COVID-19.

After the first cases of COVID-19 were identified, SARS-CoV-2 spread rapidly to all parts of the globe resulting in surges of infections as protective health measures have waxed and waned in a region-specific manner. The result of uncontrolled viral spread from approximately 400 million cases worldwide has led to the selection and spread of viral variants that are more contagious, pathogenic, or both. The WHO has announced a naming system for variants of the coronavirus that uses letters of the Greek alphabet. Under the new scheme, the B.1.1.7 variant first identified in the UK, commonly referred to as the Kent variant, is labelled “Alpha”. The B.1.351 variant identified in South Africa is “Beta”, the P.1 variant that originated in Brazil is “Gamma”, the B.1.617.2 variant first detected in India is “Delta”, and B.1.1.529 also first identified in South Africa is “Omicron”. These Greek letter labels will only be given to “variants of concern” and “variants of interest” as defined by the WHO. The current variants of concern (VOCs), specifically Delta and Omicron, have rapidly displaced previous circulating strains, spread more efficiently than previous strains, and are associated with increased risk of breakthrough infection among the vaccinated. Despite the expeditious EUA and rollout of vaccines in many counties, vaccine efficacy rates vary widely to currently circulating VOCs and relatively low percentages of people worldwide have received a booster dose important for protection against the currently dominant variant, Omicron.

Although current vaccines have been shown to protect against severe morbidity and mortality caused by current VOCs, breakthrough infections have been documented, nearly all from VOCs. As immunity wanes and booster doses become necessary, there is a critical need to enhance protection against VOCs to reduce the infection and disease burden for both the public and the health care systems across the globe. As such, Arcturus has developed the next generation of mRNA vaccines, which have demonstrated encouraging antibody data, including neutralizing antibodies against several variants of concern, including Omicron, boosting pre-existing immunity to SARS-CoV-2.

Our initial COVID-19 vaccine candidate, ARCT-021, developed in conjunction with Duke-NUS Medical School, is based on our STARR technology platform and has demonstrated antibody and cell-mediated immunogenicity and an excellent safety profile and through Phase 2 clinical trials. This vaccine was designed to promote immune responses to the spike protein of the SARS-CoV-2 virus, the critical part of the virus that allows infection to occur. In 2021, ARCT-021 was selected by a global entity for inclusion in a multinational Phase 3 vaccine trial. However, that trial has taken longer than anticipated to proceed with ARCT-021 and might not ever proceed with ARCT-021. Our clinical studies involving ARCT-021 have concluded dosing and we do not have current plans to sponsor additional development studies of ARCT-021 unless and until the global entity determines to proceed with ARCT-021 in the multinational Phase 3 vaccine trial.

Our two next generation vaccine candidates currently under development, ARCT-154 and ARCT-165, are based on the same platform as ARCT-021. We have modified the coding region to stabilize the spike protein and increase immune recognition to the receptor binding domain to improve neutralizing antibody titers and cross-protection to VOCs.

ARCT-154 is currently undergoing a fully enrolled pivotal Phase 1/2/3 study in Vietnam, sponsored and funded by Arcturus’ collaborator Vinbiocare. This vaccine is being evaluated as a primary vaccine administered in two 5-µg doses spaced 28 days apart. Evaluations include immunogenicity, efficacy and safety endpoints. A subset of participants is also receiving a third (booster) dose of ARCT-154. We have completed submission of regulatory documents for an emergency use authorization application in Vietnam.

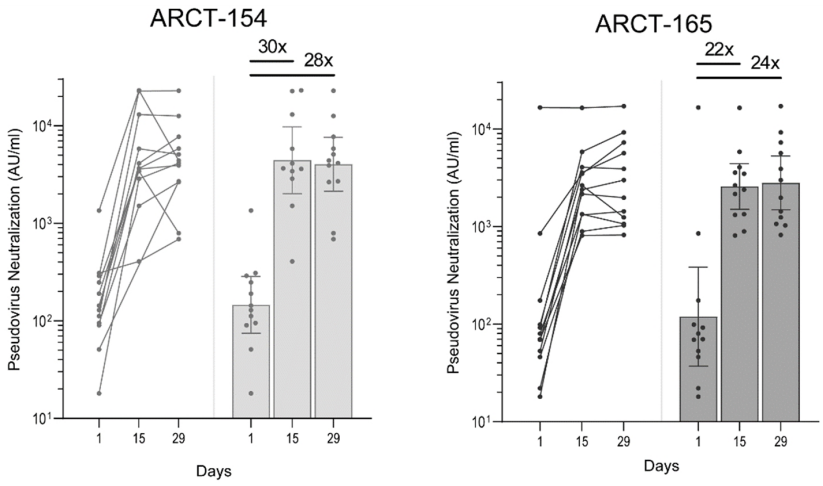
As the global market moves closer to booster administrations, Arcturus’ current next-generation vaccine candidates to COVID-19 are in trials as a booster dose of 5 µg dose, which is 6 to 10 times lower than currently-approved mRNA vaccine boosters. The purpose of a booster dose is two-fold: 1) to increase the durability of protective immunity to currently circulating strains of SARS-CoV-2 and 2) to protect against emerging VOCs that could cause breakthrough infections with currently authorized vaccines.

Two current clinical studies are exploring these next generation COVID-19 vaccines as a booster vaccination series. One of our Phase 2 studies of ARCT-021 (ARCT-021-04) has been modified to include booster vaccination with either our original or next generation COVID-19 vaccines six months after the second dose of the primary vaccine series with ARCT-021. ARCT-021-dosed participants were randomized 1:1:1:1 to receive 5 µg of one of

three Arcturus COVID-19 vaccine candidates or placebo. Participants originally receiving placebo were re-enrolled and randomized to one of three dosage groups receiving ARCT-021 as the primary vaccine series.

A second study, ARCT-165-01, evaluates ARCT-154 and ARCT-165 as boosters five months after a Comirnaty® primary vaccination series in a total of 24 subjects <60 years of age. We announced initial results from this study: increases in geometric mean neutralizing antibody concentrations of up to 30x pre-dose levels were sustained at 28 days post-boost, the last time point at which measurements were made in this ongoing study as of the announcement.

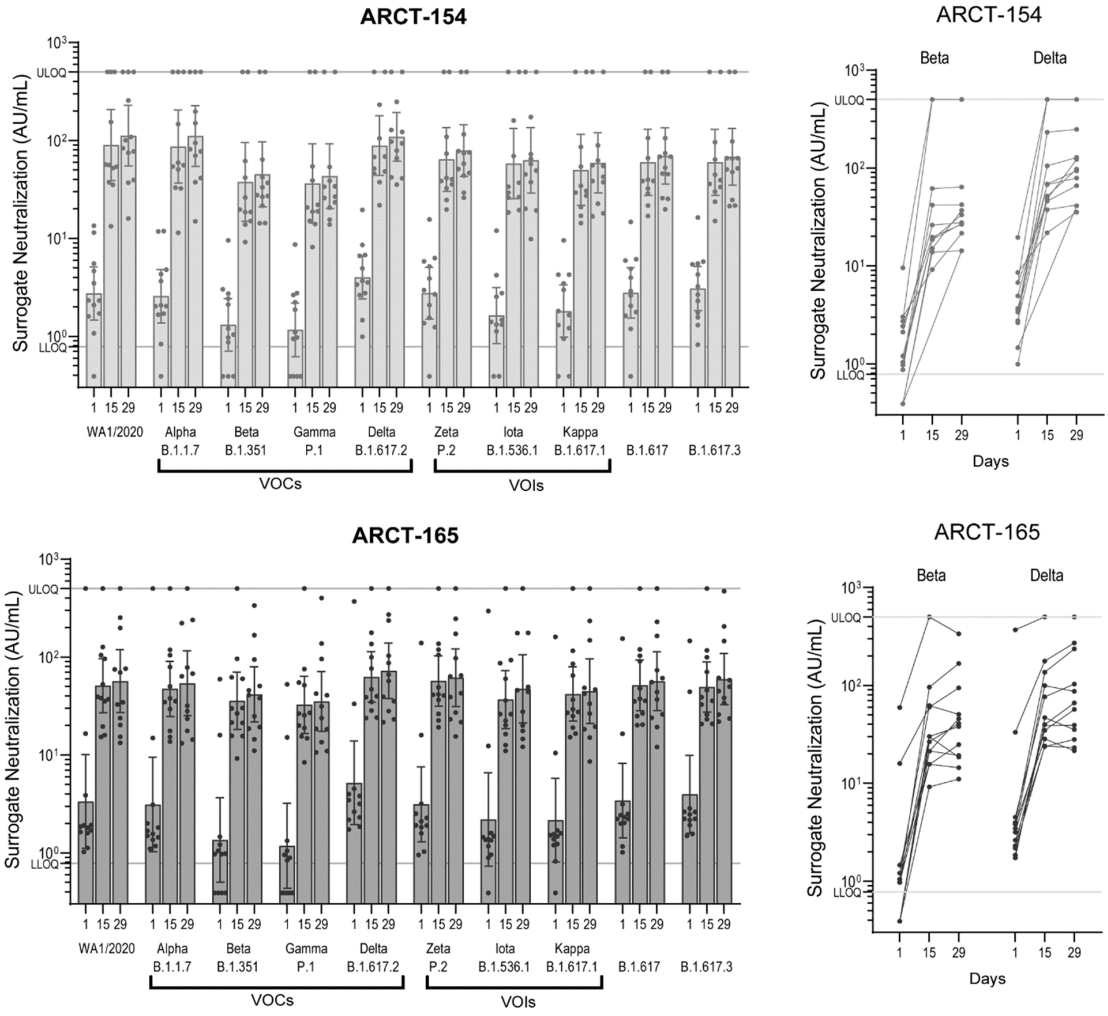
Pseudovirus (D614G variant) Microneutralization (MNT) Assay Results



Virus neutralization concentrations (arbitrary units per milliliter, AU/mL) for participants at Day 1 (prior to boosting), and Days 15 and 29 after boosting with ARCT-154 (left; n = first 8 out of 12 participants dosed) and ARCT-165 (right; n = first 9 out of 12 participants dosed). Within each panel, the left graphic shows values from individuals, and the right graphic shows the geometric means of neutralization concentrations with 95% confidence intervals. The multiples are geometric mean-fold rises (GMFR) of neutralization concentrations on Day 15 over Day 1 values. Geometric mean for Day 29 is not shown here, as data from only 4 participants are available for this time point.

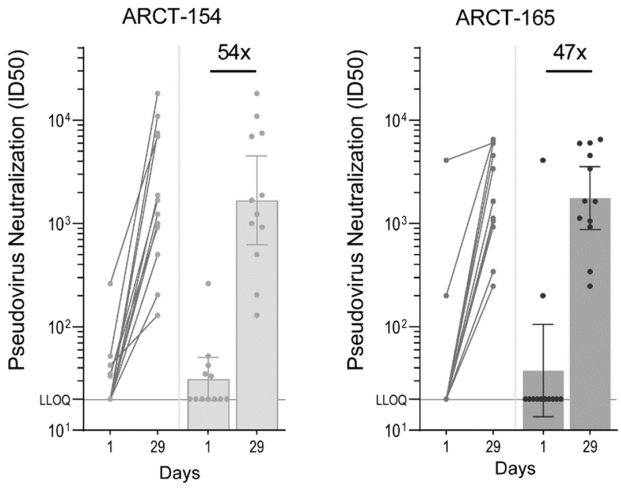
In addition, responses against a wide panel of VOC and “variants of interest” (as defined by WHO) were measured using an experimental surrogate virus neutralization assay. We found robust responses after a single booster dose across all variants tested. The different spike variants encoded by ARCT-154 and ARCT-165 may allow for broad coverage of current and emerging variants of concern and interest.

Surrogate Neutralization Assay to Variants of Concern and Interest



Top panels show geometric mean concentrations and 95% confidence intervals on Day 1 (prior to boosting), Day 15 and day 29 post-boost administration with ARCT-154 (left; n = 12 participants dosed). Line graphs on right show that responses are maintained through at least Day 29 for two variants, beta and delta. The bottom panels show the results for individual participants for the Beta and Delta variants on Day 1 (prior to boosting), and Days 15 and 29 post-boost administration with ARCT-165. Line graph on the right shows responses for each participant through Day 29. Abbreviations: VOC, variant of concern; VOI, variant of interest; ULOQ, upper limit of quantification; LLOQ, lower limit of quantification.

In a collaboration with Penny Moore, an expert in virology and immunology from the University of the Witwatersrand in Johannesburg, South Africa, we have assessed neutralizing antibody responses to Omicron, the latest WHO VOC that has displaced previous SARS-CoV-2 variants globally, using a lentiviral pseudovirus assay. We observed 54 and 47 fold increases in neutralizing titers after a single boost with ARCT-154 or ARCT-165, respectively.



Pseudovirus (Omicron variant, research use) MNT assay results. Antibody titers corresponding to 50% viral inhibition (ID50) in trial participants at Day 1 (prior to boosting) and Day 29 after boosting with ARCT-154 (left; n = 12/12) and ARCT-165 (right; n = 12/12). The bar graphs show the geometric means of neutralization titers, with 95% confidence intervals. Importantly, as this assay was performed at a different laboratory than our D614G assay and the readouts of this lentivurus based assay are different (ID50 vs AU/mL), the results from these two assays cannot be directly compared. The multiples are fold rises of neutralizing antibody titers on Day 29 over Day 1 values. ID¬50: half-maximal inhibitory dose; LLOQ: lower limit of quantitation.

LUNAR-FLU

Influenza is estimated to cause one billion infections globally every year and hundreds of thousands of deaths, especially in the elderly and individuals with underlying medical conditions. In many regions, influenza is seasonal, with infections peaking during November through April in the Northern Hemisphere and May through September in the Southern Hemisphere. Year-round surveillance by the World Health Organization in collaboration with various national health agencies informs WHO recommendations on the strains of influenza most likely to spread during the upcoming influenza season. National health agencies (such as the U.S. Food and Drug Administration (“FDA”)) then make the final decision of which strains should be covered by vaccines licensed in their country.

Our LUNAR-FLU program has the objective of producing a safe and effective seasonal vaccine candidate with significant advantages over the traditional egg-based inactivated quadrivalent vaccine. Inaccurate predictions of circulating influenza strains as well as mutations due to adaptation in egg-grown vaccines can substantially reduce efficacy on a year-to-year basis. We believe the ability of mRNA platforms to nimbly adapt to new viral strains should help improve efficacy. In addition, mRNA vaccines should not face the challenge from mutations common to egg-grown vaccines.

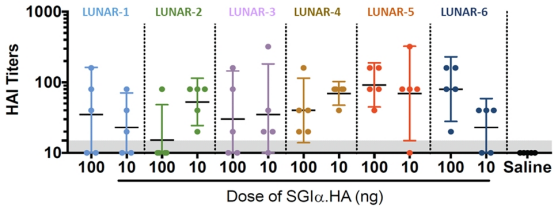
LUNAR-FLU is being designed to take advantage of our expertise in both LUNAR® lipid delivery systems, and mRNA technology to optimize the balance of acceptable reactogenicity and enhanced expression and immunogenicity of influenza antigens with the aspiration of creating a highly effective influenza vaccine for use in general and high risk populations.

Preliminary Data for Influenza

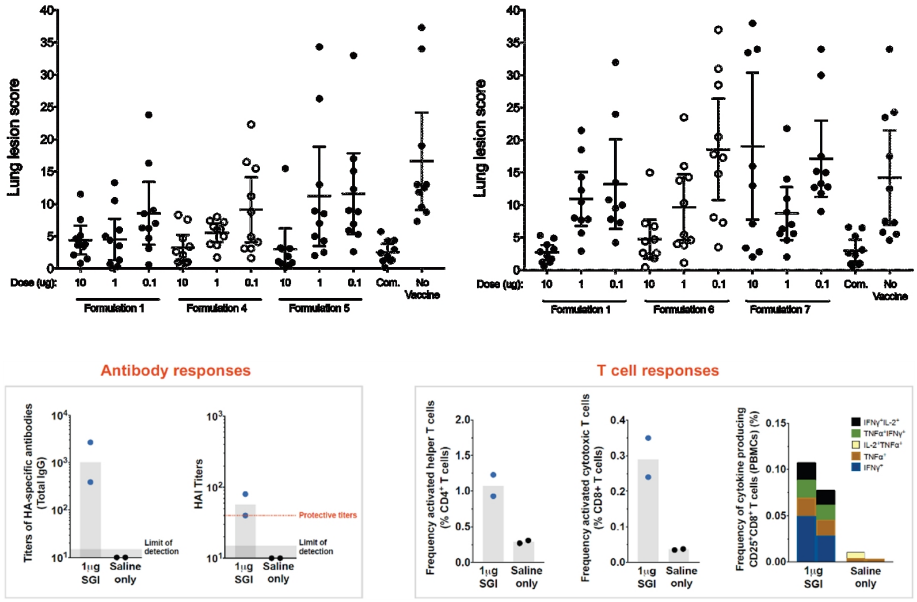
Murine Studies: An early version of our STARR platform encoding the hemagglutinin (HA) from a highly pathogenic strain of pandemic influenza (H5N1 A/Vietnam/1203/2004) formulated with several LUNAR lipids was

evaluated in mice. (HA is a glycoprotein that causes red blood cells to agglutinate or clump.) Mice primed, then boosted three weeks later, with this vaccine resulted in hemagglutinin inhibition (HAI) titers >40 two weeks after boost for two of our formulations.

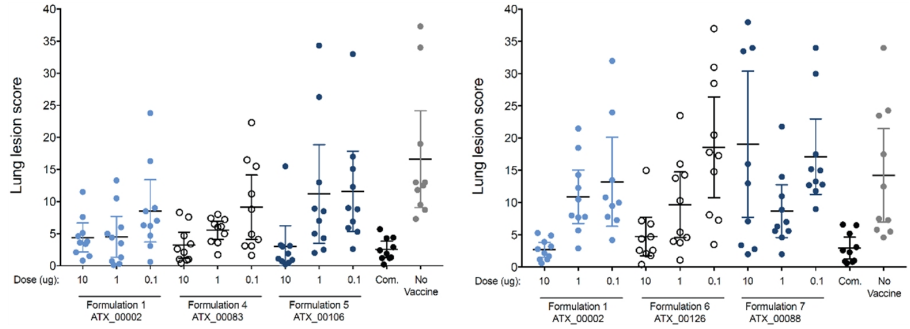
Large Animal Efficacy and Immunogenicity Studies: Experiments with a self-amplifying RNA (saRNA) encoding HA from H1N1 (A/California/07/2009) showed protection against challenge in pigs at even the 1µg dose. This protection was comparable to that elicited from an inactivated vaccine. Pigs primed, then boosted 28 days later, with our vaccine showed reduced lung lesions compared to protective responses from commercial vaccines (top). This same dose used in a small non-human primate study resulted in HAI >40 and the induction of robust polyfunctional CD8+ T cell responses (bottom).



Mice vaccinated with a previous version of STARR saRNA (in collaboration with SGI) resulted in HAI end titers >40 with several formulations of Arcturus's LNPs. Doses used are at 200-2000 times below the tolerable dose in mice.



Top: Efficacy studies performed in pigs challenged with H1N1 resulted in lung lesion scores comparable to those from a commercial inactivated vaccine. Bottom: NHPs vaccinated with saRNA encoding HA were resulted in protective HAI end titers (left) and robust polyfunctional T cell responses (middle, right)



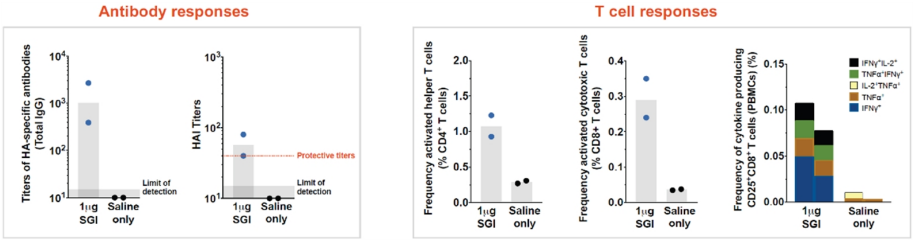
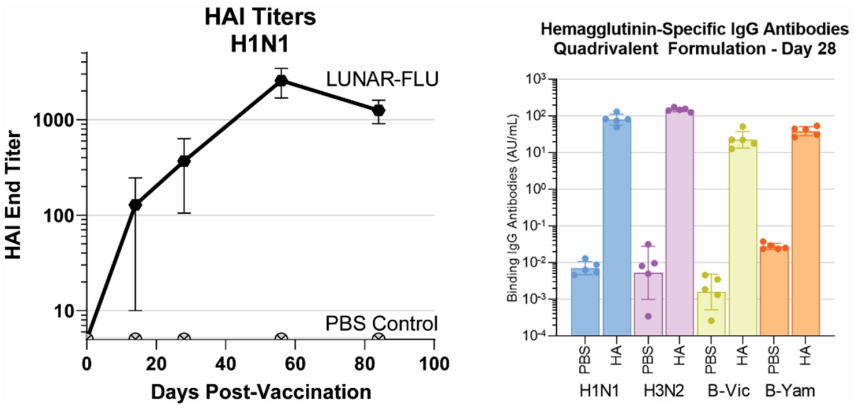


Figure TA2: Top: Efficacy studies performed in pigs challenged with H1N1 resulted in lung lesion scores comparable to those from a commercial inactivated vaccine. Bottom: NHPs vaccinated with samRNA encoding HA were resulted in protective HAI end titers (left) and robust polyfunctional T cell responses (middle, right)

Current studies use a next generation drug substance and formulation to elicit optimal influenza-specific immune responses and increase tolerability. The figure below shows that a monovalent LUNAR-FLU elicits robust HAI titers over time after a single intramuscular injection in mice. Additionally, a quadrivalent influenza vaccine also elicits robust HA-specific antibodies to all four strains present in the vaccine. Preclinical work is currently under way to optimize tolerability and immunogenicity to all four seasonal strains recommended by health authorities.



Left graph shows an increase of HAI titers after immunization of mice with monovalent LUNAR-FLU vaccine indicating robust titers maintained for at least three months post vaccination. Right graph shows robust increase in HA-binding IgG antibodies to all four seasonal influenza strains encoded by a quadrivalent LUNAR-FLU. HAI end titers over time are currently being assessed for this experiment. We plan to continue preclinical evaluations of LUNAR-FLU candidates in 2022 and to select a STARR candidate in 2022.

Rare Disease Medicines in Development

The Orphan Drug Act defines a rare disease as a disease or condition affecting fewer than 200,000 individuals in the United States. According to the National Institutes of Health (NIH), there are approximately 7,000 such diseases that, together, affect nearly 30 million people in the United States. The European Union defines a rare disease as having a prevalence of fewer than 5 in 10,000 people. Collectively, these disorders affect between 6% and 7% of the population in the developed world.

There is a pressing need for new medicines for rare diseases as few of the 7,000 known rare diseases have approved treatments. Biopharmaceutical industry researchers are making great progress in the fight against rare diseases as innovative science has opened new opportunities. More than 770 medicines have been approved by the FDA since the enactment of the Orphan Drug Act in 1983 and more than 800 medicines are currently in clinical development. Despite recent progress, there is still much more work to be done to overcome the scientific and operational challenges that arise.

We believe our technology provides an excellent platform to address genetically inherited rare diseases. Specifically, we are focusing on developing medicines to treat people with rare respiratory and liver diseases who currently have limited or no treatment options.

ARCT-810 (LUNAR-OTC)

The LUNAR-OTC development program addresses ornithine transcarbamylase (OTC) deficiency, a rare, life-threatening, genetic disease caused by mutations in the OTC gene that lead to dysfunctional or deficient OTC.

OTC deficiency is the most common of the urea cycle disorders, a group of inherited metabolic disorders that are associated with reduced ability to eliminate ammonia from the body. Ammonia is a toxic waste product produced from the breakdown of protein. OTC is a critical enzyme in the urea cycle, which takes place in liver cells and converts toxic ammonia to urea which is eliminated in the urine. In patients with OTC deficiency, ammonia accumulates in the blood and is toxic to the brain and liver. Symptoms of high ammonia levels include vomiting, headaches, coma and death. OTC deficiency can cause developmental problems, seizures and death in newborn babies. As an X-linked disorder, OTC deficiency tends to be more severe in males, though female carriers are often affected. Patients with less severe symptoms may present later in life, as adults. Currently no cure exists for OTC deficiency apart from liver transplant; however, this treatment comes with significant risk of complications such as organ rejection, and transplant recipients must take immunosuppressant drugs for the rest of their lives. Current standard of care for OTC deficiency is a low-protein diet, dietary supplements, and ammonia scavengers to try to prevent accumulation of ammonia. Life-threatening episodes of high ammonia levels can occur, requiring treatment with dialysis or hemofiltration. These treatments do not address the underlying cause of disease and there remains a high unmet need for an effective treatment.

Our LUNAR-OTC development candidate, ARCT-810, uses our LUNAR platform to deliver normal OTC mRNA into liver cells which then produce normal functioning OTC with possible disease-modifying effects. Our LUNAR-OTC approach has the potential to treat the underlying defect that causes the debilitating symptoms of OTC deficiency, rather than mitigating symptoms by sequestering ammonia. LUNAR-OTC has received orphan drug designation from the FDA for treatment of OTC deficiency. Worldwide development and commercialization rights to ARCT-810 are held entirely by Arcturus.

Preclinical data in OTC-deficient murine models have demonstrated that dosing of LUNAR-OTC results in robust OTC protein expression and activity, thereby improving ureagenesis, reducing plasma ammonia, and increasing survival.

The Phase 1, double-blind, placebo-controlled, single-dose, dose-escalation study of ARCT-810 in healthy volunteers, completed in November 2020, demonstrated favorable safety, tolerability and PK profiles.

A Phase 1b study in stable OTC-deficient patients is being conducted in the United States and Canada, and has commenced dosing. The trial plans to enroll approximately 12 patients and is designed to assess safety, tolerability and pharmacokinetics, as well as various exploratory biomarkers of drug activity. The COVID-19 pandemic has imposed numerous widespread challenges for the conduct of non-COVID clinical trials, including this study. These barriers include prolonged site closures, loss of key study personnel, prioritization of clinical care over research, and reluctance of patients to attend clinic visits. The pandemic has adversely affected startup activities for some sites and enrollment capabilities for others. Having worked closely with the investigators, the CRO and patient groups through this difficult period, we are now seeing a significant increase in patient identification and screening, such that completion of dosing of the first cohort is anticipated by the first half of 2022. Onboarding of new sites in addition to the current seven active sites in the United States is also expected to accelerate enrollment. A Phase 2 multiple-dose study of ARCT-810 in OTC-deficient patients is approved to proceed by the regulatory authorities in the UK, Belgium and Spain and clinical trial authorization applications are currently being prepared for other European countries. We anticipate that screening patients will begin in this study in the second quarter of 2022 and that we will have interim data from a subset of participants in the second half of 2022.

ARCT-032 (LUNAR-CF)

The LUNAR-CF program addresses cystic fibrosis lung disease, a progressive lung disease caused by mutations in the cystic fibrosis transmembrane conductance regulator (“CFTR”) gene. In 2020, we announced the selection and advancement of ARCT-032 as a development candidate for treatment of cystic fibrosis. ARCT-032 uses our LUNAR platform to deliver a codon-optimized human CFTR mRNA into airway epithelial cells. This

allows airway cells to produce functional human CFTR protein using their native translational machinery and protein trafficking pathways which could result in the treatment of the underlying defect that causes CF lung disease, regardless of patient's specific mutation. The Cystic Fibrosis Foundation ("CFF") has partnered with us to develop this therapy. ARCT-032 represents the first LUNAR-based mRNA therapeutic that will be delivered by the inhaled route, offering direct delivery to the affected airways with the possibility of restoring functional CFTR.

According to the NIH, cystic fibrosis is the most common rare disease in the world, with an estimated 30,000 diagnosed cases in the United States and 85,000 worldwide. Approximately 1,000 people are newly-diagnosed with cystic fibrosis each year. Cystic fibrosis is caused by one of more than 2,000 known mutations in the CFTR gene. These mutations have been grouped into several different classes based on the mechanism by which they cause reduction in the production and/or function of the CFTR protein. When CFTR is absent or defective, the airway surfaces become dehydrated and coated with a layer of thick mucus that clogs the airways, causing difficulty breathing and often resulting in chronic infections, exaggerated inflammation, structural airway damage, and other serious complications in lungs as well as in the pancreas and live. The median lifespan of CF patients in the United States is approximately 50 years, and the cause of death is usually lung-related.

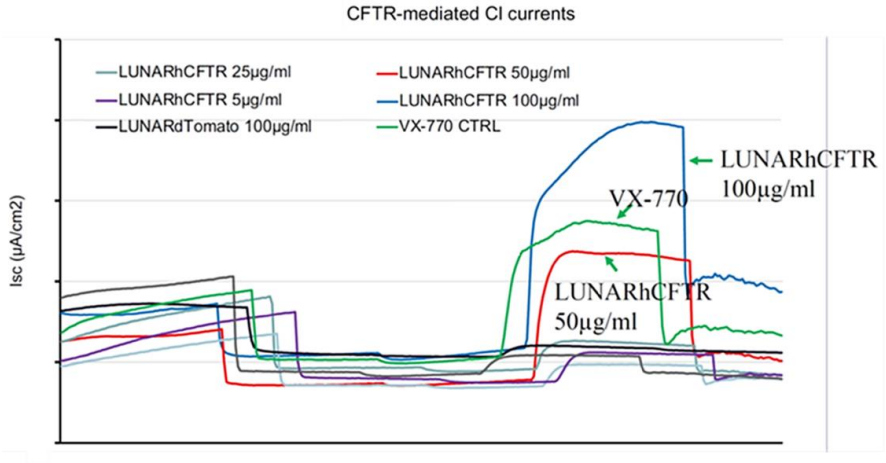
Current therapies for CF lung disease are, in effect, daily palliative treatments meant to treat existing lung disease and prevent the progression of the disease. These treatments include aerosolized mucolytics, antibiotics, and airway clearance techniques that are time-consuming and represent a significant treatment burden for people with CF. Many CF patients ultimately suffer from a critical decline in lung function and require lung transplants.

The FDA has approved several CFTR modulator therapies (Kalydeco®, Orkambi®, Symdeko®, and Trikafta®) that assist certain classes of mutant CFTR protein to reach the cell membrane and/or increase functional ion channel activity. The CFTR modulators, while effective in many patients, are mutation-specific and therefore are not effective in all persons with CF. Other treatments are required to target Class I mutations (no CFTR produced; approximately 10% of CF cases worldwide), and people who are intolerant or have poor response to CFTR modulator therapies. We are focusing ARCT-032 on these groups of patients, as they currently have the highest unmet needs for CF therapies.

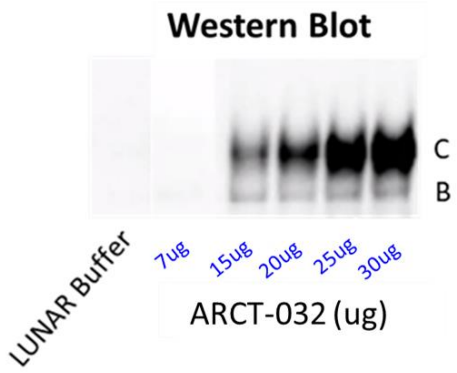
An extensive portfolio of nonclinical and preclinical studies have been performed to support the advancement of ARCT-032 towards the clinic. We presented comprehensive data that showcased the potential for ARCT-032 as a disease-modifying treatment at the North American Cystic Fibrosis Conferences in November 2021. The data presented demonstrated that (i) ARCT-032 remains stable after nebulization and retains functional activity, (ii) LUNAR protects mRNA in sputum isolated from CF patients, (iii) aerosolized LUNAR-mRNA delivers mRNA to airway epithelium across species, including rodents and non-rodents (ferrets, non-human primates), (iv) LUNAR-mRNA transduced several epithelial cell types (secretory, ionocytes, basal, ciliated) in ferret and human bronchial epithelial cells, and (v) ARCT-032 transduction demonstrated concentration-dependent expression of mature CFTR and restored chloride transport in CF human bronchial epithelial cells. In addition, we previously demonstrated restoration of CFTR activity in vivo (measured by nasal potential difference) in a CF mouse model with a Class I mutation. Cumulatively, these robust data demonstrate the proof of concept to validate ARCT-032 as a potential therapy to target the root cause of CF lung disease.

We continue to work closely with the CFF, which recently agreed to support studies with ARCT-032 in a CF ferret model to evaluate epithelial targeting and functional outcomes. These studies will be conducted in collaboration with investigators at the University of Iowa and the University of Alabama at Birmingham. We have also done several studies with the nebulizer system to optimize performance, which is important to ultimately reduce the burden on patients.

ARCT-032 generated high levels of mature (C-band) CFTR in CF human bronchial epithelial cells



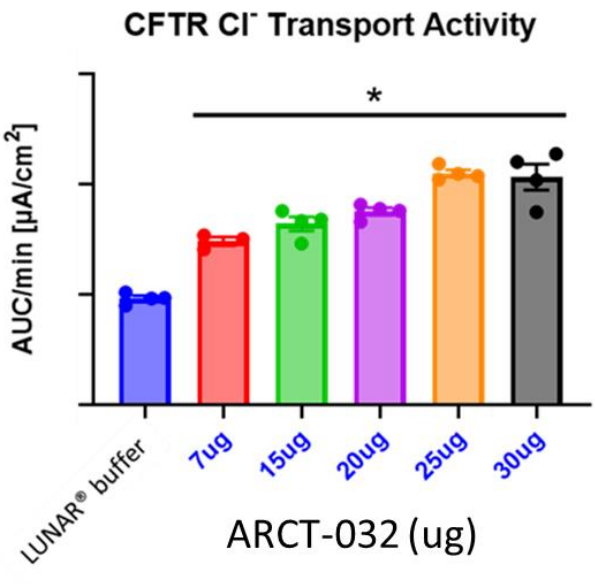
Ferret bronchial epithelial cells derived from a G551D CF ferret model were transfected in vitro with ARCT-032 (LUNARhCFTR). A dose dependent increase in chloride current was observed at the highest doses tested, comparable to the positive control VX770. The negative controls (LUNAR buffer and LUNAR-TdTomato) did not have any impact on chloride changes.



Human bronchial epithelial cells from a CF patient homozygous for F508del mutation were transfected in vitro with ARCT-032, resulting in dose-related increase in mature CFTR protein as seen in this Western blot as measured 72 hours after transfection. The increase in protein levels is specific to ARCT-032 treated samples and not present in the LUNAR buffer control.

LUNAR-CF restored CFTR activity in HBE cells carrying the F508del mutation

When CFTR is not present in the membrane or does not function properly, there is a deficit in the release of chloride and bicarbonate anions into the airways, and an associated increase of sodium uptake by the cells. The figure below demonstrates that ARCT-032 applied to human bronchial epithelial cells resulted in restored chloride transport.



Human bronchial epithelial cells from a CF patient homozygous for F508del mutation were transfected in vitro with ARCT-032. Chloride activity was significantly restored in a dose-like dependent manner at all doses tested (*, $p<0.05$).

Significant progress on the LUNAR-CF program was made in 2021, with identification of the development candidate that is now being evaluated in GLP toxicology studies. We anticipate filing a CTA for a first in human study in Q3 2022.

LUNAR Platform Program – Genome editing

Genome editing therapies are based on the ability to modify a specific DNA sequence in the human genome. All genome editing molecular tools can be programmed to target a DNA sequence of interest. Although the diversity of programmable gene editing tools is increasing, all of them are based on a DNA binding component (either a protein or, as in the case of CRISPR-clustered regularly interspaced short palindromic repeats, an RNA sequence) plus a DNA modifier component (a protein that can either make double strand breaks on the DNA (nuclease), single strand breaks (nickase), or make chemical modification in the DNA (base editors)). One of the main roadblocks to applying genome editing as a therapy to treat human disease is the delivery of the genome editing tool components into the cells either ex-vivo or in vivo, applying them directly into the human body and targeting the right organ.

The LUNAR-Genome editing program aims to leverage the ability of our LUNAR-mRNA technology to deliver any type of genome editing tools into target cells. Some of the genome editing tools are based on protein components working in pairs (TALEN-Transcriptional Activator-Like Effector Nuclease, ZFN-Zinc Finger Nuclease) or as a single protein (meganuclease), while other tools could have a combination of RNA and protein component (CRISPR). We have tested and found that we can deliver mRNAs coding for genome-editing proteins (TALEN) encapsulated in our LUNAR formulations, and also CRISPR technology, with the guide RNA together with the nuclease as an mRNA. Those mRNAs are translated into the proteins of interest that edit the targeted DNA sequence.

To test the efficacy of the different genome editing strategies as a proof of concept, we utilized target genes that encode proteins that are well known and can be detected in the plasma, which facilitated the readout of the experiments. For evaluation of the LUNAR TALEN mRNA strategy, we designed a TALEN pair targeting the mouse Pcsk9 gene which is involved in lipid metabolism. The Pcsk9 gene is expressed only in the mouse liver, and the PCSK9 protein is then secreted into the blood circulation PCSK9 protein binds and downregulates the LDL

receptors present in the hepatocytes cell membrane. Reduction of PSK9 protein levels, increases LDLR levels and its availability to take and reduce LDL-Cholesterol from the blood (Figure 1. Top drawing). A single intravenous dose of LUNAR-TALEN PCSK9 mRNA into wildtype mice lead to the production of the TALEN proteins in the mouse liver and to deletions in the targeted PCSK9 genomic DNA. Deletions in the PCSK9 genome sequence inactivated the PCSK9 gene and, consequently, there was a reduction of PCSK9 protein levels in the mouse plasma of the treated mice (Figure 1. Bottom Left). Examination of the PCSK9 targeted DNA sequence extracted from different organs did not show any DNA modifications except for the liver, which is explained by the liver specificity of this LUNAR formulation (Figure 1.Bottom Right).

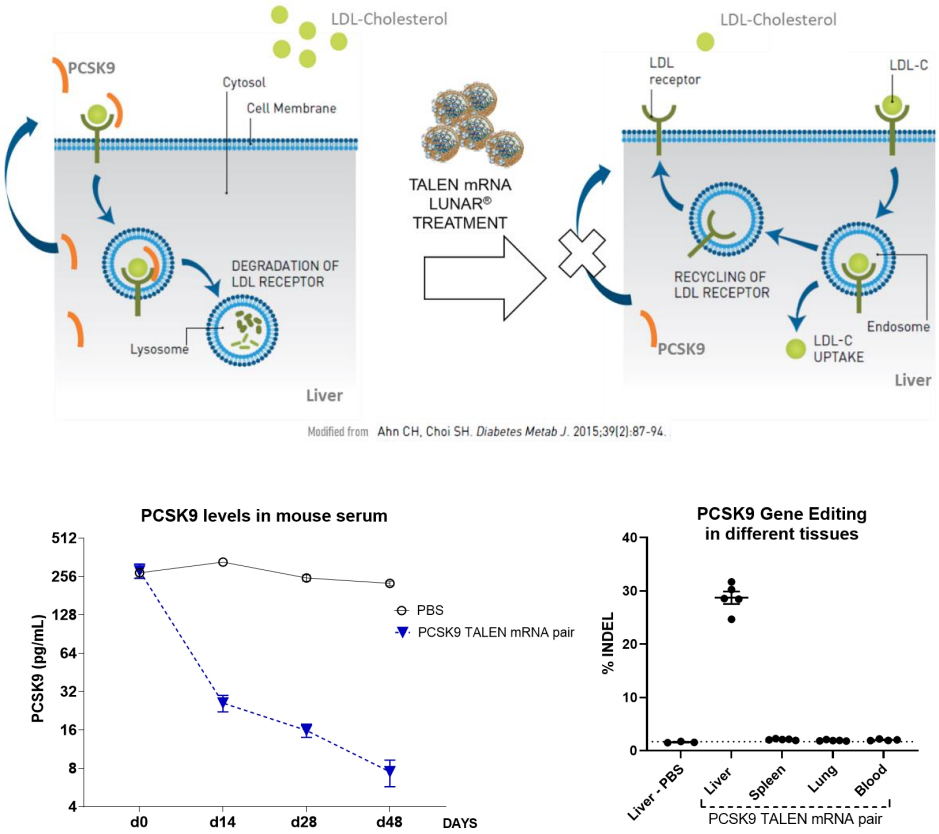


Figure1. Top: PCSK9 involvement in LDL-Cholesterol metabolism. PCSK inhibits LDL-Receptor activity and increases LDL-Cholesterol in circulation. Elimination of PCSK9 protein after editing the Pcsk9 target gene incrLeft: LUNAR-PCSK9 TALEN mRNA dosing of mice at time Day 0 irreversibly reduces levels of PCSK9 in circulation. Right: Genome editing evaluation by sequencing shows INDEL (insertion/deletions) only in DNA extracted from the liver but not from other tissues.

To test the ability to deliver CRISPR technology into the liver, we use a single guide RNA known to target the mouse Ttr gene. The transthyretin (TTR) protein is expressed only in the liver and is secreted into the blood circulation. In humans, mutations in the TTR gene can cause transthyretin amyloidosis. Mutations on the Ttr gene can alter the structure of the transthyretin protein impairing its normal function and leading to abnormal deposits of the TTR protein in different organs and tissues of the body, mainly in the nervous system and the heart. Reduction of the TTR production could stop the progression of the disease (Fig. 2 Top). LUNAR formulations containing a mouse TTR-specific single guide RNA (sgRNA) together with the Cas9 nuclease mRNA were injected intravenously into wildtype mice. After a single dose, there was a reduction in the amount of TTR protein detected in the mouse serum (Fig.2, Bottom left). This reduction of TTR protein correlated with the deletions detected in the

targeted TTR genomic DNA extracted from the liver of the LUNAR TTR-CRISPR mRNA treated mice (Fig.2, Bottom right).

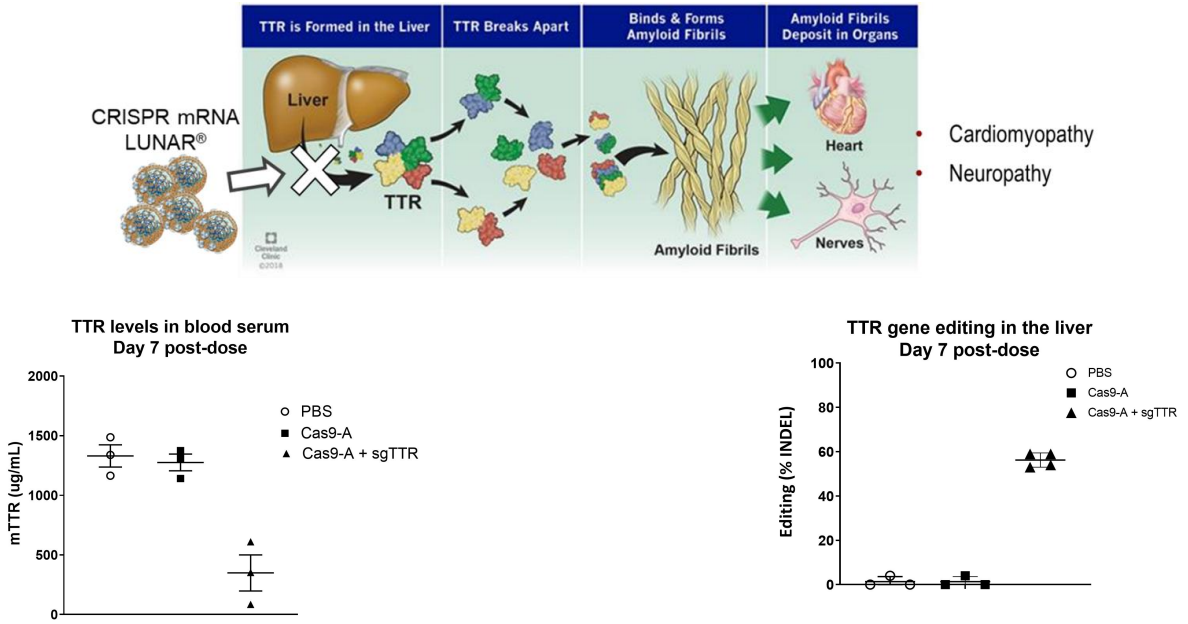


Figure 2. Top; TTR protein containing mutations aggregates and deposits forming amyloid fibers in different organs causing cardiomyopathies or neuropathies. Left: TTT levels in the serum was reduced in mice treated LUNAR-CRISPR Cas9 and sgRNA TTR mRNA but not in mice treated with LUNAR Cas9 mRNA. B. Genome editing evaluation by sequencing shows INDEL (insertion/deletions) only in the livers of the group of mice treated with LUNAR CRISPR Cas9 sgRNA TTR.

We are expanding our capabilities in the genome editing field by exploring the efficacy of LUNAR formulations carrying different genome editing tools in different organs in genomic DNA regions that could be of interest for potential therapies.

LUNAR Platform Program – Cancer vaccine (Immuno-oncology)

Our LUNAR Cancer Vaccine Program aims to develop an immunotherapy against a tumor via activated T-cells. The vaccine would encode an antigen that would be specifically presented by (or associated with) a tumor, such that the vaccination would elicit T cell responses that recognize and attack the tumor. We have applied our learnings from our more-advanced LUNAR-COVID-19 program to establish both STARR (self-amplifying) and conventional mRNA platforms for immuno-oncology therapy.

In a preclinical study, our proof of concept (POC) vaccine encoding AH1 antigen has demonstrated clear effectiveness in a syngeneic mouse model of a colorectal CT26 cell line. With intramuscular administration of the STARR vaccine (two doses of 10 ug), treatment with a checkpoint inhibitor (CPI), anti-PD1/PDL1, led to a drastic reduction of tumor growth in comparison to the CPI treatment by itself (Panel A). Moreover, the same level of efficacy was achieved with a single administration of a 0.2-ug dose of the STARR vaccine.

With various LUNAR® formulations, conventional mRNA vaccine expressing the AH1 antigen also demonstrated a robust T cell response (Panel B) and reduction of tumor growth with anti-PD1/PDL1 treatment in the syngeneic mouse model. We believe that these POC results from the two platforms premise the application to various cancer with flexibility in dosing regimens.

Our current effort focuses on the selection of neoantigens and other tumor-specific antigens encoded in the cancer vaccines. These antigens can be shared among patients, and therefore have more target patient populations. Additional advancements of LUNAR Cancer Vaccine program include the improvement of antigen cassette designs, STARR RNA elements, and immune modulator molecules, all of which significantly enhanced T cell responses.

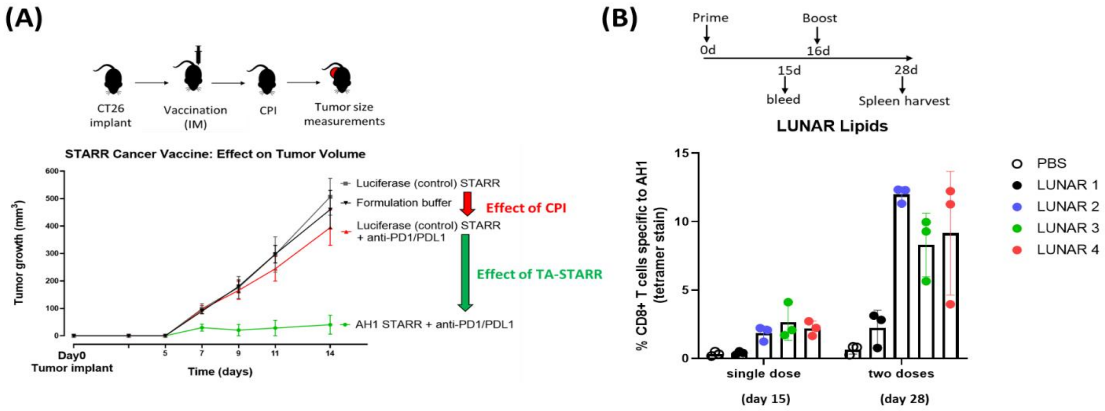


Figure. Antitumor activity and T cell response by Arcturus cancer vaccines. A. STARR vaccine expressing a tumor antigen led to a significant reduction of the tumor growth rate of a colorectal cancer cell line, CT26. **B.** T responses elicited by conventional mRNA cancer vaccine by various LUNAR® formulations.

Platform Technology Overview

Our LUNAR lipid-mediated delivery technology includes a diverse, growing library of over 250 proprietary lipids that we are rationally designing to be versatile, while maximizing efficacy and improving tolerability of a diverse selection of nucleic acids, refining the LPNs to target specific cell types, and determining the most favorable routes of administration. A key feature of our LUNAR lipids is their biodegradability, decreasing the undesired effects caused by lipid accumulation that are associated with tolerability issues present in other lipid-mediated RNA medicine delivery platforms. Our team continues to advance in the area of producing LUNAR lipid formulated nucleic acid product candidates in a scalable and highly reproducible manner, reducing the costs of goods for the therapies in our pipeline.

In addition to our LUNAR lipid-mediated delivery technology, we believe we have created innovative, proprietary advancements in producing mRNA medicines, including improvements that increase purity, scalability, efficiency in production times, and adaptability to different mRNA modification strategies. We strive to use these proprietary innovations to benefit each mRNA medicine in our pipeline.

We continue to invest in our LUNAR lipid-mediated delivery of mRNA (encoding CRISPR, TALEN, zinc finger proteins, and meganucleases), siRNA, DNA, microRNA, and antisense oligonucleotide technology platforms to improve their efficacy and safety profile, further expanding their applications. This investment has led to key innovations ensuring that our LUNAR formulated drug product candidates have optimal characteristics for therapeutic use, which we believe sets us apart from other nucleic acid therapeutics and lipid-mediated delivery platforms. As such, we consider ourselves a leader in the research and development of systemically administered mRNA therapeutics.

Key Attributes of Our LUNAR Lipid-Mediated Delivery Technology

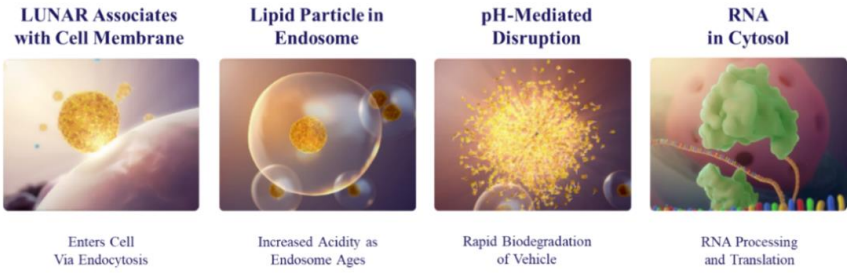
We have designed our LUNAR lipid-mediated delivery platform to address major challenges with nucleic acid medicine delivery, including transfection efficiency, adverse immune reactions and liver damage.

LUNAR formulations are a multi-component, lipid-mediated drug delivery system that utilizes our proprietary lipids, called ATX lipids. Each of our ATX lipids contains an amino head group and a biodegradable lipid backbone. The amino head group is a key chemical component of the ATX lipid, making it pH-sensitive and providing it distinct advantages as a component of our LUNAR formulation. At acidic pH, ATX lipids are positively charged,

facilitating interaction with the negatively charged nucleic acid, thereby enabling LUNAR particle formation. At physiological pH (e.g., pH 7.4), LUNAR formulations are neutrally charged, reducing the toxicity often seen with permanently positively-charged lipid-mediated delivery technology. Upon uptake into a cell by endocytosis (a process that forms a cellular structure called an endosome around the LUNAR formulated nucleic acid therapeutic), the amino head group again becomes positively charged, disrupting the endosome and the LUNAR particle, and releasing the nucleic acid therapeutic into the cell.

The disruption of the LUNAR particle also releases the components of the formulation into the cell, where the ATX lipid is degraded by enzymes in the cell allowing for the lipids to be cleared from the cell. We designed the ATX lipid to be rapidly biodegradable by engineering chemical structural components, called esters, into the ATX backbone that are sensitive to cellular enzymes, called esterases. This degradation prevents ATX lipids from accumulating inside the cell and causing toxicity.

Biodegradable, highly optimized for each cell type



LUNAR-platform development

The development of our LUNAR platform is focused on continuous innovation and advancement in the following areas:

- Design and incorporate novel ATX lipids and formulations to enrich our library of proprietary ATX lipids for target cell/tissue specificity, improved tolerability and translatability to larger species;
- Develop and improvise manufacturing processes for LUNAR formulations to ensure RNA encapsulation across compositions and scales;
- Develop stabilization strategies (e.g. lyophilized presentation) for LUNAR formulations to mitigate frozen storage; and
- Continually assess and improvise LUNAR screening funnel to enable rigorous selection of ATX lipids for various programs.

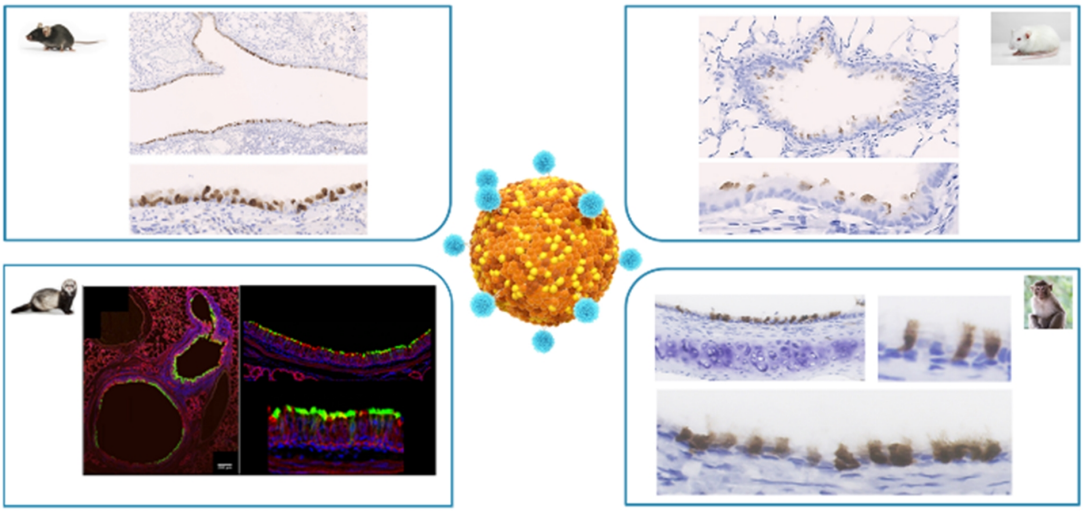
Through the above efforts, our versatile LUNAR platform continues to drive internal and partner programs.

Targeting Capabilities

As mentioned above, we have generated a growing library of more than 250 proprietary ATX lipids. ATX lipids are rationally designed to fit their respective applications and vary depending on the target cell type and route of administration. We perform extensive formulation screening for each nucleic acid therapeutic candidate to determine the optimal ATX lipid and LUNAR composition for the particular nucleic acid therapeutic candidate, the desired route of administration, and target cell type.

Lung

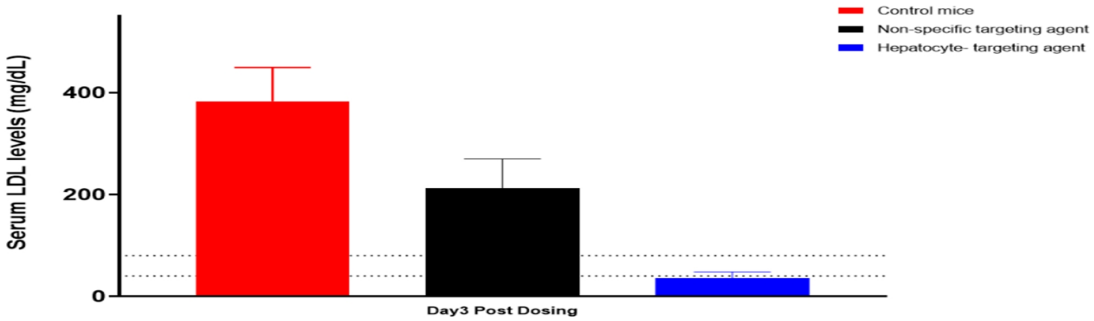
Aerosol capabilities have been developed for the Cystic Fibrosis program using Arcturus' proprietary lipid nanoparticle delivery platform, LUNAR®. Characterization and optimization of the aerosolized LUNAR® formulations in targeting airway epithelium have been achieved in rodent (mice, rat) and nonrodent models (ferret, NHP) as depicted in the image using a reporter mRNA encapsulated in LUNAR®. The validation attained for the inhaled LUNAR® platform in the Cystic Fibrosis program will serve as a "plug and play" approach to support other respiratory approaches where targeting airway epithelium is needed.



LUNAR® delivery to airways epithelium demonstrated in vivo across species (rodents, ferrets, NHPs)

Liver

As proof of concept for augmenting LUNAR liver-targeting capabilities, we are developing LUNAR formulations containing a propriety hepatocyte_targeting agent. Traditional lipid nanoparticle-mediated delivery to hepatocytes occurs via uptake by the low-density lipoprotein receptor (LDLR). We evaluated this targeting agent in an LDLR-deficient mouse model and found that only the LUNAR formulations with this targeting agent were able to deliver mRNA to the hepatocytes compared to LUNAR formulations that did not contain the targeting agent. Based on these promising data, we are expanding these platform development efforts.



LUNAR Safety (i.v. administration)

ARCT-810 Nonclinical Safety Profile

Arcturus has instituted a robust ATX lipid screening paradigm to ensure that we identify formulations with suitable properties for the intended drug's target product profile, whether is it a protein replacement therapy, a gene editing treatment, or a vaccine. Drug product safety is a key feature in that profile. An example of the outcome of these efforts is the safety profile that was obtained with ARCT-810, intended as a life-long treatment for OTC.

To support chronic administration of LUNAR-OTC (ARCT-810) in patients, nonclinical safety studies were conducted in nonhuman primates (NHPs). The findings of this study demonstrated that the nonclinical safety profile for ARCT-810 did not change from short-term dosing (3 bi-weekly infusions) to chronic administration (bi-weekly infusions for 9-months). ARCT-810 was well tolerated with no adverse findings at the highest dose administered, i.e., 1 mg/kg in the 9-month study.

	28 Day study	9 month (Chronic) study
No Observed Adverse Effect Level (NOAEL)	1 mg/kg	1 mg/kg
Complement activation	Transient non-adverse elevations	Transient non-adverse elevations, no change with chronic dosing
Cytokine activation	Transient non-adverse elevations	Transient non-adverse elevations, no change with chronic dosing
Liver enzyme function	Transient non-adverse elevations	Transient non-adverse elevations, no change with chronic dosing

With these promising results, and the advancement of ARCT-810 further into clinical development, additional nonclinical studies were performed to evaluate the safety profile to support dosing in pregnant patients. Pregnant mice were treated with ARCT-810 on gestation days 6 and 13 (a critical time for fetal development). No maternal toxicity or negative effects on the development for the fetus were observed. Both the maternal and fetal development NOAEL in this study was the highest dose tested, 5 mg/kg. The completed non-clinical safety studies support the continued clinical development of ARCT-810.

Our Proprietary mRNA and Protein Design Technology

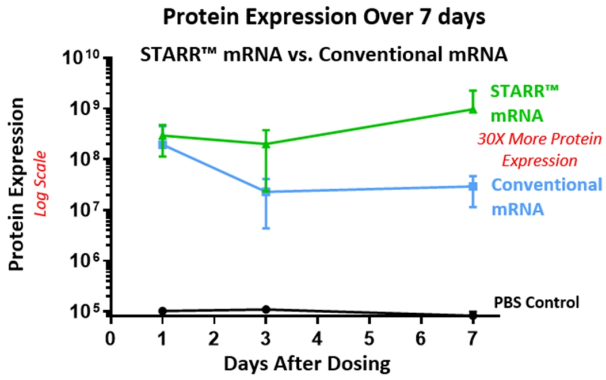
The mRNA programs in our pipeline are benefited by our in-house expertise in protein and mRNA design, which helps us address many of the known challenges that face the viability of mRNA therapeutics today. We have identified several design elements of mRNA compounds that provide improved translation (the process of making protein based on the instructions/codes in the mRNA) of our mRNA therapeutics, including untranslated regions derived from species that have not previously been combined with human mRNA sequences. This platform technology is applicable to many different human mRNA sequences that we are currently approaching in our discovery efforts. We are able to engineer human protein sequences to increase the half-life of the proteins produced by our mRNA therapies and can more efficiently direct specific types of proteins to certain cellular structures of interest. These innovations are broadly applicable to several programs that are part of our mRNA discovery efforts.

In addition to these platform technologies, we have developed a proprietary tool to aid our team in the efficient design and development of new mRNA drug candidates. Our mRNA Design Suite is a cloud-based software suite with a collection of proprietary bioinformatic algorithms aimed at achieving highly improved potency of a drug substance through optimization of mRNA sequences. The algorithms were developed in house through the integration of experimentally validated optimization processes. Through multi-layered in silico QC pipelines, mRNA Design Suite promptly generates high-quality and error-free sequences accompanied by various statistics. Additionally, mRNA Design Suite seamlessly interacts with our plasmid/mRNA production database to accelerate the process from mRNA design to gene synthesis, cloning, and mRNA production.

Our STARR mRNA Technology

Our vaccine platform is based on (1) our distinct and proprietary self-amplifying RNA (saRNA)platform (STARR) and (2) the LUNAR lipids that deliver the saRNA to cells. Our STARR platform includes proprietary algorithms that inform the design and optimization of saRNA to enhance expression of the applicable antigen while minimizing structures that might inhibit expression. The replicase, an RNA-dependent RNA polymerase, is encoded upstream of the antigen of interest and functions to amplify transcripts and increase the duration of antigen

expression compared to non-self-amplifying (conventional) mRNA. The enhanced expression leads to higher immunogenicity at lower doses than conventional mRNA vaccines in preclinical studies (Figure x).



We believe the combination of LUNAR and STARR technology could provide lower dose requirements due to superior immune response and sustained protein expression as compared to non-self-amplifying RNA-based vaccines. We believe this may enable us to simplify and increase the speed of vaccine production.

Supply and Manufacturing

Our supply and manufacturing strategy is focused on addressing the following considerations: a) multiple clinical pipeline candidates, b) commercial scale COVID vaccine products, c) regional and global product demand.

We have built a robust global manufacturing footprint with our partners, including Aldevron®, Catalent®, Recipharm, Polymun, Vingroup and ARCALIS. With such collaborations we have established an Integrated Global Supply Chain Network with our primary and secondary sourcing contract manufacturing organizations (CMOs) based in the USA, EU and Asia for producing critical raw materials, drug substance, and finished and packaged drug product. We expect our current manufacturing capabilities and completed, ongoing and planned global technology transfers to enable, by the end of 2022, a forecasted capacity of 200M doses per year of finished product for EUA, stockpiling and commercialization of COVID vaccine.

To date, we have manufactured and supplied gram quantities of drug substance, and scaled-up and validated our finished drug products (COVID Vaccine) through our CMOs for clinical studies, EUA, stockpiling and commercial readiness. We have developed, and continue to dedicate, resources to advance our sophisticated manufacturing know-how, including formulation of lipid nanoparticles, which improves manufacturing efficiency and capacity. Additionally, we are strategically exploring options to build our internal USA-based manufacturing capabilities for drug substance and finished drug product.

For the near future, we expect to continue to rely on third-party CMOs for the supply of drug substance and finished drug product for our current product candidates, including to support the launch of our first commercial products.

Our CMOs are compliant with cGMPs and other rules and regulations prescribed by foreign regulatory authorities. We believe we have established sufficient manufacturing capacity through our CMOs to meet our current internal research, development, and potential commercial needs, as well as our obligations under existing agreements with our partners. Additionally, we continue to evaluate relationships with additional suppliers to increase overall capacity and diversify our supply chain.

Revenue and Collaboration Arrangements and Other Material Agreements

In addition to our internal programs, we have a number of strategic alliances where we collaborate with other parties on discovery, development, manufacturing or other efforts based on our LUNAR lipid-mediated delivery system and our proprietary mRNA and protein design technologies. Among other collaboration arrangements,

- we are partnering with Vinbiocare, a Vingroup company, regarding a collaboration to establish a manufacturing facility in Vietnam for the manufacture of our COVID-19 vaccines, for sale and use in Vietnam;
- we are partnering with Janssen to develop nucleic acid-based therapeutic candidates for the treatment of Hepatitis B Virus (HBV);
- we are partnering with Ultragenyx to develop mRNA therapeutic candidates for rare disease targets;
- we are partnering with CureVac to develop mRNA therapeutic and vaccine candidates for various indications;
- we have received funding from the CFF to support our LUNAR-CF development program; and
- we are partnering with the Singapore Economic Development Board and Duke-NUS Medical School to develop a vaccine for the Coronavirus outbreak.

Vinbiocare

Beginning on July 29, 2021, we entered into a series of agreements with Vinbiocare, a member of Vingroup Joint Stock Company (collectively the "Vinbiocare Agreement"), whereby we will provide technical expertise and support services to Vinbiocare to assist in the build out of a manufacturing facility in Vietnam for the manufacture

of our investigational COVID-19 vaccines, for sale and use within Vietnam. The Technology License and Technical Support Agreement and Framework Drug Substance Supply Agreement became effective on July 30, 2021.

License Agreement

Within the Vinbiocare Agreement, we entered into a Technology License and Technical Support Agreement (the "License Agreement"). Pursuant to the terms of the License Agreement, Vinbiocare is, in consultation with us, building a manufacturing facility in Vietnam (the "Facility"), and we are providing to Vinbiocare access to proprietary technologies and processes for the manufacture of our investigational COVID-19 vaccines. We have granted to Vinbiocare an exclusive license to manufacture the vaccines in Vietnam at the Facility solely for distribution in Vietnam. The license and technology transfer applies to the manufacture of the final drug product of the vaccines, but not to the manufacture of mRNA drug substance or to the manufacture of our proprietary lipids used in our LUNAR ® delivery platform. Vinbiocare paid us a non-refundable upfront payment and is responsible for costs associated with the technology transfer. Vinbiocare is also required to pay us a royalty on each dose of the vaccines produced at the Facility. Other than the mRNA drug substance and our proprietary lipids, which will be sold by us to Vinbiocare, Vinbiocare is responsible for procuring all other raw materials and other inputs for the final vaccine drug product. Vinbiocare will be responsible for commercialization activities for the vaccines manufactured at the Facility for distribution within Vietnam.

Under the terms of the License Agreement, Vinbiocare is paying for our ongoing Phase 3 trial of ARCT-154 being conducted in Vietnam.

Unless earlier terminated, the License Agreement will expire on December 31, 2032. We have the right to terminate the License Agreement upon certain events, including if the Supply Agreement terminates, if Vinbiocare does not, on or prior to December 31, 2023, make a commercial dose of the vaccine in Vietnam following regulatory approval, and if we determine to cease manufacturing, development, or commercialization of the vaccines globally. Vinbiocare may terminate the License Agreement for convenience. Either party may terminate the License Agreement for uncured material breach of the other party. Vinbiocare's obligations under the License Agreement have been guaranteed by its parent company.

Supply Agreement

Within the Vinbiocare Agreement, we entered into a Framework Drug Substance Supply Agreement (the "Supply Agreement"), and pursuant to the terms of the Supply Agreement, we will supply, and Vinbiocare will pay for, mRNA drug substance for the manufacture of the vaccines under the License Agreement. The Supply Agreement will terminate contemporaneously with the License Agreement. In addition, each party may terminate the Supply Agreement for uncured material breach of the other party. Vinbiocare's obligations under the Supply Agreement have been guaranteed by its parent company.

Janssen

On October 18, 2017, we entered into a Research Collaboration and License Agreement with Janssen (the "Janssen Agreement") to collaborate on developing candidates for treating HBV with RNA therapeutics. Under the Janssen Agreement, Janssen and Arcturus will carry out their respective research obligations pursuant to agreed-upon joint research plans, and we may not engage in HBV-related research independent of the Janssen Agreement.

The Janssen Agreement provides that Janssen will develop the candidates licensed pursuant to the agreement, obtain certain regulatory approvals, and commercialize products containing the development candidates. Under the Janssen Agreement, both parties granted each other certain non-exclusive, royalty-free licenses to conduct the research covered by the agreement.

Under the Janssen Agreement, Janssen paid us an upfront fee and on a development candidate-by-development candidate basis, Janssen will pay us certain development milestone payments for each of the first two products to treat HBV as well as in each indication for which Janssen exercises its option to license certain therapeutics from us. In addition, on a research program-by-research program basis, Janssen will pay us sales milestone payments if they achieve certain annual net sales milestones in the first calendar year in which such milestones are achieved. Janssen will also pay option exercise fees within a certain range, with the precise amount depending on when Janssen exercises its license option. In addition, Janssen will pay royalties on annual net sales of licensed products up to a mid-single digit percentage, subject to (i) reduction on a country-by-country and licensed-product-by-licensed-product basis and (ii) certain events, such as expiration of program patents. In Q4 2021, Janssen

formally acknowledged that we had achieved the first milestone of showing “In Vivo Efficacy and Safety” of a nucleic acid therapeutic under investigation, and Janssen paid the corresponding milestone payment to us.

The Janssen Agreement will terminate when no further royalty payments on any licensed products are payable. Janssen may terminate the Janssen Agreement at any time on a licensed product-by-licensed product and country-by-country basis, or in its entirety, in each case upon 60 days’ written notice.

Ultragenyx

On October 26, 2015, we entered into a Research Collaboration and License Agreement with Ultragenyx, which was later amended in 2017, 2018 and during the second quarter of 2019 (as amended, the “Ultragenyx Agreement”). Ultragenyx initially selected two development targets, including Glycogen Storage Disease Type III, and the parties initially agreed to a list of eight additional reserved rare disease targets which Ultragenyx has an exclusive option to select for collaborative development. Under the Ultragenyx Agreement, we have granted Ultragenyx exclusivity (i) with respect to development targets, to the development and commercialization of products containing nucleic acid technology, and (ii) with respect to reserved targets, the development and commercialization of any product containing nucleic acid products or utilizing LUNAR lipid-mediated delivery technology.

Under the Ultragenyx Agreement, we have granted Ultragenyx a co-exclusive, royalty-free, sublicensable license of our technology for conducting collaborative development of development targets, compounds and products.

In connection with the execution of the Ultragenyx Agreement, Ultragenyx paid us an upfront fee and we are entitled to certain additional payments (i) for costs we incur in connection with our activities under agreed-upon collaborative development plans, and (ii) if Ultragenyx exercises its option to select additional reserved targets for collaborative development. For each development target for which Ultragenyx exercises this option, they will pay us a one-time option exercise fee, which will vary depending on the total number of development targets for which it has exercised such option. Ultragenyx will also pay us certain milestone payments with respect to clinical/regulatory development and commercialization, and will pay royalties as a percentage of net sales on a product-by-product and country-by-country basis.

On June 18, 2019, we expanded our collaboration with Ultragenyx and entered into a third amendment (the “Third Amendment”) to the Ultragenyx Agreement. Pursuant to the Third Amendment, the total number of targets was increased from 10 to 12, and we granted Ultragenyx exclusivity to development targets for four years at no additional cost. In connection with the Third Amendment, Ultragenyx purchased shares of our common stock and made a one-time upfront payment. Ultragenyx also received a two-year option to purchase additional shares of our common stock which they exercised in May of 2020.

On December 1, 2021, Ultragenyx announced that the first patient had been dosed in its Phase 1/2 study of UX053, an investigational messenger RNA therapy in development under the collaboration for the treatment of Glycogen Storage Disease Type III, and thus the first milestone under the collaboration agreement had been met.

CureVac

On January 1, 2018, we entered into a Development and Option Agreement with CureVac, which was amended on May 3, 2018 and later restated on September 28, 2018 (as amended and restated, the “Development and Option Agreement”). Under the terms of the Development and Option Agreement, CureVac and Arcturus agreed to conduct joint preclinical development programs and we granted CureVac a license to develop and commercialize certain products incorporating certain of our technology (the “Arcturus LMD Technology”) and CureVac technology. The products subject to the Development and Option Agreement relate to certain targets to be identified during the eight year term of the agreement. In consideration for the rights granted under the Development and Option Agreement, we received an upfront fee from CureVac.

Prior to expiration of the initial term of eight years (which was subsequently amended, as discussed below), the Development and Option Agreement also includes an option to extend the term on an annual basis for up to three years, subject to payment by CureVac to Arcturus of a non-refundable annual extension fee. The Development and Option Agreement includes potential milestone payments from CureVac for selected targets. Additionally, CureVac will pay royalties as a percentage of net sales on a product-by-product and country-by-country basis during the applicable royalty term in the low single-digit range.

On July 26, 2019, we entered into an amendment ("CureVac Amendment") to the Development and Option Agreement, pursuant to which the parties have agreed to shorten the time period during which CureVac may select potential targets to be licensed from eight years to four years, and to reduce the overall number of maximum targets that may be reserved and licensed.

Cystic Fibrosis Foundation Agreement

On May 16, 2017, pursuant to a Development Program Letter Agreement (the "CFF Agreement"), CFF agreed to award us funding for a development program to identify lead CFTR mRNA sequences and LUNAR formulations, demonstrate tolerability of LUNAR CFTR mRNA, and demonstrate translatability of aerosolized LUNAR (the "CFF Agreement"). The award includes a grant of rights to CFF know-how to assist us to research, develop, commercialize, make or otherwise exploit a product. If the award results in a successful commercialized product, we will pay CFF (i) royalties on sales of the product up to a maximum of a single-digit multiple of the total award amount actually paid to us by CFF, and (ii) thereafter, a single-digit percentage of annual net sales. Further, in the event of a license, sale or other transfer of the product or our development program technology (including a change of control transaction), we will pay CFF a percentage of such license, sale of transfer payments actually received by us or our shareholders (subject to a royalty cap).

On August 1, 2019, we amended the CFF Agreement. Pursuant to the amendment, (i) CFF will increase the amount it will award to advance LUNAR-CF, (ii) we will provide a certain amount of matching funds for remaining budgeted costs, (iii) the related disbursement schedule from CFF to us will be modified such that (a) a disbursement was made upon execution of the amendment, (b) an agreed upon amount will be disbursed to us within 30 days of the first day of each of January, April, July and October 2020, and (c) the last payment will be disbursed upon us invoicing CFF to meet good manufacturing practices and submitting an IND application. In January 2022, the parties signed an amendment for CFF to fund the development of a CF ferret model for application in the development of ARCT-032, our LUNAR-CF candidate.

Singapore Economic Development Board

On March 4, 2020, we were awarded a grant from the EDB to support the co-development of ARCT-021 with Duke-NUS Medical School. In exchange for the grant, we agreed to supply ARCT-021 to the EDB for use within Singapore and we retained the right to sell and market ARCT-021 outside of Singapore. We have agreed to pay Duke-NUS Medical School a low single digit royalty based on annual net sales of the vaccine in markets or jurisdictions outside of Singapore. On October 2, 2020, we were awarded an additional grant from the EDB to support the further development of ARCT-021.

On November 7, 2020, we entered into a Manufacturing Support Agreement (the "Support Agreement") with the EDB pursuant to which they agreed to make a term loan to us, subject to the satisfaction of customary deliveries, to further support the development of the LUNAR-COV19 vaccine candidate. On January 29, 2021, we elected to borrow the full amount available under the Support Agreement. Subject to certain exceptions, the Singapore Loan is a limited recourse loan that is intended to be repaid solely through a royalty payment on sales of the LUNAR-COV19 vaccine candidate, with a portion of the proceeds on all such vaccine sales being applied on a quarterly basis to prepay outstanding principal and interest under the Singapore Loan. However, all unpaid principal and interest under the Singapore Loan will be due and payable five years after draw date, if net sales of the LUNAR-COV19 vaccine exceed a certain minimum threshold during this five year period or we obtain clearance to sell the vaccine in specified jurisdictions. Unpaid principal and interest under the Singapore Loan will also become due and payable upon an event of default under the Support Agreement.

Other Collaboration Arrangements

On December 6, 2016, we entered into a research agreement with Millennium Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited ("Takeda"). Under the agreement, we conducted a joint research program with Takeda to discover siRNA medicines for the treatment of NASH. The program involved development of siRNA compounds formulated in LUNAR lipid-mediated delivery technology for in vivo studies. On March 8, 2019, we entered into a subsequent research agreement with Takeda, which was subsequently amended on June 3, 2019. Under this amended agreement, Takeda received a non-exclusive, worldwide, sublicensable license to certain of our technology, including mRNA compounds formulated for LUNAR lipid-mediated delivery technology, for the purpose of conducting a joint research program on additional targets in in-vitro and in-vivo models of liver diseases.

On August 20, 2021, we received notice from Providence Therapeutics, Inc. to terminate the Amended and Restated Joint Venture, Research Collaboration and License Agreement, dated as of July 15, 2018. No termination penalties were incurred by Providence or Arcturus in connection therewith.

Other Material Agreements

Alexion License Agreement

On February 17, 2021, we entered into an exclusive license agreement with Alexion Pharmaceuticals, Inc. ("Alexion") pursuant to which Alexion granted to Arcturus Therapeutics, Inc. an exclusive, worldwide license to exploit certain specified Alexion patents. In accordance with the terms of the license agreement, and in exchange for the license, we issued shares of our common stock to Alexion. The per share price was determined based on the volume weighted average closing price of our common stock on The NASDAQ Global Market for the thirty trading days ending on February 17, 2021.

Israel Supply Agreement

On August 17, 2020, our wholly owned subsidiary entered into a definitive Supply Agreement (the "Supply Agreement") with the Israeli MOH which provides for the supply of LUNAR-COV19 to the MOH. The MOH has elected to reserve an initial 500,000 doses of LUNAR-COV19 vaccinations. On October 14, 2020, we received a non-refundable first reserve payment from the MOH. This first reserve payment is associated with a specified clinical trial milestone and was provided after a data review process during which the MOH had access to material preclinical and clinical data for our LUNAR-COV19 vaccine candidate.

Intellectual Property

Our business success depends in part on our ability to obtain and maintain intellectual property protection for our proprietary technologies, inventions and know-how, and on our ability to operate without infringing on the proprietary rights of others. We strive to protect our intellectual property through a combination of patents, trademarks, trade secrets, licensing agreements and confidentiality agreements with employees, advisors, consultants and contractors.

We rely on continuing technological innovation to strengthen our proprietary position in the field of nucleic acid medicines. Therefore, we plan to continue to file patent applications in jurisdictions around the world as we discover and develop novel nucleic acid technology platforms and novel nucleic acid therapeutic candidates. We cannot guarantee that future applications will be issued.

Our Patent Portfolio

As of February 22, 2022, we own over 253 patents and pending patent applications including 38 U.S. patents, 33 pending U.S. patent applications, 12 pending international applications under Patent Cooperation Treaty ("PCT"), 82 foreign patents and 88 pending foreign patent applications. The claims of these patents and pending applications include compositions of matter, methods of use, manufacturing process and drug product formulations. These claims cover the use of our core platform technologies including the use of LUNAR and lipid components to deliver nucleic acids, the use of UNA oligomers for therapeutics and reagents, the use of LNA oligomers for therapeutics, specific nucleic acid modalities for treating disease, as well as our proprietary technology regarding the design, manufacture, and purification of nucleic acids for use in therapy. Claims also cover the composition of matter, formulation, and use of our therapeutic candidates to prevent and/or treat target diseases including OTC deficiency, CF, HBV, and COVID-19. Our issued patents are expected to expire between 2028 and 2042, without taking into account any possible patent term extensions.

Our patent portfolio includes the following patents and pending patent applications for LUNAR, UNA and the use of LNA in certain RNA medicines:

- LUNAR – As of February 28, 2022, we own 18 U.S. patents, 8 U.S. pending patent applications, 1 international patent application ("PCT"), 18 foreign granted patents, and 33 foreign pending patent applications covering the composition of matter, manufacture of lipid nanoparticles (including lyophilization), and use of our LUNAR technology for nucleic acid delivery and drug delivery.
- UNA, mRNA and LNA – As of February 28, 2022, we own 19 U.S. patents, 10 U.S. pending patent applications, 3 PCT applications, 63 foreign patents and 26 foreign pending patent applications

covering methods and uses of LNA, UNA oligomer and mRNA therapeutics, and compositions of UNA oligomers or mRNA to treat specific target diseases.

- STARR – In 2019, we began to develop our STARR platform which combines our proprietary LUNAR delivery systems with technologies that enable self-transcribing and self-amplifying RNA. As noted above, our robust LUNAR portfolio of over 60 patents and patent applications, provides protection for delivery vehicles that can enable specific and effective delivery of STARR drug substances. In particular, we own two pending U.S. nonprovisional patent applications and one pending PCT application directed to the manufacture of compositions that can comprise STARR RNA in a lipid delivery vehicle. In addition, we have begun to develop our STARR patent portfolio, and as of February 28, 2022, we own one pending U.S. provisional patent application, one pending U.S. nonprovisional application, and one pending PCT application directed to specially designed RNA constructs, specific nucleotide and amino acid sequences, and lipid formulations comprising the same under the STARR technology. We anticipate that further patents will be filed as we continue to innovate with respect to our STARR platform and that current applications covering these developments in our STARR platform, if granted, will last until 2041, not including any patent term extensions.

Patent Terms

The term of individual patents depends on the countries in which they are obtained. The patent term is 20 years from the earliest effective date of filing a non-provisional patent application in most of the countries in which we file.

Under the Drug Price Competition and Patent Term Restoration Act (also known as the Hatch-Waxman Act), U.S. patent holders can apply for a patent term extension to compensate for the patent term lost during the FDA regulatory review process. Patent extension is only available for patents covering FDA-approved drugs. The extension can be up to five years beyond the original expiration date of the patent and cannot extend a patent term for longer than 14 years from the date of product approval. Only one patent extension is granted per approved drug. Similar provisions may be available in foreign jurisdictions including Europe. We intend to apply for patent term extensions where possible.

Trade Secrets

We also rely on trade secrets to protect our product candidates. Our commercial success also depends in part on our non-infringement of the patents or proprietary rights of third parties. For a more comprehensive discussion of the risks related to our intellectual property, please see Item 1A “Risk Factors” – “Risks Related to Our Intellectual Property.”

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions.

Our success depends in part on our ability to:

- preserve trade secrets;
- prevent third parties from infringing upon our proprietary rights; and
- operate our business without infringing the patents and proprietary rights of third parties, both in the United States and internationally.

Certain Risks to Intellectual Property

We also protect our proprietary technology and processes, in part, by confidentiality and invention assignment agreements with our employees, consultants, scientific advisors and other contractors. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our employees, consultants, scientific advisors or other contractors use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Product Approval and Government Regulation

Government authorities in the United States, at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of products such as those we are developing. Any product candidate that we develop must be authorized or approved by the FDA before it may be legally marketed in the United States and by the appropriate foreign regulatory agency before it may be legally marketed in foreign countries.

U.S. Drug Development Process

In the United States, the development, manufacturing, and marketing of human drugs and vaccines are subject to extensive regulation. The FDA regulates drugs under the Federal Food, Drug and Cosmetic Act ("FDCA") and implementing regulations, and biological products, including vaccines, under provisions of the FDCA and the Public Health Service Act ("PHSA"). Drugs and vaccines are also subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to administrative or judicial civil or criminal sanctions. FDA sanctions could include refusal to approve pending applications, withdrawal of an approval, clinical hold, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, debarment, restitution, disgorgement or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us. The process required by the FDA before a drug or biological product may be marketed in the United States generally involves the following:

- completion of nonclinical laboratory tests, animal studies and formulation and stability studies according to good laboratory practices ("GLP") or other applicable regulations;
- submission to the FDA of an application for an IND, which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials according to the FDA's regulations commonly referred to as current good clinical practices ("GCPs") to establish the safety and efficacy of the proposed drug for its intended use;
- submission to the FDA of a new drug application ("NDA") or biologics license application ("BLA") for a new drug or biologics;
- satisfactory completion of FDA inspections of the manufacturing facility or facilities where the drug is produced to ensure compliance with the FDA's current good manufacturing practice standards ("cGMP"), to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- potential FDA audit of the nonclinical and clinical trial sites that generated the data in support of the NDA or BLA; and
- FDA review and approval of the NDA or BLA.

The lengthy process of seeking required approvals and the continuing need for compliance with applicable statutes and regulations require the expenditure of substantial resources and approvals are inherently uncertain.

Before testing any compounds with potential therapeutic value in humans, the drug candidate enters the preclinical study stage. Preclinical tests, also referred to as nonclinical studies, include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and pharmacological activity of the drug candidate. The conduct of the preclinical tests must comply with federal regulations and requirements including GLP. The sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA imposes a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a drug candidate at any time before or during clinical trials due to safety concerns or non-compliance.

Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that suspend or terminate such trial.

Clinical trials involve the administration of the drug candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's direct control. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety. Each protocol must be submitted to the FDA as part of the IND. Clinical trials must be conducted in accordance with the FDA's regulations comprising the good clinical practices requirements. Further, each clinical trial must be reviewed and approved by an independent institutional review board ("IRB") at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the form and content of the informed consent that must be signed by each clinical trial subject or his or her legal representative and provides oversight for the clinical trial until completed.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- Phase 1. The drug is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing may be conducted in patients;
- Phase 2. The drug is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule; and
- Phase 3. Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for product labeling. Generally, a well-controlled Phase 3 clinical trial is required by the FDA for approval of an NDA or BLA.

Post-approval clinical trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These clinical trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication.

Annual progress reports detailing the results of the clinical trials must be submitted to the FDA and written IND safety reports must be promptly submitted to the FDA and the investigators for serious and unexpected adverse events or any finding from tests in laboratory animals that suggests a significant risk for human subjects. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor or its data safety monitoring board may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

Concurrently with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

U.S. review and approval processes

The results of product development, nonclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA or BLA requesting approval to market the product. The

submission of an NDA or BLA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances.

In addition, under the Pediatric Research Equity Act ("PREA"), an NDA or BLA or supplement to an NDA or BLA must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan designation has been granted.

The FDA reviews all NDAs or BLAs submitted to determine if they are substantially complete before it accepts them for filing. If the FDA determines that an NDA or BLA is incomplete or is found to be non-navigable, the filing may be refused and must be re-submitted for consideration. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA or BLA. Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act ("PDUFA"), the FDA has 10 months from acceptance of filing in which to complete its initial review of a standard NDA or BLA and respond to the applicant, and six months from acceptance of filing for a priority NDA or BLA. The FDA does not always meet its PDUFA goal dates. The review process and the PDUFA goal date may be extended by three months or longer if the FDA requests or the NDA or BLA sponsor otherwise provides additional information or clarification regarding information already provided in the submission before the PDUFA goal date.

After the NDA or BLA submission is accepted for filing, the FDA reviews the NDA or BLA to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, strength, quality and purity. The FDA may refer applications for novel drug or biological products or drug or biological products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. During the drug approval process, the FDA also will determine whether a risk evaluation and mitigation strategy ("REMS") is necessary to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the NDA or BLA must submit a proposed REMS; the FDA will not approve the NDA or BLA without a REMS, if required.

Before approving an NDA or BLA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The FDA requires vaccine manufacturers to submit data supporting the demonstration of consistency between manufacturing batches, or lots. The FDA works together with vaccine manufacturers to develop a lot release protocol, the tests conducted on each lot of vaccine post-approval. Additionally, before approving an NDA or BLA, the FDA will typically inspect the sponsor and one or more clinical sites to assure that the clinical trials were conducted in compliance with IND study requirements. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable it will outline the deficiencies in the submission and often will request additional testing or information.

The NDA or BLA review and approval process is lengthy and difficult and the FDA may refuse to approve an NDA or BLA if the applicable regulatory criteria are not satisfied or may require additional clinical data or other data and information. Even if such data and information are submitted, the FDA may ultimately decide that the NDA or BLA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data. The FDA will issue a complete response letter if the agency decides not to approve the NDA or BLA. The complete response letter usually describes all of the specific deficiencies in the NDA or BLA identified by the FDA. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. Additionally, the complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete response letter is issued, the applicant may either submit new information, addressing all of the deficiencies identified in the letter, or withdraw the application.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the

product labeling. In addition, the FDA may require post marketing clinical trials, sometimes referred to as Phase 4 clinical trials, which are designed to further assess a product's safety and effectiveness and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized.

Emergency Use Authorization ("EUA")

The Commissioner of the FDA, under delegated authority from the Secretary of the U.S. Department of Health and Human Services ("DHHS") may, under certain circumstances, issue an authorization in the form of an EUA that would permit, for the duration of the declaration by the DHHS described below or until revocation of the EUA, the distribution and use of a drug or biological product that is not approved or licensed. Before an EUA may be issued, the Secretary must make a declaration that circumstances exist to justify the authorization based on one of the following grounds:

- a determination by the Secretary of the Department of Homeland Security that there is a domestic emergency, or a significant potential for a domestic emergency, involving a heightened risk of attack with a biological, chemical, radiological, or nuclear agent or agents;
- a determination by the Secretary of the Department of Defense that there is a military emergency, or a significant potential for a military emergency, involving a heightened risk to U.S. military forces of attack with a specified biological, chemical, radiological, or nuclear agent or agents or other agent or agents that may cause, or are otherwise associated with, an imminently life-threatening and specific risk to U.S. military forces;
- a determination by the Secretary of the DHHS that there is a public health emergency, or significant potential for such, that affects, or has the significant potential to affect, national security or the health and security of U.S. citizens living abroad, and that involves a biological, chemical, radiological, or nuclear agent or agents, or a disease or condition that may be attributable to such agent or agent; or
- the identification of a material threat pursuant to Section 319F-2 of the Public Health Service Act, authorizing the creation of the Strategic National Stockpile and security countermeasure procurements, sufficient to affect the national security or the health and security of United States citizens living abroad.

In order to be the subject of an EUA, the FDA Commissioner must conclude that, based on the totality of scientific evidence available, it is reasonable to believe that the product may be effective in diagnosing, treating or preventing a disease attributable to the agents described above, that the product's potential benefits outweigh its potential risks and that there is no adequate approved alternative to the product. The FDA has issued EUAs to companies for products intended for the prevention and treatment of COVID-19. The FDA expects EUA holders to work toward submission of an NDA, BLA, or other applicable approval.

In addition to the United States, other countries such as UK and Vietnam have a similar mechanism to facilitate the availability and use of medical countermeasures, including vaccines, during public health emergencies.

Post-approval requirements

Any drug or biological products for which we or our strategic alliance partners receive FDA approvals are subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the product, providing the FDA with updated safety and efficacy information, product sampling and distribution requirements, complying with certain electronic records and signature requirements and complying with FDA promotion and advertising requirements, which include, among others, standards for direct-to-consumer advertising, promoting drugs for uses or in patient populations that are not described in the drug's approved labeling (known as "off-label use"), industry-sponsored scientific and educational activities, and promotional activities involving the internet. Failure to comply with FDA requirements can have negative consequences, including adverse publicity, enforcement letters from the FDA, mandated corrective advertising or communications with doctors, and civil or criminal penalties. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such off-label uses.

Manufacturers of our product candidates are required to comply with applicable FDA manufacturing requirements contained in the FDA's cGMP regulations. cGMP regulations require among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation. Following approval, the FDA continues to monitor vaccine quality through real-time monitoring of lots by requiring manufacturers to submit certain information for each vaccine lot. Vaccine manufacturers may only distribute a lot

following release by the FDA. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved NDA or BLA, including withdrawal of the product from the market. In addition, changes to the manufacturing process require notice to or prior approval from the FDA before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

Regulation in Europe and Other Regions

In addition to regulations in the United States, we and our strategic alliance partners are subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our products.

Whether or not we or our collaborators obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like the IND prior to the commencement of human clinical trials. Once the CTA is approved in accordance with a country's requirements, clinical trial development may proceed.

The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials are conducted in accordance with GCPs and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

To obtain regulatory approval of an investigational drug or biological product under European Union regulatory systems, we or our strategic alliance partners must submit a marketing authorization application. The application in the United States is similar to that required in the European Union, with the exception of, among other things, country-specific document requirements.

For other countries outside of the European Union, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, again, the clinical trials are conducted in accordance with GCPs and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

Competition

Our Business in General

We believe that our scientific knowledge and expertise in nucleic acid-based therapies provide us with competitive advantages over the various companies and other entities that are attempting to develop similar treatments. However, we face competition at the technology platform and therapeutic indication levels from both large and small biopharmaceutical companies, academic institutions, governmental agencies and public and private research institutions. Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Our success will be based in part upon our ability to identify, develop and manage a portfolio of product candidates that are safer and more effective than competing products in the treatment of our targeted patients. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, are more convenient or are less expensive than any products we may develop.

We are aware of several other companies that are working to develop nucleic acid medicines, including gene therapy, gene editing, mRNA, siRNA, and antisense therapeutics. Many of these companies, such as the newly formed Genevant, are also developing nucleic acid delivery platforms which compete with LUNAR technology.

Below we have included what we believe to be the competitive landscape for certain of the medicines that we currently have in development.

Vaccine Franchise

LUNAR-COV19 Vaccines (ARCT-021, ARCT-154, ARCT-165)

Our vaccine franchise is based on our self-amplifying and self-replicating STARR® technology platform and our lipid nanoparticle delivery platform called LUNAR®. This franchise has advanced into late stage clinical development including ARCT-154 in Phase 3 clinical development and ARCT-165 and ARCT-021 in phase 2 clinical development. We consider the following companies with approved or late stage clinical development vaccines as some of our competitors or future competitors to Arcturus' COVID-19 vaccine franchise: Pfizer, BioNTech, Moderna, Janssen, AstraZeneca, Novavax, Sinovac and the Russian Gamaleya National Research Centre for Epidemiology and Microbiology. Dozens of other companies are also developing COVID-19 vaccines. These companies generally use conventional mRNA (not self-amplifying) and egg-based vaccine technology as the basis for their COVID-19 vaccines, and we are not aware of any saRNA COVID-19 pipeline that has advanced in clinical studies as far as ours.

LUNAR-FLU Vaccine

We consider the following companies as some of the competitors or future competitors to LUNAR-Flu: Pfizer, BioNTech, Moderna, Sanofi, and Seqirus. The flu industry is shifting to using mRNA based platforms in addition to traditional (egg-based) technologies.

Liver Franchise ARCT-810 (LUNAR-OTC)

Our liver franchise has advanced into mid-stage clinical development with ARCT-810 in phase 2 clincial development. Potential competitors include, but are not limited to, Ultragenyx which is advancing a gene therapy program for OTC in clinical development.

Lung Franchise: ARCT-032 (LUNAR-CF)

The lead candidate of our lung franchise is ARCT-032, which is an mRNA therapeutic candidate for cystic fibrosis based on our proprietary drug substance mRNA technology platform and our LUNAR lipid nanoparticle delivery platform.

We are aware of product candidates of the following companies that we consider as competitors or future competitors to ARCT-032: Translate Bio, Eloxx Pharmaceuticals, Recode, 4DMT and Splisense.

Employees

As of December 31, 2021, we had 177 employees, all of which were full-time. None of our employees are represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

Available Information

Our Internet address is www.arcturusrx.com. Our Annual Reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and proxy statements, and all amendments thereto, are available free of charge on our Internet website. These reports are posted on our website as soon as reasonably practicable after they are electronically filed with the SEC. The public may read and copy any materials that we file with the SEC electronically through the SEC website (www.sec.gov). The information contained on the SEC's website is not incorporated by reference into this Annual Report on Form 10-K and should not be considered to be part thereof.

Item 1A. Risk Factors

In conducting our business, we face many risks that may interfere with our business objectives. Some of these risks could materially and adversely affect our business, financial condition and results of operations. In particular, we are subject to various risks resulting from inherent unknowns and uncertainties in the drug development process, as well as changing economic, political, industry, regulatory, business and financial conditions. The risks and uncertainties described below are not the only ones we face.

You should carefully consider the following factors and other information in this Annual Report before you decide to invest in our common stock. If any of the negative events referred to below occur, our business, financial condition and results of operations could suffer. In any such case, the trading price of our common stock could decline, and you may lose all or part of your investment.

Risk Factor Summary

The following is a summary of certain important factors that may make an investment in our company speculative or risky. You should carefully consider the fuller risk factor disclosure set forth in this Annual Report, in addition to the other information herein, including the section of this report titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our financial statements and related notes.

We have a limited operating history, have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future.

We have never generated any revenue from product sales, have generated only limited revenue since inception, and may never be profitable.

The coronavirus pandemic has caused interruptions and delays of our business plan for the past two years and may continue to have a significant adverse effect on our business.

We expect that we will need to raise additional capital, which may not be available on acceptable terms, or at all.

The clinical studies involving our initial COVID-19 vaccine candidate, ARCT-021, have concluded dosing and we might not proceed with further development of ARCT-021. If we cannot quickly develop and achieve approval of a COVID-19 vaccine candidate, we may be unable to effectively market and sell a COVID-19 vaccine.

Even if we successfully develop a COVID-19 vaccine, we may not be able to sell it profitably, or it may not be accepted in the market.

Our next generation COVID-19 vaccine candidate, ARCT-154, does not have marketing approval and may never achieve marketing approval. Regulators may refuse to approve ARCT-154 as a booster shot because we have not yet received approval for ARCT-154 as a primary vaccination series for COVID-19.

There is significant competition in the development of a vaccine against COVID-19, some competitors' vaccines are already widely accepted in the market, and many of our competitors have substantially greater financial, scientific and other resources than we have.

If we are unable to generate successful results from preclinical and clinical studies of our product candidates, or experience significant delays in doing so, our business may be materially harmed..

Our platform focuses on nucleic acid technology, and mRNA drug products in particular, which are relatively new and any adverse results from nucleic acid or mRNA technologies in the industry could significantly impact our ability to develop and commercialize marketable products..

We may not be successful in our efforts to identify or discover potential product candidates.

If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

We may find it difficult to identify and enroll patients in our clinical studies, and the limited number of patients who have the diseases for which certain of our product candidates are being studied could delay or prevent clinical studies of certain of our product candidates.

If any of our product candidates cause undesirable side effects or have other properties impacting safety, their regulatory approval could be prevented, delayed or limited.

Even if we complete the necessary preclinical studies and clinical trials, we cannot predict whether or when we will obtain regulatory approval to commercialize a product candidate and we cannot, therefore, predict the timing of any revenue from a future product.

Even if we obtain regulatory approval for a product candidate, we will still face extensive regulatory requirements and our products may face future development and regulatory difficulties.

We may use our financial and human resources to pursue a particular research program or product candidate and fail to capitalize on programs or product candidates that may be more profitable or for which there is a greater likelihood of success.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

Manufacturing issues may arise that could increase product and regulatory approval costs or delay or hinder commercialization.

If our alliance partners do not perform in accordance with the terms of our agreements, our potential to generate future revenue from these programs would be significantly reduced and our business would be materially and adversely harmed.

We face significant competition from other biotechnology and pharmaceutical companies and our operating results will suffer if we fail to compete effectively.

The commercial success of our product candidates will depend upon the acceptance of these product candidates by the medical community, including physicians, patients and healthcare payors.

If we are unable to establish cost-effective sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to generate any revenues.

If we obtain approval to commercialize any approved products outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.

If our strategic alliances are unsuccessful or are terminated, we may be unable to commercialize certain product candidates and generate revenues.

If the outside contractors we rely on to conduct some aspects of our compound formulation, research and studies do not perform satisfactorily and meet deadlines, development of our product candidates could be delayed or precluded.

If the contract manufacturers we rely on to produce the supply of our preclinical and clinical product candidates, including materials for the manufacture of our product candidates, do not timely deliver adequate quantities of quality materials, development and commercialization of our product candidates would be hindered.

Any disruption in the supply chain of raw materials for, or in the manufacturing capacity and timing for the manufacture of drug substance or drug product for, our product candidates may cause a delay in developing and commercializing these product candidates and limit the revenues that we could generate.

If the contract research organizations and clinical trial sites we rely on to conduct, supervise and monitor our clinical trials perform in an unsatisfactory manner, it may harm our business.

If we are unable to obtain or protect intellectual property rights related to our future products and product candidates, we may not be able to compete effectively in our markets.

Claims that we infringe the intellectual property rights of others, especially in the crowded and competitive field of mRNA patents, may prevent or delay our development and commercialization efforts.

If we fail to obtain licenses to necessary intellectual property or do not comply with our obligations in license agreements, we could lose important rights.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensees, which could be expensive, time consuming and unsuccessful.

RISKS RELATED TO OUR FINANCIAL CONDITION AND NEED FOR ADDITIONAL CAPITAL

We have a limited operating history, have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future.

We are a global clinical-stage messenger RNA medicines company with a limited operating history. Since inception, our operations have been primarily limited to acquiring and licensing intellectual property rights, developing our product platform, undertaking basic research and conducting studies for our initial product development programs. We have not yet obtained regulatory approval for any product candidates. Consequently, any predictions about our future success or viability, or any evaluation of our business and prospects, is difficult and may not be accurate.

We have incurred losses in each year since our inception. Our net losses were $203.7 million and $72.1 million for the years ended December 31, 2021 and 2020, respectively. As of December 31, 2021, we had an accumulated deficit of $347.5 million.

We have devoted most of our financial resources to research and development, including our preclinical and clinical development activities. To date, we have funded our operations primarily through upfront payments, research funding and milestone payments from strategic alliances and collaborations, and through the sale of equity and convertible securities. We expect to continue to incur substantial and increased expenses, losses and negative cash flows as we expand our development activities and advance our programs. If our product candidates are not successfully developed or commercialized, including because of a lack of capital, or if we do not generate enough revenue following marketing approval, we will not achieve profitability and our business may fail. Even if we or our strategic alliance partners successfully obtain regulatory approval to market a product candidate, our revenues will also depend upon the size of any markets in which our product candidates have received market approval and our ability to achieve sufficient market acceptance and adequate market share for our products.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if and as we:

- continue our research and development of our product candidates, both independently and under our strategic alliance agreements;
- seek to identify additional targets and product candidates;
- acquire or in-license other products and technologies;
- advance product candidates into and through clinical trials;
- seek marketing approvals for any product candidates that successfully complete clinical trials;
- ultimately establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, regulatory, research, executive and administrative personnel; and
- create additional infrastructure to support our operations and our product development and planned future commercialization efforts.

We have never generated any revenue from product sales, have generated only limited revenue since inception, and may never be profitable.

Our ability to generate revenue and achieve profitability depends on our ability, alone or with strategic alliance partners, to successfully complete the development of, obtain the necessary regulatory approvals for and commercialize our product candidates. Our ability to generate revenues from product sales depends heavily on our success in:

- completing our research and development of product candidates;
- initiating and completing clinical trials for product candidates with favorable results;

- seeking, obtaining, and maintaining marketing approvals for product candidates that successfully complete clinical trials;
- establishing and maintaining supply and manufacturing relationships with capable parties;
- launching and commercializing product candidates for which we may obtain marketing approval, with an alliance partner or, if launched independently, successfully establishing a sales force, marketing and distribution infrastructure;
- maintaining, protecting and expanding our intellectual property portfolio; and
- attracting, hiring and retaining qualified personnel.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to predict reliably the timing or amount of increased expenses and when we will be able to achieve or maintain profitability, if ever. In addition, our expenses could increase beyond expectations if we are required by the FDA, or other foreign regulatory agencies to perform studies and trials in addition to those that we currently anticipate.

Even if one or more of the product candidates that we independently develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations.

The coronavirus pandemic has caused interruptions and delays of our business plan for the past two years and may continue to have a significant adverse effect on our business.

In December 2019, a strain of coronavirus, COVID-19, was reported to have surfaced in Wuhan, China, and on March 12, 2020, the World Health Organization declared COVID-19 to be a pandemic. In an effort to contain and mitigate the spread of COVID-19, many countries, including the United States, Canada and China, have imposed unprecedented restrictions on travel, quarantines, and other public health safety measures. This pandemic has adversely affected our operations in many ways, including:

- delayed enrollment and difficulty retaining patients in clinical trials;
- shortages, delays and higher prices for clinical supply materials and other resources used in our business;
- suspensions and delays in completion of clinical trials;
- diverted resources and priorities at hospitals and clinics in areas where we are conducting trials;
- disruption in supply chain, including difficulties in procuring materials and components for our clinical trials;
- limited availability and losses of key management, scientific and technical personnel; and
- slower expected development timelines for our product candidates.

The extent to which the pandemic will continue to adversely affect our business and the global economy and its full impact will depend on future developments, which are highly uncertain and cannot be reliably predicted.

We expect that we will need to raise additional capital, which may not be available on acceptable terms, or at all.

Developing pharmaceutical products, including conducting studies and clinical trials, is extremely expensive. We expect our research and development expenses to substantially increase in connection with our ongoing activities, particularly as we advance our product candidates towards and through clinical trials. We may need to raise additional capital to support our operations and such funding may not be available to us on acceptable terms, or at all. As of December 31, 2021, we had unrestricted cash and cash equivalents of $370.5 million, which we expect should be sufficient to fund currently planned operations for at least one year. But if our plans change or we face unexpected circumstances, our capital resources may be depleted more rapidly than we currently anticipate. For example, our clinical trials may encounter technical, regulatory or other difficulties. Additionally, our strategic alliance collaborators may elect not to pursue the development and commercialization of any of our product

candidates that are subject to their respective strategic alliance agreements with us. Any of these events would increase our development costs more than we expect. In order to support our long-term plans, we will need to raise additional capital or otherwise obtain funding through additional strategic alliances if we choose to initiate preclinical or clinical trials for product candidates that are not currently subject to a collaboration. In any event, we will require additional capital to obtain regulatory approval for, and to commercialize, future product candidates.

A significant portion of our current cash balance is expected to be utilized during 2022 to fund our continued preclinical and clinical development activities for our pipeline, including manufacturing activities to support such development activities and corresponding manufacturing activities and resources to preparing filings with regulatory authorities.

Any additional Phase 3 trial of our LUNAR-COV19 vaccine candidate, if any, may need to be primarily or exclusively funded through our cash reserves. If we achieve EUA approval to market our LUNAR-COV19 vaccine candidate, we will need to raise additional funds through equity transactions, additional debt or prepayments from potential customers, among other options, to fund commercialization of LUNAR-COV19.

Any additional fundraising efforts may divert our management from our day-to-day activities, which may delay and hinder our ability to develop and commercialize future product candidates. We may be unable to raise sufficient amounts of additional capital when needed and on acceptable terms, which could require us to:

- significantly delay, scale back or discontinue the development or commercialization of any future product candidates;
- seek strategic alliances for research and development programs or clinical trials at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available; or
- relinquish or license on unfavorable terms, our rights to technologies or any future product candidates that we otherwise would seek to develop or commercialize ourselves.

We are exposed to interest rate risk, including under our loan agreements.

We are exposed to market risk from changes in interest rates. Exposure to interest rate risk results from our debt obligations, including the loan agreement entered into on October 12, 2018 by our wholly-owned subsidiary, Arcturus Therapeutics, Inc., with Western Alliance Bank (the "Western Loan Agreement"). The Western Loan Agreement bears a variable interest rate of 1.25% above the prime rate published by the western edition of the Wall Street Journal. As of December 31, 2021, we had $15.2 million outstanding under the Western Loan Agreement. If we were to experience a 10% adverse change in the prime rate referenced above, the annual effect such change would have on our statement of operations, based on the amount we had outstanding as of December 31, 2021, under the Western Loan Agreement, would be negligible.

Additionally, on November 7, 2020, we entered into a Manufacturing Support Agreement with the EDB. Pursuant to the Manufacturing Support Agreement, the Economic Development Board of the Republic of Singapore (the "EDB") agreed to make a term loan (the "Singapore Loan") of up to S$62.1 million, subject to the satisfaction of customary deliveries, to support the manufacture of the LUNAR-COV19 vaccine candidate (ARCT-021). The Singapore Loan accrues interest at a rate of 4.5% per annum calculated on a daily basis. We elected to borrow the full amount available under the Support Agreement of S$62.1 million, or US$46.6 million, as a result of applicable exchange rates, on January 29, 2021.

Our indebtedness could materially and adversely affect our business, financial condition and results of operations.

Agreements with our lenders, including with Western Alliance Bank, create several limitations on us, including but not limited to:

- limiting our flexibility in planning for, or reacting to, changes in our business and our industry;
- placing us at a competitive disadvantage compared to our competitors who may have less debt or comparable debt at more favorable interest rates or less strict covenants and other limitations or requirements;

- limiting our ability to incur specified types of additional indebtedness which may be desired for working capital, capital expenditures, research and development efforts, acquisitions, debt service requirements, execution of our business strategy or other purposes; and
- resulting in an acceleration of our obligations upon the occurrence of an event of default.

Our ability to comply with these covenants in future periods will depend on our financial and operating performance, which in turn will be subject to economic conditions and to financial, market and competitive factors, many of which are beyond our control. Any of these factors or others described in the Western Loan Agreement could materially and adversely affect our business, financial condition and results of operations.

Our debt contains customary default clauses, a breach of which may result in acceleration of the repayment of some or all of this debt.

The Western Loan Agreement contains customary default clauses. In the event we were to default on our obligations under our debt and were unable to cure or obtain a waiver of such default, the repayment of our debt may be accelerated. If such acceleration were to occur, we would be required to promptly secure alternative sources of equity or debt financing to be able to repay the debt. Alternative financing may not be available on terms satisfactory to us, or at all. New debt financing may require the cooperation and agreement of our existing lenders. If acceptable alternative financing were unavailable, we would have to consider alternatives to fund the repayment of the debt, which could materially and adversely affect our business, financial condition and results of operations.

RISKS RELATED TO THE DEVELOPMENT AND COMMERCIALIZATION OF PRODUCT CANDIDATES

The clinical studies involving our initial COVID-19 vaccine candidate, ARCT-021, have concluded dosing and we might not proceed with further development of ARCT-021. If we cannot quickly develop and achieve approval of a COVID-19 vaccine candidate, we may be unable to effectively market and sell a COVID-19 vaccine.

The planned multinational Phase 3 vaccine trial against COVID-19 with a global entity, for which our initial COVID-19 vaccine candidate, ARCT-021, was selected, has taken longer than anticipated to proceed with ARCT-021 and might not ever proceed with ARCT-021. We have completed dosing in the studies involving ARCT-021 and do not have current plans to sponsor additional development studies of ARCT-021 unless and until the global entity determines to proceed with ARCT-021 in the multinational Phase 3 vaccine trial. We have developed next generation COVID-19 candidates, namely ARCT-154, that we have progressed further in clinical development, but advancing these next generation candidates has taken significant time and resources. Further, the existence of several other COVID-19 vaccines that have achieved approval and widespread global adoption makes it significantly more challenging for us to run clinical trials on, and to achieve marketing approvals (including emergency use authorizations) for, any of our COVID-19 vaccine candidates. Data from our ongoing Phase 1/2/3 clinical trials of ARCT-154 in Vietnam may not provide sufficient evidence to the Vietnamese regulatory authorities, the US FDA or regulatory authorities in other jurisdictions that it is sufficiently safe and effective to achieve any marketing approval (including any emergency use authorization) or to have a plausible clinical path to an approval.

Clinical trial results are inherently uncertain, and a significant portion of our potential success and business prospects currently depend on our COVID-19 vaccine program. If we cannot demonstrate sufficient safety and efficacy and complete these clinical trials on a timely basis, we likely will have missed a substantial market opportunity for COVID-19 vaccines, after dedicating significant efforts and financial resources to this program.

Even if we successfully develop a COVID-19 vaccine, we may not be able to sell it profitably.

If the prevalence of COVID-19 continues to decline and more people get vaccinated, the potential market opportunity is likely shrinking for any vaccine, including any booster we may be able to develop. As further COVID-19 vaccines are approved, production of existing COVID-19 vaccines improves and the COVID-19 impact transitions from pandemic to endemic stage, there may be downward pressure on prices. Although many developing countries have large populations for whom COVID-19 vaccines have not been available, it may not be easy or profitable to get vaccines to those populations. The price at which COVID-19 vaccines could be sold to developing countries is not likely to be as high as prices paid by wealthier countries eager to get vaccines when first available. Therefore, even if we can get through the extremely costly, long and risky process of developing and obtaining

regulatory approval to market a vaccine, it may not be commercially successful. This failure could be due to reduced demand for COVID-19 vaccines, lower prices, distribution problems, competitors' products or many other reasons. Our manufacturing process for our current COVID-19 vaccine candidates include a step for lyophilization to enhance the stability of the vaccine product. The additional step of lyophilization adds time and costs to the overall production output, which could adversely impact the production volumes and profitability of our COVID-19 vaccines if approval to market a vaccine is achieved.

Our next generation COVID-19 vaccine candidate, ARCT-154, does not have marketing approval and may never achieve marketing approval. Regulators may refuse to approve ARCT-154 as a booster shot because we have not yet received approval for ARCT-154 as a primary vaccination series for COVID-19.

In the coming months, we expect to receive important clinical data on ARCT-154, and the data may not support a regulatory approval (including emergency use authorization). Regulatory authorities, including the FDA, may deem the data we expect to collect from studies outside of the United States to be inadequate or unacceptable. Regulatory authorities, including the FDA, may also determine to foreclose or make more difficult a path to emergency use authorization. If key regulatory authorities, such as the FDA, determine that our data is inadequate or unacceptable, or make the path to regulatory approval more difficult, we may not be able to achieve regulatory approval (including EUA) and any additional study may prove too costly for us to conduct without a strategic partner

Though we have exciting preliminary clinical data on ARCT-154 as a booster series, we do not have approval for ARCT-154 (or any vaccine candidate) as a primary vaccination series anywhere in the world. We have completed EUA submission in Vietnam for ARCT-154 on the primary vaccination series. But we cannot provide any assurance that the Vietnam Ministry of Health will approve the EUA, or that any other country will provide an EUA or other approval on the primary vaccination series. We are not aware of the FDA authorizing use of any COVID-19 vaccine or any other vaccine as a booster shot unless the FDA has previously authorized that vaccine to be used as a primary vaccine series. We cannot provide any assurance that the FDA would be willing in the future to approve a COVID-19 vaccine as a booster shot without prior approval as a primary vaccine series. The FDA and regulators in other jurisdictions may still refuse to approve ARCT-154 or any other vaccine as a booster even if our COVID-19 vaccine candidate demonstrates safety and efficacy. In such event, we will not be able to sell a COVID-19 vaccine and our financial condition could be substantially harmed.

Even if one of our vaccine candidates is approved for sale, it may not be accepted in the market, despite limitations on the effectiveness of some approved vaccines.

Notwithstanding the ongoing rollout of vaccines, it will still take a substantial amount of time to produce, distribute and administer the vaccines worldwide and, as a result, to achieve broad protection of the global population. It is also still unclear if the vaccines will enable adequate long-term protection, as (i) many vaccinated individuals have become ill due to "breakthrough infections" and have transmitted the virus to many others, (ii) there are millions of individuals who refuse to be vaccinated or who cannot be vaccinated due to pre-existing conditions, (iii) it is unclear how long the vaccine protection will last, and (iv) genetic mutations or variants of the virus already have had, and are expected to continue to have, an adverse impact on the efficacy of available vaccines. If we cannot develop and commercialize a vaccine that adequately addresses some of these shortcomings of vaccines currently on the market, we cannot expect to have commercial success.

There is significant competition in the development of a vaccine against COVID-19, some competitors' vaccines are already widely accepted in the market, and many of our competitors have substantially greater financial, scientific and other resources than we have.

A large number of biopharmaceutical companies, academic institutions and other organizations currently have programs to develop COVID-19 vaccine candidates and many are further along in development of their vaccine candidates. Pfizer, Moderna and Johnson & Johnson have received full approvals or emergency use authorization from the FDA and many other health regulatory authorities throughout the world, and other biopharmaceutical companies have received approvals or authorizations from many health regulatory authorities other than the FDA, for their COVID-19 vaccines and have already commercialized them on a large scale and have vaccinated billions of people around the world.

Despite funding provided to us to date, we are already at a significant competitive disadvantage to those companies with vaccines on the market, as well as many other competitors pursuing vaccine candidates. Many other

competitors have significantly greater product candidate development, manufacturing and marketing resources than we do. Larger pharmaceutical and biotechnology companies have extensive experience in clinical testing and obtaining regulatory approval for their products, and may have the resources to heavily invest to accelerate discovery and development of their vaccine candidates. Our business could be further materially and adversely affected by our competitors commercialization of their vaccines before we complete development and seek approval for our vaccine candidate; if they develop and commercialize one or more COVID-19 vaccines that are safer, more effective against multiple variants, have fewer or less severe side effects, have broader market acceptance, are more convenient or are less expensive than any vaccine candidate that we may develop. Furthermore, if any competitors are successful in producing a more efficacious vaccine or other treatment for COVID-19, or if any competitors are able to manufacture and distribute any such vaccines or treatments with greater efficiency, there may be a diversion of potential governmental and other funding away from us and toward such other parties.

If we are unable to generate successful results from preclinical and clinical studies of our product candidates, or experience significant delays in doing so, our business may be materially harmed.

We have no products approved for commercial marketing and all of our product candidates are in preclinical or clinical development. Before obtaining regulatory approval for the commercial distribution of our product candidates, we or an existing or future collaborator must conduct extensive preclinical studies and clinical trials to demonstrate the safety and efficacy of our product candidates.

The success of our product candidates will depend on several factors, including the following:

- successfully designing preclinical studies which may be predictive of clinical outcomes;
- successful enrollment in clinical trials and completion of preclinical and clinical studies with favorable results;
- receipt of marketing approvals from applicable regulatory authorities;
- obtaining and maintaining patent and trade secret protection for future product candidates;
- establishing and maintaining manufacturing relationships with third parties or establishing our own manufacturing capability; and
- successfully commercializing our products, if approved, including successfully establishing a sales force, marketing and distribution infrastructure, whether alone or in collaboration with others.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully complete the development or commercialization of our product candidates, which would materially harm our business.

Our platform focuses on nucleic acid technology, and mRNA drug products in particular, which are relatively new and any adverse results from nucleic acid or mRNA technologies in the industry could significantly impact our ability to develop and commercialize marketable products.

We have concentrated our therapeutic product research and development efforts on nucleic acid technology, and mRNA in particular, and our future success depends on the successful development and acceptance of this technology for drug products. The development and commercialization of drug products based on nucleic acid technologies, including mRNA, are relatively new. The scientific evidence to support the feasibility of developing product candidates based on these discoveries is both preliminary and limited. If nucleic acid or mRNA approaches to drug products encounter setbacks based on the safety, efficacy, distribution, costs or other factors, it will significantly hurt our prospects and the value of our common stock.

Our focus on nucleic acid technology for developing drugs as opposed to more proven technologies for drug development increases the risks associated with the ownership of our common stock. If we are not successful in developing any product candidates using nucleic acid technology, we may be required to change the scope and direction of our product development activities. In that case, we may not be able to identify and implement successfully an alternative product development strategy.

We may not be successful in our efforts to identify or discover potential product candidates.

The success of our business depends primarily upon our ability to identify, develop and commercialize messenger RNA medicines. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons, including:

- our research methodology or that of our strategic alliance partners may be unsuccessful in identifying potential product candidates;
- potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval; or
- our strategic alliance partners may change their development profiles for potential product candidates or abandon a therapeutic area.

If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations. Research programs to identify new product candidates require substantial technical, financial and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful.

If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

Before obtaining marketing approval from regulatory authorities for the sale of product candidates, we or our strategic alliance partners must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates in humans. Clinical trials are expensive, difficult to design and implement, can take many years to complete and are uncertain as to the outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical studies and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for their products. Furthermore, even if prior animal studies have demonstrated the potential safety and efficacy of our product candidates, there can be no guarantee that such results will be reproducible in preclinical studies and clinical trials involving human subjects.

Events which may result in a delay or unsuccessful completion of clinical development include:

- delays in reaching an agreement with the FDA or other regulatory authorities on final trial design;
- delays in submitting or acceptance of, an application for authorization to administer an investigational new drug product to humans through the submission or acceptance of an IND application to the FDA, or foreign regulatory authority;
- imposition of a clinical hold of our clinical trial operations or trial sites by the FDA or other regulatory authorities;
- delays in reaching agreement on acceptable terms with prospective contract research organizations (“CROs”) and clinical trial sites;
- our inability to adhere to clinical trial requirements directly or with third parties such as CROs;
- clinical trial site or CRO non-compliance with GCPs, GLPs, or other regulatory requirements;
- inability or failure of clinical trial sites to adhere to the clinical trial protocol;
- delays in obtaining required IRB approval at each clinical trial site, or an IRB suspending or terminating a trial;
- delays in recruiting suitable patients to participate in a trial;
- delays in the testing, validation, manufacturing and delivery of the product candidates to the clinical sites;
- delays in having patients complete participation in a trial or return for post-treatment follow-up;
- delays caused by patients dropping out of a trial due to protocol procedures or requirements, product side effects or disease progression;

- clinical sites dropping out of a trial to the detriment of enrollment;
- time required to add new clinical sites; or
- delays by our contract manufacturers to produce and deliver sufficient supply of clinical trial materials.

If we or our strategic alliance partners are required to conduct additional clinical trials or other testing of any product candidates beyond those that are currently contemplated, are unable to successfully complete clinical trials of any such product candidates or other testing, or if the results of these trials or tests are not positive, are only modestly positive or if there are safety concerns, we or our strategic alliance partners may:

- be delayed in obtaining marketing approval for our future product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as originally intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

Our product development costs will also increase if we experience delays in testing or marketing approvals. We face risks that clinical trials may not begin as planned, may need to be restructured or may not be completed on schedule, or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or could allow our competitors to bring products to market before we do, which would impair our ability to successfully commercialize our product candidates. Any inability to timely and successfully complete preclinical and clinical development, whether independently or with our strategic alliance partners, could result in additional costs to us or impair our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties.

We may find it difficult to identify and enroll patients in our clinical studies, and the limited number of patients who have the diseases for which certain of our product candidates are being studied could delay or prevent clinical studies of certain of our product candidates.

Identifying and qualifying patients to participate in clinical studies of our product candidates is critical to our success. The timing of our clinical studies depends in part on the speed at which we can recruit patients to participate in testing our product candidates, and we may experience delays in our clinical studies if we encounter difficulties in enrollment.

Because of the aggressive roll-out of COVID-19 vaccines, we have found it challenging to enroll sufficient subjects in our LUNAR-COV19 trials who have not otherwise received a vaccine. Additionally, competing COVID-19 vaccine clinical trials make it more difficult to enroll subjects in our LUNAR-COV19 trials. We may also find it more difficult to identify subjects willing to participate in our studies. The regulatory authorities of certain countries have restricted placebo-controlled trials in studies for COVID-19 vaccine candidates. Such restrictions may make it more difficult to seek approval to proceed with certain clinical trial designs, and for the ultimate likelihood of approval of such candidates.

In addition, certain conditions for which we plan to evaluate our current product candidates are rare genetic diseases, and have limited patient pools from which to draw for clinical studies. For example, we estimate that approximately 8,000 patients in the developed world suffer from late-onset OTC deficiency, for which LUNAR-OTC is being studied. In addition to the rarity of these diseases, the eligibility criteria of our clinical studies will further limit the pool of available study participants as we will require patients to have specific characteristics that we can measure or to assure their disease is either severe enough or not too advanced to include them in a study. The process of finding and diagnosing patients may prove costly, especially since the rare diseases we are studying are commonly underdiagnosed. We also may not be able to identify, recruit, and enroll a sufficient number of appropriate patients to complete our clinical studies because of demographic criteria for prospective patients, the perceived risks and benefits of the product candidate under study, the proximity and availability of clinical study sites for prospective patients, and the patient referral practices of physicians. The availability and efficacy of competing therapies and clinical studies can also adversely impact enrollment.

If we are unable to promptly enroll an adequate number of patients in our studies for the foregoing or other reasons, the timeline for conducting studies and obtaining regulatory approval of potential products may be delayed,

the commercial prospects of our product candidates will be harmed, and our ability to generate product revenue from any of these product candidates could be delayed or prevented. Furthermore, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical studies may also ultimately lead to the denial of regulatory approval of our product candidates. Delays in achieving approval to conduct and in completing our clinical studies will increase our costs, slow down our product candidate development and approval process, and jeopardize our ability to commence product sales and generate revenue. Any of these occurrences may harm our business, financial condition, and prospects significantly.

If any of our product candidates cause undesirable side effects or have other properties impacting safety, their regulatory approval could be prevented, delayed or limited.

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other regulatory authorities. It is likely that there will be side effects associated with use of our product candidates. If results of our trials reveal a high and unacceptable severity and prevalence of side effects, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of, or deny approval of, our product candidates for any or all targeted indications. Such side effects could also affect patient recruitment, the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may materially and adversely affect our reputation and financial condition.

Further, clinical trials by their nature test product candidates in only samples of the potential patient populations. With a limited number of patients and limited duration of exposure in such trials, rare and severe side effects of our product candidates may not be uncovered until a significantly larger number of patients are exposed to the product candidate.

If any of our product candidates receives marketing approval, and causes serious, unexpected, or undesired side effects, a number of potentially significant negative consequences could result after we begin commercialization, including:

- regulatory authorities may withdraw, suspend, or limit their approval of the product or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation strategy;
- regulatory authorities may require the addition of labeling statements, such as warnings or contraindications;
- we may be required to change the way the product is administered or conduct additional clinical trials or post-marketing surveillance;
- we could be sued and held liable for harm caused to patients; or
- our reputation may suffer.

Any of these events could prevent us or our partners from achieving or maintaining market acceptance of the affected product and could substantially increase the costs of commercializing our future products and impair our ability to generate revenues from the commercialization of these products either by us or by our strategic alliance partners.

Even if we complete the necessary preclinical studies and clinical trials, we cannot predict whether or when we will obtain regulatory approval to commercialize a product candidate and we cannot, therefore, predict the timing of any revenue from a future product.

The extent and timing of any product revenue is highly unpredictable because regulatory authorities may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval for many reasons including:

- regulatory authorities disagreeing with the design or implementation of our clinical trials;
- such authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- such authorities may not accept clinical data from trials which are conducted at clinical facilities or in countries where the standard of care is potentially different from that of the United States, such as our phase 1/2/3 clinical trial of ARCT-154 currently being conducted in Vietnam;

- unfavorable or unclear results from our clinical trials or results that may not meet the level of statistical significance required by the FDA or foreign regulatory agencies for approval;
- serious and unexpected drug-related side effects experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates;
- the population studied in the clinical trial may not be sufficiently broad or representative to assure safety in the full population for which we seek approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- such authorities may not agree that the data collected from clinical trials of our product candidates are acceptable or sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the United States or elsewhere, and such authorities may impose requirements for additional preclinical studies or clinical trials;
- such authorities may disagree regarding the formulation, labeling and/or the specifications of our product candidates;
- such authorities may find deficiencies in the manufacturing processes or facilities of manufacturers with which we contract for clinical and commercial supplies; or
- regulations or interpretations of such authorities may significantly change in a manner rendering our or any of our potential future collaborators' clinical data insufficient for approval.

Additional delays may result if an FDA advisory committee recommends restrictions on approval or recommends non-approval. In addition, we or our strategic alliance partners may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical trials and the review process.

Even if we obtain regulatory approval for a product candidate, we will still face extensive regulatory requirements and our products may face future development and regulatory difficulties.

Even if we obtain regulatory approval in the United States, the FDA may still impose significant restrictions on the indicated uses or marketing of our product candidates, or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance. The FDA may also require a risk evaluation and mitigation strategy as a condition of approval of our product candidates, which could include requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Additionally, the manufacturing processes, packaging, distribution, adverse event reporting, labeling, advertising, promotion, and recordkeeping for the product will be subject to extensive and ongoing FDA regulatory requirements, in addition to other potentially applicable federal and state laws. These requirements include monitoring and reporting of adverse events and other post-marketing information and reports, registration, as well as continued compliance with current good manufacturing practice, or cGMP, regulations. The holder of an approved NDA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. If we or a regulatory agency discovers previously unknown problems with a product such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions relative to that product or the manufacturing facility, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

If we or our strategic partners fail to comply with applicable regulatory requirements following approval of any of our product candidates, a regulatory agency may:

- issue a warning letter asserting that we are in violation of the law;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve a pending NDA or supplements to an NDA submitted by us;
- seize product or require a product recall; or
- refuse to allow us to enter into supply contracts, including government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our future products, if approved, and generate revenues.

We may use our financial and human resources to pursue a particular research program or product candidate and fail to capitalize on programs or product candidates that may be more profitable or for which there is a greater likelihood of success.

As a result of our limited financial and human resources, we will have to make strategic decisions as to which targets and product candidates to pursue and may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. For example, we have allocated significant resources to the testing and development of our LUNAR-COV19 and LUNAR-OTC vaccine candidates, but competitors Pfizer, Moderna and Johnson & Johnson have already received full approvals or emergency use authorization from the FDA for their COVID-19 vaccines, which have achieved regulatory approval and widespread global adoption. Although we are seeking to develop a next-generation COVID-19 vaccine candidate, our spending on research and development programs and product candidates for COVID-19 may prove to have been unwise. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through strategic alliance, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate, or we may allocate internal resources to a product candidate in a therapeutic area in which it would have been more advantageous to enter into a partnering arrangement.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed applicable insurance coverage we may have as well as our financial resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Manufacturing issues may arise that could increase product and regulatory approval costs or delay or hinder commercialization.

As we scale-up manufacturing of product candidates and conduct required stability testing, product, packaging, equipment and process-related issues may require refinement or resolution in order to proceed with any clinical trials and obtain regulatory approval for commercial marketing. We may identify significant impurities, which could result in increased scrutiny by the regulatory agencies, delays in clinical programs and regulatory approval, increases in our operating expenses, or failure to obtain or maintain approval for product candidates or any approved products. We have limited stability data on ARCT-154, and though we have more extensive stability data for ARCT-021 and believe that our LUNAR platform should persuade regulatory authorities to consider ARCT-021 stability data for ARCT-154, regulatory authorities may disagree and require additional data. We are performing long term stability studies on ARCT-154 and are continuing storage shipping validation studies and continuous process and quality verification programs, but we cannot be sure of the outcomes of such studies and programs. Poor results could impact the prospects, timing and cost of our programs. Furthermore, we are required by our contract manufacturers to make financial commitments in advance of the receipt of clinical data or feedback from regulatory authorities, which could result in significant financial obligations.

If our alliance partners do not perform in accordance with the terms of our agreements, our potential to generate future revenue from these programs would be significantly reduced and our business would be materially and adversely harmed.

If our strategic alliance partners elect to further pursue the development and commercialization of any of the product candidates that are subject to our strategic alliance agreement, we will have limited influence and/or control over their approaches to development and commercialization. If strategic alliance partners do not perform in the manner that we expect or fail to fulfill their responsibilities in a timely manner, or at all, the clinical development, regulatory approval and commercialization efforts related to product candidates we have licensed to such strategic alliance partners could be delayed or terminated. If we terminate any of our strategic alliances or any program thereunder, we may have the right to assume the responsibility at our own expense for the development of the applicable product candidates. Assuming sole responsibility for further development will increase our expenditures, and may mean we will need to limit the size and scope of one or more of our programs, seek additional funding and/or choose to stop work altogether on one or more of the affected product candidates. This could result in a limited potential to generate future revenue from such product candidates and our business could be materially and adversely affected.

We face significant competition from other biotechnology and pharmaceutical companies and our operating results will suffer if we fail to compete effectively.

The biotechnology and pharmaceutical industries are intensely competitive. We have competitors both in the United States and internationally, including major multinational pharmaceutical companies, biotechnology companies and universities and other research institutions. Many of our competitors have substantially greater financial, technical and other resources, such as larger research and development staff and experienced marketing, regulatory and manufacturing organizations. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring or licensing on an exclusive basis, drug products that are more effective or less costly than any product candidate that we may develop.

The commercial success of our product candidates will depend upon the acceptance of these product candidates by the medical community, including physicians, patients and healthcare payors.

The degree of market acceptance of any product candidates will depend on a number of factors, including:

- demonstration of clinical safety and efficacy compared to other products;
- the relative convenience, ease of administration and acceptance by physicians, patients and healthcare payors;
- the prevalence and severity of any adverse events;
- limitations or warnings contained in the FDA-approved label for such products;
- availability of alternative treatments;
- pricing and cost-effectiveness;
- the effectiveness of our, or any of our collaborators', sales and marketing strategies;
- our ability to obtain hospital or payor formulary approval;
- our ability to obtain and maintain sufficient coverage from healthcare payors and adequate reimbursement; and
- the willingness of patients to pay out-of-pocket in the absence or inadequacy of coverage by healthcare payors.

Unless other formulations are developed in the future, we expect our compounds to be formulated in an injectable form. Injectable medications may be disfavored by patients or their physicians in the event drugs which are easy to administer, such as oral medications, are available. If any of our products is approved, but does not achieve an adequate level of acceptance by physicians, patients and healthcare payors, we may not generate sufficient revenues from such product and we may not become or remain profitable. Such increased competition may decrease any future potential revenue for future product candidates due to increasing pressure for lower pricing and higher discounts in the commercialization of our product.

If we are unable to establish cost-effective sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to generate any revenues.

In order to market any products that may be approved, we must build our sales, marketing, managerial and other non-technical capabilities or make arrangements with outside parties to perform these services. With respect to certain of our current programs as well as future programs, we may rely completely on a strategic alliance partner for sales and marketing. In addition, we intend to enter into strategic alliances with other parties to commercialize other product candidates, if approved, including in markets outside of the United States or for other large markets that are beyond our resources. Although we intend to establish a sales organization if we are able to obtain approval to market any product candidates for niche markets in the United States, we will also consider the option to enter into strategic alliances for future product candidates in the United States if commercialization requirements exceed our available resources. This will reduce the potential profit generated from the sales of these products.

Our current and any future strategic alliance partners may not dedicate sufficient resources to the commercialization of our product candidates, if approved, or may otherwise fail in their commercialization due to factors beyond our control. If we are unable to establish effective alliances to enable the sale of our product candidates, if approved, to healthcare professionals and in geographical regions, including the United States, that will not be covered by our own marketing and sales force, or if our potential future strategic alliance partners do not successfully commercialize the product candidates that may be approved, our ability to generate revenues from product sales will be adversely affected.

If we are unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, we may not be able to generate sufficient product revenue and may not become profitable. We will be competing with many companies that currently have extensive and well-funded marketing and sales operations. Without an internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

If we obtain approval to commercialize any approved products outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.

If we obtain approval to commercialize any approved products outside of the United States, we expect that we will be subject to additional risks related to entering into international business relationships, including:

- different regulatory requirements for drug approvals in foreign countries;
- differing payor reimbursement regimes, governmental payors or patient self-pay systems and price controls;
- reduced protection for intellectual property rights;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires.

If coverage and adequate reimbursement is not available for any of our future products, it would be difficult for us to sell that product profitably.

Market acceptance and sales of any product candidates that we develop will depend on coverage and reimbursement policies and may be affected by future healthcare reform measures. Government authorities and third-party payors, such as private health insurers, government payors and health maintenance organizations, decide which drugs they will pay for and establish reimbursement levels. We cannot be sure that coverage and adequate reimbursement will be available for any future product candidates. In the United States, the Centers for Medicare &

Medicaid Services (“CMS”), an agency within the U.S. Department of Health and Human Services, decides whether and to what extent a new drug will be covered and reimbursed under Medicare. Private payors tend to follow the coverage reimbursement policies established by CMS to a substantial degree. It is difficult to predict what CMS will decide with respect to reimbursement for novel product candidates. Inadequate reimbursement amounts could substantially reduce the demand for, or the price of, our future products. Further, one payor’s determination to provide coverage for a product does not assure that other payors will also provide coverage for the product. If reimbursement is not available, or is available only at limited levels, we may not be able to successfully commercialize product candidates that we develop and that may be approved. Thus, even if we succeed in bringing a product to market, it may not be considered medically necessary or cost-effective, and the amount reimbursed for any products may be insufficient to allow us to sell our products on a competitive basis.

In addition, we cannot be certain if and when we will obtain formulary approval to allow us to sell any products into our target markets. Obtaining formulary approval from hospitals and from pharmacy benefits payors can be an expensive and time-consuming process. Failure to obtain timely formulary approval will limit our commercial success.

There have been a number of legislative and regulatory proposals to change the healthcare system in the United States and in some foreign jurisdictions that could affect our ability to sell products profitably. These legislative and/or regulatory changes may negatively impact the reimbursement for drug products, following approval. The availability of numerous generic treatments may also substantially reduce the likelihood of reimbursement for our future products. We expect to experience pricing pressures in connection with the sale of any products that we develop, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, and prescription drugs in particular, has and is expected to continue to increase in the future. For instance, government and private payors who reimburse patients or healthcare providers are increasingly seeking greater upfront discounts, additional rebates and other concessions to reduce prices for pharmaceutical products. If we fail to successfully secure and maintain sufficient reimbursement coverage for our future products or are significantly delayed in doing so, we will have difficulty achieving market acceptance of our future products and our business will be harmed.

In addition, in some non-U.S. jurisdictions, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the EU provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. If any country that has price controls or reimbursement limitations for pharmaceutical products does not allow favorable reimbursement and pricing arrangements for any of our products, our sales and profits from that product could be severely limited. Historically, products launched in the EU do not follow price structures of the U.S. and generally tend to be priced significantly lower

RISKS RELATED TO OUR RELIANCE ON OUTSIDE PARTIES

If our strategic alliances are unsuccessful or are terminated, we may be unable to commercialize certain product candidates and generate revenues.

We depend on alliance partners for financial and scientific resources for the clinical development, manufacture and commercialization of certain of our nucleic acid product candidates. These alliances will likely provide us with limited control over the course of development of a nucleic acid product candidate, especially once a candidate has reached the stage of clinical development. Our ability to ultimately recognize revenue from our strategic relationships will depend upon the ability and willingness of our alliance partners to successfully meet their respective responsibilities under our agreements with them.

Our ability to recognize revenues from strategic alliances may be impaired by several factors, including:

- an alliance partner may shift its priorities and resources away from our programs due to a change in its business strategies, or a merger, acquisition, sale or downsizing of its company or business unit;
- an alliance partner may cease development in therapeutic areas which are the subject of our strategic alliances;
- an alliance partner may change the success criteria for a particular program or potential product candidate thereby delaying or ceasing development of such program or candidate;
- a significant delay in initiation of certain development activities by an alliance partner will also delay payment to us of milestones tied to such activities, thereby impacting our ability to fund our own activities;
- an alliance partner could develop a product that competes, either directly or indirectly, with our product candidate;
- an alliance partner with commercialization obligations may not commit sufficient financial or human resources to the marketing, distribution or sale of a product;
- an alliance partner with manufacturing responsibilities may encounter regulatory, resource or quality issues and be unable to meet demand requirements;
- an alliance partner may exercise its rights under the agreement to terminate a strategic alliance;
- a dispute may arise between us and an alliance partner concerning the research, development or commercialization of a program or product candidate resulting in a delay in payments of milestones or royalties, or the termination of a program, and possibly resulting in costly litigation or arbitration which may divert management attention and resources; and
- an alliance partner may use our proprietary information or intellectual property in such a way as to invite litigation from a third party or fail to maintain or prosecute intellectual property rights such that our rights in such property are jeopardized.

If any of our alliance partners do not elect to pursue the development and commercialization of our nucleic acid development candidates or if they terminate the strategic alliance, then, depending on the event:

- development of product candidates subject to our alliances may be terminated or significantly delayed;
- our cash expenditures could increase significantly if it is necessary for us to hire additional employees and allocate limited resources to the development and commercialization of product candidates that were previously funded, or expected to be funded, by our alliance partners;
- we would bear all of the risks and costs related to the further development and commercialization of product candidates that were previously the subject of our strategic alliance, including the reimbursement of third parties; and
- in order to fund further development and commercialization, we may need to seek out and establish alternative strategic alliances with other parties; this may not be possible, or we may not be able to do so on terms which are acceptable to us, in which case it may be necessary for us to limit the size or scope of one or more of our programs, increase our expenditures, or seek additional funding by other means.

Any of these events would have a material adverse effect on our results of operations and financial condition.

If the outside contractors we rely on to conduct some aspects of our compound formulation, research and studies do not perform satisfactorily and meet deadlines, development of our product candidates could be delayed or precluded.

We do not independently conduct all aspects of our drug discovery activities, compound formulation research or preclinical and clinical studies of product candidates. We currently rely and expect to continue to rely on outside contractors to conduct some aspects of our preclinical and clinical studies and formulation development, but we remain responsible for ensuring that each of our IND-enabling studies and clinical trials are conducted in accordance with the study plan and protocols for the trial.

If these outside parties terminate their engagements with us or do not successfully carry out their contractual duties, meet expected deadlines or conduct our studies in accordance with regulatory requirements or our stated

study plans and protocols, we will not be able to complete, or may be delayed in completing, the necessary preclinical studies to enable us or our strategic alliance partners to select viable product candidates for IND submissions and will not be able to, or may be delayed in our efforts to, successfully develop and commercialize such product candidates.

If the contract manufacturers we rely on to produce the supply of our preclinical and clinical product candidates, including materials for the manufacture of our product candidates do not timely deliver adequate quantities of quality materials, development and commercialization of our product candidates would be hindered.

We rely on outside contractors to produce the supply of our preclinical and clinical product candidates, and we intend to rely on outside contractors to produce future clinical supplies of product candidates and commercial supplies of any approved product candidates. Reliance on outside suppliers and manufacturers entails risks, some of which we would not be subject to if we manufactured the product candidates ourselves, including:

- the inability to meet any product specifications and quality requirements consistently;
- a delay or inability to procure or expand sufficient manufacturing capacity;
- manufacturing and product quality issues related to scale-up of manufacturing;
- costs and validation of new equipment and facilities required for scale-up;
- a failure to comply with cGMP and similar foreign standards;
- the inability to negotiate manufacturing or supply agreements with outside parties on commercially reasonable terms;
- termination or nonrenewal of manufacturing agreements with outside parties in a manner or at a time that is costly or damaging to us;
- the reliance on a limited number of sources, and in some cases, single sources for raw materials, such that if we are unable to secure a sufficient supply of these product components, we will be unable to manufacture and sell future product candidates in a timely fashion, in sufficient quantities or under acceptable terms;
- the lack of qualified backup suppliers for any raw materials that are currently purchased from a single source supplier;
- operations of our contract manufacturers or suppliers could be disrupted by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier;
- carrier disruptions or increased costs that are beyond our control; and
- the failure to deliver products under specified storage conditions and in a timely manner.

Any of these events could lead to clinical study delays or failure to obtain regulatory approval, or impact our ability to successfully commercialize future products, if approved. Some of these events could be the basis for detrimental FDA action, including injunction, product recall or seizure, or total or partial suspension of production.

Any disruption in the supply chain of raw materials for, or in the manufacturing capacity and timing for the manufacture of drug substance or drug product for, our product candidates may cause a delay in developing and commercializing these product candidates and limit the revenues that we could generate.

We have established manufacturing relationships with a limited number of suppliers to supply raw materials used to create our product candidates and with a limited number of contract manufacturers to manufacture drug substance and drug product. The availability of continued supply and manufacturing capacity from our current vendors, and the availability of additional suppliers and manufacturers, is limited. We have experienced some supplier shortages and delivery delays since the COVID-19 pandemic began in early 2020. If our vendors fail to supply materials or to manufacture substances or products in the required quantities on a timely basis and at commercially reasonable prices, and we are unable to secure one or more replacement vendors in a timely manner at a substantially equivalent cost, our clinical trials may be delayed and our commercialization prospects could be materially diminished.

Prior to marketing approval for any of our product candidates, a manufacturer and its processes are required to be qualified by the FDA. If supply from the approved manufacturer is interrupted, there could be a significant disruption in our sales of any product. An alternative vendor would need to be qualified through an NDA supplement which could result in further delay. The FDA or other regulatory agencies outside of the United States may also require additional studies if a new supplier is relied upon for commercial production. Switching vendors may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

In addition, if our alliance partners elect to pursue the development and commercialization of certain programs, we will lose control over the manufacturing of the product candidate subject to the agreement. Also, we will not be able to ensure that the product candidates will be manufactured under the correct conditions to permit the product candidates to be used in such clinical trials.

If the contract research organizations and clinical trial sites we rely on to conduct, supervise and monitor our clinical trials perform in an unsatisfactory manner, it may harm our business.

We and our strategic alliance partners rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials. We and our strategic alliance partners have limited control or influence over their actual performance, but remain responsible for ensuring that clinical trials are conducted in accordance with the applicable protocol, legal, regulatory and scientific standards.

If we or our CROs fail to comply with applicable good clinical practices , the clinical data generated in our clinical trials may be deemed unreliable and the FDA or applicable non-U.S. regulatory agency may require us to perform additional clinical trials before approving any marketing applications. In addition, our future clinical trials will require a sufficiently large number of test subjects to adequately evaluate the safety and effectiveness of a potential drug product. Accordingly, if our CROs fail to comply with these regulations or fail to recruit a sufficient number of patients, we may be required to repeat such clinical trials, which would delay the regulatory approval process and increase our costs.

Our CROs are not our employees, and we are not be able to control whether or not they devote sufficient time and resources to our clinical and nonclinical programs. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities, which could possibly harm our competitive position. If our future CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements, or for any other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize our product candidates. As a result, the commercial prospects for such products and any product candidates that we develop would be harmed, our costs could increase, and our ability to generate revenues could be delayed.

We rely on other outside parties to store and distribute drug products for clinical trials. Any performance failure or delays by our distributors could delay clinical development, marketing approval or commercialization of our product candidates, resulting in additional losses and depriving us of potential product revenue.

RISKS RELATED TO OUR INTELLECTUAL PROPERTY

If we are unable to obtain or protect intellectual property rights related to our future products and product candidates, we may not be able to compete effectively in our markets.

Our success depends in part on our ability to obtain and maintain patents and other forms of intellectual property rights, including in-licenses of intellectual property rights of others, for our product candidates, methods used to develop and manufacture our product candidates and methods for treating patients using our product candidates, as well as our ability to preserve our trade secrets, to prevent third parties from infringing upon our proprietary rights and to operate without infringing upon the proprietary rights of others. As of February 28, 2022, we own over 253 patents and pending patent applications including 38 U.S. patents, 33 pending U.S. patent applications, 12 pending international applications under Patent Cooperation Treaty (“PCT”), 82 foreign patents and 88 pending foreign patent applications. The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be highly uncertain. The patent applications that we own or in-license may fail to result in patents with claims that cover our products or methods in the United States or in other countries.

Our patents could be prevented from issuing or be invalidated after issuance for many reasons, including:

- relevant prior art relating to our patents and patent applications; or

- Claims that others were first to file a patent application covering the same subject matter, which could require an interference proceeding to determine which applicant is entitled to a patent on that subject matter; or
- third party challenges to their validity, enforceability or scope, which may result in patents being narrowed or invalidated.

If the patent applications we hold or have in-licensed with respect to our programs or product candidates fail to issue or are invalidated or if their breadth or strength of protection is threatened, it could dissuade companies from collaborating with us to develop product candidates, and threaten our ability to commercialize, future products. For example, we have been subjected to re-examination of, or oppositions to, patents owned by or licensed to us. Although we believe these concluded proceedings did not result in a commercially relevant impact on the individual patents, future challenges could deprive us of rights necessary for the successful commercialization of any product candidates that we or our strategic alliance partners may develop.

If we do not prevail in any challenge to our intellectual property rights, we could be required to cease using the related technology or to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license at all, or on commercially reasonable terms. Our defense of a patent or patent application in such a proceeding may not be successful and, even if successful, may result in substantial costs and distract our management and other employees. Even if our patent are issued and are not challenged or invalidated, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing around our claims. In addition, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available however the life of a patent, and the protection it affords is limited. Once the patent life has expired for a product, we may be open to competition from generic medications. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable, including processes for which patents are difficult to enforce and any other elements of our drug discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. Although each of our employees agrees to assign their inventions to us through an employee inventions agreement, and all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology are required to enter into confidentiality agreements, such agreements may not be effective in preventing our trade secrets and other confidential proprietary information from being disclosed or accessed by competitors. In addition, competitors and others may independently discover our trade secrets and proprietary information or independently develop substantially equivalent information and techniques. For example, the FDA, as part of its Transparency Initiative, is currently considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA's disclosure policies may change in the future, if at all.

Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent material disclosure of the non-patented intellectual property related to our technologies to third parties, and there is no guarantee that we will have any such enforceable trade secret protection, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business.

Claims that we infringe the intellectual property rights of others, especially in the crowded and competitive field of mRNA and delivery technology patents, may prevent or delay our development and commercialization efforts.

As the biotechnology and pharmaceutical industries expand and more patents are issued and as our activities expand, the risk increases that our product candidates and activities may be subject to claims of infringement of the patent rights of others. This risk is significantly heightened because of the many patents and other intellectual property rights in messenger RNA and delivery technology, which is being relied on by many companies, including us, developing mRNA-based vaccines.

Since the outbreak of the COVID-19 pandemic, many companies have devoted substantial effort to developing vaccines and therapeutics that use mRNA technology and have developed their own intellectual property

rights, applied for patents, and licensed rights to patents held by other companies or research institutions. Some of these patents may have broad claims that cover our current or expected activities.

We are aware of patent challenging and enforcement activities in connection with technologies used in mRNA-based COVID-19 vaccines. The outcomes of such activities and the advancement of our programs could give rise to third party claims of infringement against us and our partners.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize a COVID-19 vaccine or one or more of our other product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee and financial resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay significant royalties, or try to redesign our infringing products, which may be impossible or require substantial time and monetary expenditure, further delaying and commercialization and substantially reducing potential market revenue. Or, in order to continue development, manufacture or sale of a product, we may need to obtain a license from the owner of intellectual property, which may not be available on commercially reasonable terms or at all.

If we fail to obtain licenses to necessary intellectual property or do not comply with our obligations in license agreements, we could lose important rights.

We may need to obtain licenses from owners of intellectual property to advance our research or allow commercialization of our product candidates, and we have done so from time to time. If may fail to obtain any of these licenses at a reasonable cost and on reasonable terms, we would be unable to further develop and commercialize one or more of our product candidates, which could harm our business significantly.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensees, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our patents or the patents of our licensees. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours or of our licensees is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing.

Our defense in a lawsuit may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensees, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during the course of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

If we are subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties, we could incur substantial expenses.

We employ individuals who were previously employed at other biotechnology or pharmaceutical companies. We may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed confidential information of our employees' former employers or other third parties. We may also be subject to claims that former employers or other parties have an ownership interest in our patents. Litigation may be necessary to defend against these claims. We may not be successful in defending these claims, and if we are successful, litigation could result in substantial cost and be a distraction to our management and other employees.

RISKS RELATED TO OUR BUSINESS OPERATIONS AND INDUSTRY

We may need to expand our organization and may experience difficulties in managing this growth, which could disrupt our operations.

As of December 31, 2021, we had 177 employees. In the future we may expand our employee base to increase our managerial, scientific, operational, commercial, financial and other resources and we may hire more consultants and contractors. Future growth would impose significant additional responsibilities on our management, including the need to identify, recruit, maintain, motivate and integrate additional employees, consultants and contractors. Also, our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure or give rise to operational mistakes, loss of business opportunities, loss of employees or reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. Moreover, if our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenues could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

We have recently experienced high turnover and if we cannot continue to attract, retain and motivate key executives and qualified scientists and other personnel, we will not be able to effectively operate our business.

We are highly dependent on principal members of our executive team, and any reduction or loss of their services may adversely impact the achievement of our objectives. While we have entered into employment agreements with each of our executive officers, any of them could leave our employment at any time, as all of our employees are “at will” employees. Recruiting and retaining other qualified employees for our business, including scientific and technical personnel, will also be critical to our success. During the COVID-19 pandemic over the past two years, we have experienced a high number of resignations, as well as our Chief Medical Officer stepping down recently to a part-time role. There was already a shortage of skilled executives as well as scientific and technical personnel in our industry prior to COVID-19, which was exacerbated by the pandemic and is likely to continue. As a result, competition for skilled personnel is intense and the turnover rate can be high, as we have recently seen. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical companies for individuals with similar skill sets. In addition, failure to succeed in preclinical studies and clinical trials may make it more challenging to recruit and retain qualified personnel. The inability to recruit any executive or key employee or the loss of the services of any executive or key employee might impede the progress of our research, development and commercialization objectives.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of employee fraud or other misconduct. Employee misconduct could have significant negative impacts on our business. Misconduct by employees could include intentional or nonintentional failures to comply with the regulations of the FDA and other regulators, to provide accurate information to the FDA and other regulators, to comply with healthcare fraud and abuse laws and regulations in the United States and abroad, to report financial information or data accurately or to disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements.

Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. Although we have adopted a code of conduct and procedures, we may not always be effective in identifying and deterring employee misconduct, controlling unknown or unmanaged risks or losses, or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could result in the imposition of civil, criminal and administrative penalties, damages, fines, possible exclusion from Medicare, Medicaid and other government healthcare programs, additional reporting requirements

and/or oversight, particularly if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance, disgorgement, imprisonment, and contractual damages. Even if we are ultimately successful in defending any such action, we could be required to divert financial and managerial resources in doing so and adverse publicity could result, all of which could harm our business.

If we do not fully comply with applicable healthcare fraud and abuse laws, false claims laws and health information privacy and security laws, we could face criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

If we obtain FDA approval for any of our product candidates and begin commercializing those products in the United States, our operations may be directly, or indirectly through our customers, further subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act. These laws may impact, among other things, our proposed sales, marketing and education programs. In addition, we may be subject to patient privacy regulation by the federal government and by the U.S. states and foreign jurisdictions in which we conduct our business. The healthcare laws and regulations that may affect our ability to operate include:

- The federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, either the referral of an individual, or the purchase or recommendation of an item or service for which payment may be made under a federal healthcare program, such as the Medicare and Medicaid programs. Remuneration has been interpreted broadly to include anything of value. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution, the exemptions and safe harbors are drawn narrowly, and those activities may be subject to scrutiny or penalty if they do not qualify for an exemption or safe harbor. A conviction for violation of the Anti-Kickback Statute requires mandatory exclusion from participation in federal healthcare programs. This statute has been applied to arrangements between pharmaceutical manufacturers and those in a position to purchase products or refer others, including prescribers, patients, purchasers and formulary managers. In addition, the Affordable Care Act amended the Social Security Act to provide that the U.S. government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act penalties for which are described below.
- Federal civil and criminal false claims laws and civil monetary penalty laws, including the federal False Claims Act (“FCA”), which imposes criminal or civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, claims for payment to the federal government, including Medicare or Medicaid, that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. FCA liability is potentially significant in the healthcare industry because the statute provides for treble damages and mandatory penalties in 2021 of $11,803 to $23,607 per false claim or statement, which are adjusted for inflation.
- The civil monetary penalties statute, which imposes penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to a federal healthcare program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.
- The federal Health Insurance Portability and Accountability Act of 1996 (“HIPAA”), which imposes civil and criminal penalties for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations or promises, any money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private), knowingly and willfully embezzling or stealing from a health care benefit program, willfully obstructing a criminal investigation of a healthcare offense and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare.

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 ("HITECH"), and its implementing regulations, which imposes certain requirements on certain types of individuals and entities, such as healthcare providers, health plans and healthcare clearing houses, known as "covered entities," as well as their "business associates," independent contractors or agents of covered entities that receive or obtain individually identifiable health information in connection with providing a service on behalf of a covered entity, relating to the privacy, security and transmission of individually identifiable health information.
- The federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to CMS, information related to payments or other transfers of value made to physicians, and further requires applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by physicians and their immediate family members. The SUPPORT for Patients and Communities Act expanded the scope of reporting, such that beginning January 1, 2021 companies must also report payments and transfers of value provided to other types of healthcare professionals. Failure to submit timely, accurately and completely the required information for all covered payments, transfers of value and ownership or investment interests may result in civil monetary penalties.; and
- Many state and foreign law equivalents of each of the above federal laws, such as: anti-kickback and false claims laws which may apply to items or services reimbursed by any third party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; state and local laws that require the registration of pharmaceutical sales representatives; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

In addition, the European Union ("EU") has established its own data security and privacy legal framework, including but not limited to Directive 95/46/EC (the "Data Protection Directive"). The European General Data Protection Regulation ("GDPR") took effect on May 25, 2018, which contains new provisions specifically directed at the processing of health information, higher sanctions and extra-territoriality measures intended to bring non-EU companies under the regulation. We anticipate that over time we may expand our business operations to include additional operations in the EU, including potentially conducting preclinical and clinical trials. With such expansion, we would be subject to increased governmental regulation in the EU countries in which we might operate, including regulation due to the GDPR.

If our operations are found to be in violation of any of the laws described above or any other governmental regulations or laws that apply to us, we may be subject to substantial penalties, including, without limitation, civil, criminal and administrative penalties, damages, fines, possible exclusion from Medicare, Medicaid and other government healthcare programs, additional reporting requirements and/or oversight, particularly if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance, disgorgement, imprisonment, contractual damages, reputational harm, diminished profits and future earnings, and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Recent and future healthcare legislation may further impact our business operations.

The United States and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our products profitably. Among policymakers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (the "ACA") was enacted, which made a number of substantial changes in the way healthcare is financed by both governmental

and private insurers. The ACA included a number of provisions that may reduce the profitability of drug products, including revising the rebate methodology for covered outpatient drugs under the Medicaid Drug Rebate Program, extending Medicaid rebates to individuals enrolled in Medicaid managed care plans, and requiring drug manufacturers to pay an annual fee based on their market share of prior year total sales of branded programs to certain federal health care programs.

There remain executive, legal and political challenges to certain aspects of the ACA. For example, in December 2017, Congress repealed the tax penalty for an individual's failure to maintain ACA-mandated health insurance as part of the Tax Cuts and Jobs Act of 2017 (the "Tax Act"), effective January 1, 2019. On December 14, 2018, a Texas U.S. District Court Judge ruled that the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Act. On December 18, 2019, the U.S. Court of Appeals for the Fifth Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. On March 2, 2020, the U.S. Supreme Court granted the petitions for writs of certiorari to review the case and held oral arguments on November 10, 2020. Although the U.S. Supreme Court has not yet ruled on the constitutionality of the ACA, on January 28, 2021, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through May 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructs certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare. It is unclear how the U.S. Supreme Court ruling, other such litigation, and the healthcare reform measures of the Biden administration will impact the ACA and our operations.

In addition, other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. On August 2, 2011, the Budget Control Act of 2011 among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of 2% per fiscal year, which started in April 2013, and, due to subsequent legislative amendments, will remain in effect through 2030 unless additional Congressional action is taken, except for a temporary suspension from May 1, 2020 through March 31, 2021 due to the COVID-19 pandemic. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, also reduced Medicare payments to several categories of healthcare providers. Additionally, the Bipartisan Budget Act of 2018, among other things, amended the ACA to increase from 50% to 70% the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole."

Further, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level, Congress and the Biden administration may seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, to encourage importation from other countries and bulk purchasing.

We expect that healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria and lower reimbursement, and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private payors.

We cannot predict what healthcare reform initiatives may be adopted in the future. Further federal, state and foreign legislative and regulatory developments are likely, and we expect ongoing initiatives to increase pressure on drug pricing. Such reforms could have an adverse effect on anticipated revenues from product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop product candidates.

We face potential product liability, and, if successful claims are brought against us, we may incur substantial liability and costs.

The use of our product candidates in clinical trials and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our product candidates or products. For example, unanticipated adverse effects could result from the use of our future products or product candidates which may result in a potential product liability claim. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- impairment of our business reputation;
- withdrawal of clinical trial participants;
- costs due to related litigation;
- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- the inability to commercialize our product candidates; and
- decreased demand for our products approved for commercial sale.

We have a limited amount of product liability insurance relating to the use of our therapeutics in clinical trials. However, such insurance coverage may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive and in the future we may not be able to obtain or maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If and when we obtain marketing approval for product candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated adverse effects. A successful product liability claim or series of claims brought against us could cause our share price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business.

Cyber security risks and the failure to maintain the confidentiality, integrity, and availability of our computer hardware, software, and Internet applications and related tools and functions could result in damage to our reputation and/or subject us to costs, fines or lawsuits.

Our business requires manipulating, analyzing and storing large amounts of data. In addition, we rely on a global enterprise software system to operate and manage our business. We also maintain personally identifiable information about our employees and participants in our clinical trials. Our business therefore depends on the continuous, effective, reliable, and secure operation of our computer hardware, software, networks, Internet servers, and related infrastructure. To the extent that our hardware or software malfunctions or access to our data by internal research personnel is interrupted, our business could suffer. The integrity and protection of our employee and company data is critical to our business and our employees and participants in our clinical trials have a high expectation that we will adequately protect their personal information. The regulatory environment governing information, security and privacy laws is increasingly demanding and continues to evolve. Maintaining compliance with applicable security and privacy regulations may increase our operating costs. Although our computer and communications hardware is protected through physical and software safeguards, it is still vulnerable to fire, storm, flood, power loss, earthquakes, telecommunications failures, physical or software break-ins, software viruses, and similar events. These events could lead to the unauthorized access, disclosure and use of non-public information. The techniques used by criminal elements to attack computer systems are sophisticated, change frequently and may originate from less regulated and remote areas of the world. As a result, we may not be able to address these techniques proactively or implement adequate preventative measures. If our computer systems are compromised, we could be subject to fines, damages, litigation and enforcement actions, and we could lose trade secrets, the occurrence of which could harm our business. In addition, any sustained disruption in internet access provided by other companies could harm our business.

Business interruptions could delay us in the process of developing our future products.

Our headquarters are located in San Diego, California. We are vulnerable to natural disasters such as earthquakes, mudslides, floods and wildfires, as well as other events that could disrupt our operations. We do not carry insurance for earthquakes or other natural disasters and we may not carry sufficient business interruption insurance to compensate us for losses that may occur. Any losses or damages we incur could have a material adverse effect on our business operations.

RISKS RELATED TO OUR COMMON STOCK

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

Under the Tax Cuts and Jobs Act, as modified by the Coronavirus Aid, Relief, and Economic Security Act, or CARES Act, U.S. federal net operating losses ("NOLs") incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such federal NOLs is limited. It is uncertain if and to what extent various states will conform to the Tax Cuts and Jobs Act. To the extent that we continue to generate taxable losses for United States federal income tax purposes, unused NOLs will carry forward to offset future taxable income (subject to any applicable limitations), if any. Under Sections 382 and 383 of the Internal Revenue Code, as amended, if a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change NOLs and other pre-change tax attributes (such as research tax credits) to offset its post-change income may be significantly limited. We believe we may have triggered an "ownership change" limitation; however, we have not completed a study in accordance with Sections 382 and 383 of the Code to determine whether this ownership change has occurred or what the possible effects of an ownership change would be on our ability to use NOLs. We may also experience ownership changes in the future as a result of subsequent shifts in our share ownership. As a result, if we earn net taxable income, our ability to use our pre-change NOL carryforwards to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. Similar provisions of U.S. state tax law may also apply to limit our use of accumulated state tax attributes, including our state NOLs. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. As a result, even if we attain profitability, we may be unable to use a material portion of our NOLs and other tax attributes, which could negatively impact our future cash flows.

We do not intend to pay dividends on our common stock so any returns to investors will be limited to the value of our shares.

We have never declared or paid any cash dividends on our common stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future.

GENERAL RISK FACTORS

The market price of our common stock has been, and is expected to continue to be, highly volatile and investors may not be able to resell shares at or above the price at which they purchased the shares.

The trading price of our common stock is likely to continue to be volatile. Our share price could be subject to wide fluctuations in response to a variety of factors, including but not limited to the following factors:

- adverse results or delays in preclinical studies or clinical trials;
- inability to obtain additional funding;
- any delay in filing an application for authorization to commence a clinical trial of, or for authorization or approval to market, any of our product candidates and any adverse development or perceived adverse development with respect to the FDA's review of that IND or BLA;
- failure to maintain our existing strategic alliances or enter into new alliances;
- failure of our strategic alliance partners to elect to develop and commercialize product candidates under our alliance agreements or the termination of any programs under our alliance agreements;
- failure by us or our licensors and strategic alliance partners to prosecute, maintain or enforce our intellectual property rights;
- failure to successfully and timely develop and commercialize our product candidates;

- changes in laws or regulations applicable to our preclinical and clinical development activities, product candidates or future products;
- inability to obtain adequate product supply for our product candidates or the inability to do so at acceptable prices;
- adverse regulatory decisions;
- introduction of new products, services or technologies by our competitors;
- failure to meet or exceed financial projections we may provide to the public;
- failure to meet or exceed the estimates and projections of the investment community;
- the perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us, our strategic alliance partners or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- additions or departures of key scientific or management personnel;
- significant lawsuits, including patent or licensing matters;
- changes in the market valuations of similar companies;
- sales of our common stock by us or our shareholders in the future; and
- trading volume of our common stock.

In addition, companies trading in the stock market in general, and Nasdaq in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance.

The requirements of being a publicly traded company may strain our resources and divert management's attention.

As a publicly traded company, we have incurred, and will continue to incur, significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act, as well as rules subsequently implemented by the SEC and Nasdaq have imposed various requirements on public companies. In July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act (the "Dodd-Frank Act") was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas such as "say on pay" and proxy access. Shareholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain our current levels of such coverage.

Failure to comply with these requirements could subject us to enforcement actions by the SEC, divert management's attention, damage our reputation, and adversely affect our business, results of operations, or financial condition. In particular, if our independent registered public accounting firm is not able to render the required unqualified attestation, it could result in a loss of investor confidence in the accuracy, reliability, and completeness of our financial reports. Our loss of "emerging growth company" status and our current status as a "large accelerated filer," and compliance with these additional requirements will require management to expend additional time while also condensing the time frame available to comply with certain requirements, which can be expected to further increase our legal and financial compliance costs.

If we are subject to securities class action litigation, we would incur substantial costs and diversion of management's attention.

We may be at risk of securities class action litigation. This risk is especially relevant for us due to our dependence on positive clinical trial outcomes and regulatory approvals of each of our product candidates. In the past, medicines, biotechnology and pharmaceutical companies have experienced significant stock price volatility,

particularly when associated with binary events such as clinical trials results and product approvals. If we face such litigation, it could result in substantial costs, divert management's attention and resources, and have a very material adverse effect on our business, operating results and prospects.

Sales of a substantial number of shares of our common stock in the public market by our existing shareholders could cause our share price to fall.

If our existing shareholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline significantly. In particular, the former shareholders, warrant holders and noteholders of Arcturus Therapeutics, Inc. received an aggregate of 6,631,712 of our common stock pursuant to the merger with Alcobra Ltd. in an unregistered transaction, which shares may be sold pursuant to Rule 144 under the Securities Act of 1933, as amended (the "Securities Act"). Those shareholders are eligible to sell those shares in the public market without restriction, except for shareholders who are deemed our "affiliates" under Rule 144 under the Securities Act. In addition, common stock that is either subject to outstanding options or reserved for future issuance under our employee benefit plans, may become eligible for sale in the public market to the extent permitted by vesting schedules and Rule 144 under the Securities Act. If common stock is sold, or if it is perceived that it will be sold, in the public market, that could cause the trading price to decline.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our shareholders and could cause our share price to fall.

We expect that significant additional capital will be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our shareholders may experience substantial dilution. Pursuant to our 2019 Omnibus Equity Incentive Plan, our management is authorized to grant options and other equity-based awards to our employees, directors and consultants. We may issue and sell additional shares of common stock, convertible securities or other equity securities in one or more capital-raising or other transactions at prices and in a manner we determine from time to time, any of which may result in material dilution to investors and/or our existing shareholders. New investors could also be issued securities with rights superior to those of our existing shareholders.

We may be unable to comply with the applicable continued listing requirements of Nasdaq.

Our common stock is currently listed on Nasdaq. In order to maintain this listing, we must satisfy minimum financial and other continued listing requirements and standards, including a minimum closing bid price requirement for our common stock of $1.00 per share. There can be no assurance that we will be able to comply with the applicable listing standards. For example, if we were to fail to meet the minimum bid price requirement for 30 consecutive business days, we could become subject to delisting. Although Nasdaq may provide us with a compliance period in which to regain compliance with the minimum bid price requirement, we may not be able to regain compliance within the period provided by Nasdaq. In order to regain compliance with such requirement, the closing bid price of our common stock would need to meet or exceed $1.00 per share for at least 10 consecutive business days during the compliance period. If we were not able to regain compliance within the allotted compliance period for this requirement or any other applicable listing standard, including any extensions that may be granted by Nasdaq, our common stock would be subject to delisting. In the event that our common stock is delisted from Nasdaq, liquidity will be reduced and the trading price of our common stock can be expected to decline immediately. If our common stock is not eligible for quotation or listing on another market or exchange, trading of our common stock could be conducted only in the over-the-counter market or on an electronic bulletin board established for unlisted securities such as the Pink Sheets or the OTC Bulletin Board. In such event, it could become more difficult to dispose of, or obtain accurate price quotations for our common stock and there would likely also be a reduction in our coverage by securities analysts and the news media, which could cause the price of our common stock to decline further.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

We have three properties located in San Diego, California. Our principal place of business is located at 10628 Science Center Drive, Suite 250, and consists of approximately 24,700 square feet of office space and laboratory space leased through March 2025. We have the right to extend this lease for an additional five-year term.

On February 16, 2020, we entered into a short-term lease for additional office and laboratory space located in close proximity to our main office at 10578 Science Center Drive, Suite 150. The additional space of approximately 11,750 square feet is leased through March 2025.

On February 26, 2021, we entered into a short-term lease for additional office and laboratory space located in close proximity to our main office at 10240 Science Center Drive, Suite 100. The additional space of approximately 4,312 square feet is leased for a term of twelve months. We have the right to extend this lease for an additional twelve months.

On September 29, 2021, we entered into a lease agreement for office, research and development, engineering and laboratory space located at 10285 Science Center Drive, San Diego, California. The additional space of approximately 43,234 square feet is leased for a term of 10 years and 8 months. The leased premises will serve as an addition to Arcturus' existing properties.

We believe that our properties are suitable for the conduct of our business.

Item 3. Legal Proceedings

From time to time, we may be involved in various legal proceedings and subject to claims that arise in the ordinary course of business. Although the results of litigation and claims are inherently unpredictable and uncertain, we are not currently a party to any legal proceedings.

On December 13, 2019, a former employee of the Company filed a complaint in San Diego County Superior Court, captioned Adonary Munoz v. Arcturus Therapeutics, Inc., et al, Case No. 37-2019-00066358-CU-PO-CTL. The lawsuit alleged sexual assault by an acquaintance of one of our employees and sought to hold the Company liable on a number of causes of action. On May 5, 2021, the parties settled the dispute, and the parties agreed to dismiss the legal proceedings. The settlement did not result in any material liability to the Company as the settlement payment was covered by the Company's insurance.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Holders of Common Stock

As of February 23, 2022, there were 14 holders of record of our common stock. As of such date, there were 26,375,002 shares of our common stock outstanding.

Dividends

We have never declared or paid any cash dividends on our common stock. We currently intend to retain all available funds and any future earnings to support our operations and finance the growth and development of our business. Any future determination related to our dividend policy will be made at the discretion of our board of directors and will depend upon, among other factors, our results of operations, financial condition, capital requirements, contractual restrictions, business prospects and other factors our board of directors may deem relevant.

Recent Sales of Unregistered Securities

None.

Issuer and Affiliated Purchaser – Purchases of Equity Securities

During the fiscal year 2018, we completed the sale of our intangible assets related to the ADAIR technology. Pursuant to the asset purchase agreement for ADAIR, we received a 30% ownership interest in the common stock of Vallon Pharmaceuticals, Inc. ("Vallon") in consideration for the sale of the ADAIR technology. Vallon completed an initial public offering and began trading on The Nasdaq Capital Market under the ticker "VLON" in February 2021. After this offering and other previous stock issuances of Vallon, Arcturus owns 843,750 shares of Vallon's total post-IPO 6,812,836 outstanding shares, or approximately 12%.

Item 6. Selected Financial Data

In accordance with Item 301 of Regulation S-K as amended effective February 10, 2021, we are omitting this disclosure.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

You should read the following discussion and analysis together with the consolidated financial statements and related notes included elsewhere herein.

This report includes forward-looking statements which, although based on assumptions that we consider reasonable, are subject to risks and uncertainties which could cause actual events or conditions to differ materially from those currently anticipated and expressed or implied by such forward-looking statements.

Overview

Arcturus is a late-stage global clinical messenger RNA medicines company focused on the development of infectious disease vaccines and significant opportunities within liver and respiratory rare diseases. In addition to our messenger RNA platform, our proprietary lipid nanoparticle delivery system, LUNAR®, has the potential to enable multiple nucleic acid medicines, and our proprietary self-amplifying mRNA technology (Self-Transcribing and Replicating RNA, or STARR™, technology) has the potential to provide longer-lasting RNA and sustained protein expression.

We are leveraging our proprietary LUNAR platform and our nucleic acid technologies to develop and advance a pipeline of mRNA-based vaccines and therapeutics for infectious diseases and rare genetic disorders with significant unmet medical needs. Our key proprietary technology has the potential to address the major hurdles in RNA development, namely the effective and safe delivery of RNA therapeutics to disease-relevant target tissues. We believe the versatility of our platform to target multiple tissues, its compatibility with various nucleic acid therapeutics, and our expertise in developing scalable manufacturing processes puts us in a leading position to deliver on the next generation of nucleic acid medicines.

During 2021, together with Vinbiocare, we advanced ARCT-154, our investigational next generation, self-amplifying mRNA-based vaccine for COVID-19, into a Phase 1/2/3 study in Vietnam, which is being funded by Vinbiocare. With Vinbiocare, we completed submission of regulatory documents to the Ministry of Health in Vietnam with respect to application for an Emergency Use Authorization for ARCT-154 (LUNAR-COV19).

Our activities since inception have consisted principally of performing research and development activities, clinical research activities, general and administrative activities and raising capital to fund those efforts. Our activities are subject to significant risks and uncertainties, including failing to secure additional funding before we achieve sustainable revenues and profit from operations. As of December 31, 2021, we had an accumulated deficit of $347.5 million.

Liquidity and Capital Resources

Overview

Since our inception, we have funded our operations principally with proceeds from the sale of capital stock and revenues earned through collaborative agreements. At December 31, 2021, we had $370.5 million in unrestricted cash and cash equivalents.

Pursuant to the Third Amendment to the Loan and Security Agreement with Western Alliance Bank (the "Loan"), the Bank agreed to make a term loan to us on October 30, 2019, in the amount of $15.0 million (the "Term Loan"). The Term Loan bears interest at a floating rate ranging from 1.25% to 2.75% above the prime rate. The amendment further provides that the Term Loan has a maturity date of October 30, 2023. In October of 2021, we entered into a Fifth Amendment to Loan Agreement which provided for a six month extension to the interest only period which moves the first principal payment to May 1, 2022.

Grants from the Economic Development Board of the Republic of Singapore

On March 4, 2020, we were awarded a grant ("Grant 1") from the Economic Development Board of the Republic of Singapore (the "EDB") to support the co-development of a potential COVID-19 vaccine program with the Duke-NUS Medical School. The Grant provides for up to S$14.0 million (approximately US$10.0 million using the exchange rate at the time the grant contract was entered into) in grants to support the development of the vaccine. The Grant has been paid in full by the EDB as a result of the achievement of certain milestones related to the progress of the development of the vaccine, as set forth in the award agreement. The funds received have been recognized as contra research and development expense. The parties are in continued negotiations with respect to amendments of Grant 1. Currently, we are liable for certain expenses during the program and are also subject to certain conditions including the requirement to pay an agreed upon royalty rate to Duke-NUS on future net sales of the LUNAR-COV19 vaccine candidate developed with Duke-NUS in markets or jurisdictions outside of Singapore.

On October 2, 2020, we were awarded another grant ("Grant 2") from the Singapore EDB to support the clinical development of a potential COVID-19 vaccine (ARCT-021). The grant provides for up to S$9.3 million (approximately US$6.7 million) to support the clinical development of the vaccine candidate for costs incurred in Singapore subject to certain conditions. The grant is paid in two installments upon the achievement of certain milestones related to the progress of the development of the vaccine candidate. We received the first installment of $3.6 million in the fourth quarter of 2020. A portion of the funds received were recognized as contra research and development expense as costs were incurred during the fourth quarter of 2020. As costs were incurred during fiscal year 2021, we recognized the remaining amount of the first installment as contra expense for Grant 2. The parties are in continued negotiations with respect to amendments of Grant 2 that could include initiation of a clinical trial for a variant COVID-19 vaccine.

Manufacturing Support Agreement

On November 7, 2020, we entered into a Manufacturing Support Agreement (the "Support Agreement") with the EDB. Pursuant to the Support Agreement, the EDB agreed to make a term loan (the "Singapore Loan") of S$62.1 million, subject to the satisfaction of customary deliveries, to support the manufacture of the LUNAR-COV19 vaccine candidate (ARCT-021). The EDB has agreed to an extension of the reconciliation period to March 31, 2022 with unused funds as of such date to be subsequently returned within thirty days, subject to any further agreed upon extension of the reconciliation date. The parties are in continued negotiations with respect to amendments of the Singapore Loan terms. Under current terms, (i) we are to provide a quarterly reconciliation report within forty-five days of each financial quarter end, (ii) we will provide a projection of expenditures through March 31, 2022 followed by an audited statement of actual expenditures through March 31, 2022 by June 30, 2022, (iii) we are to provide EDB with a right of first refusal on GMP manufacturing slots of the LUNAR-COV19 vaccine candidate up to an agreed-upon maximum amount, (iv) and the obligation to repay the Singapore Loan will be secured by an interest in the raw materials and manufacturing equipment purchased by us with the funds from the Singapore Loan in form and substance satisfactory to the EDB in its sole discretion. We elected to borrow the full amount available under the Support Agreement of S$62.1 million ($46.6 million) on January 29, 2021. As of December 31, 2021, we have reported a portion of the Singapore Loan as current to reflect a potential payment in fiscal year 2022. As of December 31, 2021, we reported a portion of the Singapore Loan as current to reflect a potential principal repayment of approximately 20.9 million Singapore dollars (US $15.2 million) in fiscal year 2022 based on amounts not used toward the manufacture of ARCT-021.

The Singapore Loan accrues interest at a rate of 4.5% per annum calculated on a daily basis. Subject to certain exceptions, the Singapore Loan is intended to be a limited recourse loan that will be repaid solely through a royalty payment of 10% of net sales proceeds of the LUNAR-COV19 vaccine candidate, up to the amount of the outstanding principal and interest under the Singapore Loan. However, all unpaid principal and interest under the Singapore Loan will be due and payable five years after draw date, if net sales of the LUNAR-COV19 vaccine exceed a certain minimum threshold during this five year period or we obtain clearance to sell the vaccine in specified jurisdictions. Unpaid principal and interest under the Singapore Loan will also become due and payable upon an event of default under the Support Agreement. The first vaccine sales, including the amount of net sales, shall be reported to EDB within 10 days of delivery and quarterly reports of aggregate vaccine sales, including net sales proceeds shall be provided within 30 days after quarter end.

The Singapore Loan is forgivable if we have not obtained regulatory approval by the final repayment date and net sales of LUNAR-COV19 are less than $100 million. If, any portion of the Singapore Loan is required to be forgiven pursuant to the terms of the Support Agreement, the EDB has the right to take ownership of certain raw

materials and equipment that were purchased by us with proceeds of the Singapore Loan (the "Specified Assets"). We entered into a security agreement (the "Security Agreement") for the benefit of the EDB to provide that repayment of the Singapore Loan and related obligations are secured by a lien on the Specified Assets.

In connection with the entry into the Support Agreement, we entered into a consent agreement with Western Alliance Bank (the "Bank") and an amendment to the Loan and Security Agreement, dated as of October 12, 2018, to exclude the Specified Assets from Western Alliance Bank's lien on certain assets.

Vinbiocare Agreement

On August 2, 2021, we announced an agreement with Vinbiocare, a member of Vingroup Joint Stock Company, to establish a manufacturing facility in Vietnam for the manufacture of our investigational COVID-19 vaccine program, for sale and use within Vietnam. In addition, Vinbiocare agreed to execute a phase 1/2/3 study in Vietnam.

Under the terms of the arrangement, Vinbiocare is building out a manufacturing facility in Vietnam, and we have provided to Vinbiocare access to proprietary technologies and processes for the manufacture of our investigational COVID-19 vaccine candidate. We also provided Vinbiocare with an exclusive license to manufacture the vaccines in Vietnam at the facility solely for distribution in Vietnam. The license and technology transfer applies toward drug product manufacturing but not toward mRNA drug substance manufacturing. Vinbiocare made an upfront payment of $40 million and is responsible for costs associated with the technology transfer. Vinbiocare will also pay for mRNA drug substance supplied by us and royalties on vaccines produced at the manufacturing facility.

General Financial Resources

A significant portion of our current cash balance of $370.5 million is expected to be utilized during fiscal year 2022 to fund (i) further progress of our COVID and FLU vaccine programs, (ii) the continued Phase 2 trial of ARCT-810, our LUNAR-OTC candidate, (iii) advances to our LUNAR-CF program toward submission of a CTA during the second half of 2022 and (iv) continued expansion of our platform and other general administrative activities.

We expect to receive in the near term significant data from studies of our COVID 19 vaccine and regulatory guidance which will determine our course of action with respect to the development and commercialization of our vaccine candidate. Commercialization of ARCT-154 will require significant additional funds. We are considering additional partnering opportunities to assist in these efforts. We cannot be certain that we will identify a partner or enter into an acceptable arrangement. We will continue to evaluate our business opportunities in a surgical manner to maximize our ability to develop approved products while making most efficient use of our available resources.

We entered into binding agreements with third party contract manufacturing organizations with upfront financial commitments of not less than $13 million.

Our future capital requirements are difficult to forecast and will depend on many factors that are out of our control. If we are unable to maintain sufficient financial resources, our business, financial condition and results of operations will be materially and adversely affected. There can be no assurance that we will be able to obtain additional needed financing on acceptable terms or at all. Additionally, equity or debt financings may have a dilutive effect on the holdings of our existing shareholders.

We expect to continue to incur additional losses for the foreseeable future, and we will need to raise additional debt or equity financing or enter into additional partnerships to fund development. Our ability to transition to profitability is dependent on identifying and developing successful mRNA drug and vaccine candidates. If we are not able to achieve planned milestones, incur costs in excess of our forecasts, or do not meet covenant requirements of our debt, we will need to reduce discretionary spending, discontinue the development of some or all of our programs, which will delay part of our development programs, all of which will have a material adverse effect on our ability to achieve our intended business objectives.

The following table shows a summary of our cash flows for the year ended December 31, 2021, 2020 and 2019 (in thousands):

	Year Ended December 31,		
(Dollars in thousands)	**2021**	**2020**	**2019**
Cash provided by (used in):			
Operating activities	$ (135,043)	$ (42,861)	$ (6,445)
Investing activities	(3,406)	(1,742)	(818)
Financing activities	48,016	436,145	41,907
Net increase (decrease) in cash and restricted cash	$ (90,433)	$ 391,542	$ 34,644

Operating Activities

Our primary use of cash is to fund operating expenses, which consist mainly of research and development and general and administrative expenditures. We have incurred significant expenses which have been partially offset by cash collected through our collaboration agreements. Cash collections under the collaboration agreements can vary from year to year depending on the terms of the agreement and work performed. These changes on cash flows primarily relate to the timing of cash receipts for upfront payments, reimbursable expenses and achievement of milestones under these collaborative agreements.

Net cash used in operating activities was $135.0 million on a net loss of $203.7 million for 2021, $42.9 million on a net loss of $72.1 million for 2020 and $6.4 million on a net loss of $26.0 million for 2019. Adjustments for non-cash charges which includes share-based compensation expense and depreciation and amortization were $37.4 million for 2021, $8.1 million for 2020 and $3.6 million for 2019. Changes in working capital resulted in adjustments to operating net cash inflows of $31.2 million for 2021, $21.2 million for 2020 and $16.0 million for 2019. The significant adjustments to operating net cash inflows for 2021 were primarily due to the agreement with Vinbiocare signed in the third quarter of 2021 along with increased accrued liabilities from LUNAR-COV19 and LUNAR-OTC (ARCT-810) clinical trial activities, which expenses were incurred as discussed below. Adjustments to operating net cash inflows for 2020 were primarily due to the supply agreement with Israeli MOH signed in the third quarter of 2020 along with increased accounts payable and accrued liabilities from LUNAR-COV19 and LUNAR-OTC (ARCT-810) clinical trial activities. Lastly, adjustments to operating net cash inflows for 2019 were primarily due to the third amendment to the collaboration agreement with Ultragenyx during the second quarter of 2019 along with increased accounts payable and accrued liabilities from LUNAR-OTC (ARCT-810).

Investing Activities

Net cash used in investing activities of $3.4 million for 2021, $1.7 million for 2020 and $0.8 million for 2019 reflected the acquisition of property and equipment.

Financing Activities

Net cash provided by financing activities of $48.0 million for 2021 consisted of net proceeds from the Singapore Loan of $46.6 million, proceeds from the exercise of stock options of $0.9 million and proceeds from the issuance of common stock related to our employee stock purchase plan of $0.5 million. Net cash provided by financing activities of $436.1 million for 2020 consisted of net proceeds from the issuance of common stock in three underwritten public offerings totaling $423.8 million, net proceeds of $9.6 million from the issuance of common stock to Ultragenyx upon the exercise of its option and proceeds from the exercise of stock options of $2.7 million. Net cash provided by financing activities of $41.9 million for 2019 consisted of net proceeds from the issuance of common stock of $15.5 million to Ultragenyx, net proceeds from the issuance of common stock of $21.3 million related to public offerings, net proceeds from long-term debt of $4.9 million, and proceeds from the exercise of stock options of $0.1 million.

Funding Requirements

We anticipate that we will continue to generate annual net losses for the foreseeable future, and we expect the losses to increase as we continue the development of, and seek regulatory approvals for, our product candidates, and begin commercialization of our products. As a result, we will require additional capital to fund our operations in order to support our long-term plans. We believe that our current cash position will be sufficient to meet our anticipated cash requirements through at least the next twelve months, assuming, among other things, no significant unforeseen

expenses, continued funding from partners at anticipated levels and our payment obligations continuing to follow the current maturity schedule under our long-term credit facility referenced in Note 7 to our consolidated financial statements in this Annual Report. We intend to seek additional capital through equity and/or debt financings, collaborative or other funding arrangements with partners or through other sources of financing. Should we seek additional financing from outside sources, we may not be able to raise such financing on terms acceptable to us or at all. If we are unable to raise additional capital when required or on acceptable terms, we may be required to scale back or discontinue the advancement of product candidates, reduce headcount, liquidate our assets, file for bankruptcy, reorganize, merge with another entity, or cease operations.

Our future funding requirements are difficult to forecast and will depend on many factors, including the following:

- the development of our LUNAR-COV19 and LUNAR-FLU vaccine candidates;
- the achievement of milestones under our strategic alliance agreements;
- maintaining and/or expanding our manufacturing network and capabilities;
- the terms and timing of any other strategic alliance, licensing and other arrangements that we may establish;
- the initiation, progress, timing and completion of preclinical studies and clinical trials for our product candidates;
- the number and characteristics of product candidates that we pursue;
- the outcome, timing and cost of regulatory approvals;
- delays that may be caused by changing regulatory requirements;
- the cost and timing of hiring new employees to support our continued growth;
- the costs involved in filing and prosecuting patent applications and enforcing and defending patent claims;
- the costs and timing of procuring clinical and commercial supplies of our product candidates;
- the costs and timing of establishing sales, marketing and distribution capabilities;
- the costs associated with legal proceedings;
- the costs associated with potential litigation related to collaboration agreements; and
- the extent to which we acquire or invest in businesses, products or technologies.

Results of Operations

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with the consolidated financial statements included in this Annual Report. Our historical results of operations and the year-to-year comparisons of our results of operations that follow are not necessarily indicative of future results.

Revenues

We enter into arrangements with pharmaceutical and biotechnology partners and government agencies that may contain upfront payments, license fees for research and development arrangements, research and development funding, milestone payments, option exercise and exclusivity fees and royalties on future sales. The following table summarizes our total revenues for the periods indicated (in thousands):

	Year Ended December 31,		
(Dollars in thousands)	**2021**	**2020**	**2019**
Revenue	$ 12,359	$ 9,539	$ 20,789

Revenue increased by $2.8 million during the year ended December 31, 2021 as compared to the year ended December 31, 2020. The increase in revenue primarily relates to $4.4 million of increased revenue related to the agreement with Vinbiocare executed in the third quarter of 2021. The overall increase in revenue was primarily offset by a decrease in revenue of $1.6 million from our existing collaboration partners.

Revenue decreased by $11.3 million during the year ended December 31, 2020 as compared to the year ended December 31, 2019. The decrease in revenue primarily relates to (i) $5.6 million of decreased revenue from reduced reimbursements associated with the CureVac co-development agreement that terminated in the second quarter of 2019, (ii) a decrease in one-time sublicense revenue from Synthetic Genomics as we recognized sublicense revenue of $3.3 million during the second quarter of 2019, (iii) a reduction of $1.9 million in revenue recognized related to the Ultragenyx Agreement, as we recorded a large amount of upfront payment amortization upon the execution of the Ultragenyx Third Amendment during the second quarter of 2019 and also recognized fewer research and development expense reimbursements related to the Ultragenyx Agreement during 2020, and (iv) lower research and development expense reimbursements recognized in 2020 related to other collaboration agreements, including with Providence Therapeutics and Takeda. The decrease in revenue was partially offset by increased revenue recognition related to the Janssen agreement and other collaboration agreements.

Operating Expenses

Our operating expenses consist of research and development and general and administrative expenses.

	Year Ended December 31,		
(Dollars in thousands)	**2021**	**2020**	**2019**
Operating expenses:			
Research and development, net	$ 173,760	$ 57,846	$ 33,640
General and administrative	41,451	23,217	12,662
Total	$ 215,211	$ 81,063	$ 46,302

The following table presents our total research and development expenses by category:

	Year Ended December 31,		
(Dollars in thousands)	**2021**	**2020**	**2019**
External pipeline development expenses:			
LUNAR-COV19, net	$ 100,626	$ 20,896	$ —
LUNAR-CF (ARCT-032), net	4,761	4,405	813
LUNAR-OTC (ARCT-810)	7,296	13,008	15,616
Discovery technologies	20,279	1,748	3,937
External platform development expenses:			
Partnered discovery technologies	812	1,515	1,894
Total development expenses	$ 133,774	$ 41,572	$ 22,260
Personnel related expenses	$ 34,861	$ 12,824	$ 9,005
Facilities and equipment expenses	5,125	3,450	2,375
Total research and development expenses, net	$ 173,760	$ 57,846	$ 33,640

Research and Development Expenses, net

Our research and development expenses consist primarily of external manufacturing costs, in-vivo research studies and clinical trials performed by contract research organizations, clinical and regulatory consultants, personnel related expenses and laboratory supplies related to conducting research and development activities. Costs to acquire and manufacture pre-launch inventory, mRNA supply for preclinical studies and clinical trials are recognized and included in external pipeline development expenses for the specific program.

LUNAR-COV19 expenses increased by $79.7 million during the year ended December 31, 2021 as compared to the year ended December 31, 2020. Expenses incurred were partially offset with funds awarded by the Singapore

EDB. The LUNAR-COV19 program did not commence until late in the first quarter of 2020 and is now in late-stage clinical trials.

LUNAR-CF expenses were $4.8 million in the year ended December 31, 2021, $4.4 million in the year ended December 31, 2020 and $0.8 million in the year ended December 31, 2019. Expenses incurred were partially offset with funds awarded by the CFF. The increase in LUNAR-CF expenses was due primarily to increased research and development cost incurred in association with the amendment to the CFF Agreement executed in July 2019, and we expect that our development efforts and associated costs will increase over the next several years as the LUNAR-CF program moves toward expected CTA submission in the second half of 2022.

LUNAR-OTC expenses were $7.3 million for the year ended December 31, 2021, $13.0 million for the year ended December 31, 2020 and $15.6 million for the year ended December 31, 2019. The decreases for each year are related to slower than expected recruiting for the ARCT-810 clinical trial caused in part by the ongoing Covid environment.

Discovery technologies represents our efforts to expand our product pipeline and are expected to increase in the near future. Discovery technology expenses were $20.3 million in the year ended December 31, 2021, $1.7 million in the year ended December 31, 2020 and $3.9 million in the year ended December 31, 2019. The increase in 2021 when compared to 2020 is primarily due to increased investment in new capabilities. Further, in the first quarter of 2021, we acquired an exclusive license from Alexion Pharmaceuticals to certain intellectual property for approximately $5.0 million of our common stock, which we expensed in 2021. The decrease in discovery technology expenses from 2019 to 2020 was due to focusing our efforts on the advancement of our LUNAR-OTC and LUNAR-COV19 programs.

Partnered discovery technologies expenses were $0.8 million in the year ended December 31, 2021, $1.5 million in the year ended December 31, 2020 and $1.9 million in the year ended December 31, 2019. The decreases in partnered discovery technologies expenses from 2020 to 2021 and 2019 to 2020 were primarily caused by decreased activity in rare disease targets and a greater focus on vaccine technology. We expect partnered discovery technologies expenses to fluctuate based on the needs of our collaboration partners.

Personnel related expenses, net of funds received from CFF and the Singapore EDB, were $34.9 million in the year ended December 31, 2021, $12.8 million in the year ended December 31, 2020 and $9.0 million in the year ended December 31, 2019. The increases were associated with increased headcount costs necessary to advance our external pipeline, platform and clinical trial efforts as well as increased share-based compensation expense.

Facilities and equipment expenses were $5.1 million in the year ended December 31, 2021, $3.5 million in the year ended December 31, 2020 and $2.4 million in the year ended December 31, 2019. The increases resulted primarily from higher rent and related costs associated with an additional lease that we entered into in February 2020. We expect that the facility and equipment expenses will increase in 2022 as we have added an additional facility in the second quarter of 2022 in order to support our research and development activities.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and related benefits for our executive, administrative and accounting functions and professional service fees for legal and accounting services as well as other general and administrative expenses.

General and administrative expenses were $41.5 million in the year ended December 31, 2021, $23.2 million in the year ended December 31, 2020 and $12.7 million in the year ended December 31, 2019. The increases resulted primarily from personnel expense due to increased headcount and increased share-based compensation expense. We expect general and administrative expenses to increase in 2022 as we expand our headcount, facilities and professional services to execute our business plan.

Finance income (expense), net

	Year Ended December 31,		
(Dollars in thousands)	**2021**	**2020**	**2019**
Finance income (expense), net:			
Interest income	$ 753	$ 470	$ 408
Interest expense	(2,674)	(831)	(854)
Total	$ (1,921)	$ (361)	$ (446)

Interest income is generated on cash and cash equivalents. The increases in interest income from 2020 to 2021 and from 2019 to 2020 resulted from increased interest on bank deposits due to higher cash balances, partially offset by lower interest rates earned.

Interest expense during the year ended December 31, 2021 was incurred in conjunction with our Loan and Security Agreement with Western Alliance Bank and the Singapore Loan. The increase in interest expense during 2021 as compared to the prior year period was primarily a result of additional accrued interest expense related to the Singapore Loan that was funded in January 2021. Interest expense was relatively flat for the year ended 2020 as compared to 2019 and was related to the Loan and Security Agreement with Western Alliance Bank.

Critical Accounting Policies and Estimates

We prepare our consolidated financial statements in conformity with accounting principles generally accepted in the United States ("U.S. GAAP"). As such, we make certain estimates, judgments and assumptions that we believe are reasonable, based upon information available to us. These judgments involve making estimates about the effect of matters that are inherently uncertain and may significantly impact our results of operations and financial condition. We describe our significant accounting policies more fully in Note 2 to our consolidated financial statements for the year ended December 31, 2021. In the following paragraphs, we describe the specific risks associated with these critical accounting policies and we caution that future events may not reflect exactly as one may expect, and that best estimates may require adjustment.

The following are our significant accounting policies which we believe are the most critical to aid in fully understanding and evaluating our reported financial results.

Revenue Recognition

Research and development revenue under collaborative agreements

We recognize research and development revenue from several collaboration agreements. Our collaboration agreements typically contain promised goods and services, including technology licenses or options to obtain technology licenses, research and development services, and manufacturing services. Upon entering into a collaboration agreement, we are required to make the following judgments:

Identifying the performance obligations contained in the agreement

Our assessment of what constitutes a separate performance obligation requires us to apply judgment. Specifically, we are required to identify which goods and services we are required to provide under the contract are distinct, if any.

Determining the transaction price, including any variable consideration

To determine the transaction price, we review the amount of consideration we are eligible to earn under the agreement. We do not typically include any payments we may receive in the future in our initial transaction price since the payments are typically not probable because they are contingent upon certain future events.

We are required to reassess the total transaction price at each reporting period to determine if we should include additional payments that have become probable in the transaction price.

Allocating the transaction price to each of our performance obligations

If we were to allocate the transaction price to more than one performance obligation, we would make estimates of the relative stand-alone selling price of each performance obligation, as it is not typical for us to sell our goods or services on a stand-alone basis. The estimate of the relative stand-alone selling price would require us to make significant judgments. To date, we have not entered into a collaboration agreement with more than one performance obligation.

The research and development revenue we recognize each period is comprised of several types of revenue, including amortization from upfront payments, milestone payments, option exclusivity fees and other services. Each of these types of revenue require us to make various judgments and estimates.

Amortization from Upfront Payments

For certain agreements, we recognize revenue from the amortization of upfront payments as we perform research and development, technology transfer and consulting services. We use an input method to estimate the amount of revenue to recognize each period. This method requires us to make estimates of the total costs we expect to incur in order to complete our promised research and development services or the total length of time it will take us to complete our promised research and development services. If we change our estimates, we may have to adjust our revenue.

Milestone Payments

When recognizing revenue related to milestone payments, we typically judge and estimate whether the milestone payment is probable (discussed in detail above under “Determining the transaction price, including any variable consideration”).

Research and Development Expenses, Including Clinical Trial Accruals/Expenses

Research and development costs consist of salaries and benefits, including related stock-based compensation, laboratory supplies and facility costs, as well as fees paid to other entities that conduct certain research and development activities on our behalf, such as clinical research organizations, or CROs, and contract manufacturing organizations, or CMOs. Research and development costs are expensed as incurred.

Clinical trial expenses are a significant component of research and development expenses, and we outsource a significant portion of these clinical trial activities to third parties. Third-party clinical trial expenses include investigator fees, site and patient costs, CRO costs, and costs for central laboratory testing and data management. The accrual for site and patient costs includes inputs such as estimates of patient enrollment, patient cycles incurred, clinical site activations, and other pass-through costs. These inputs are required to be estimated due to a lag in receiving the actual clinical information from third parties. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected on the balance sheets as prepaid assets or accrued expenses. These third-party agreements are generally cancelable, and related costs are recorded as research and development expenses as incurred. Non-refundable advance clinical payments for goods or services that will be used or rendered for future research and development activities are recorded as a prepaid asset and recognized as expense as the related goods are delivered or the related services are performed. When evaluating the adequacy of the accrued expenses, we analyze progress of the studies, including the phase or completion of events, invoices received and contracted costs. We make estimates of our accrued balances as of each balance sheet date based on facts and circumstances known to our internal personnel at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. Significant judgments and estimates may be made in determining the accrued balances at the end of any reporting period. Actual results could differ from the estimates made. Our historical clinical accrual estimates have not been materially different from our actual costs.

Off-balance sheet arrangements

None.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Our primary exposure to market risk is interest income and expense sensitivity, which is affected by changes in the general level of United States interest rates. Due to the nature of our investments and term loan, we believe that we are not subject to any material market risk exposure. We do not have any foreign currency or other derivative financial instruments.

Item 8. Financial Statements and Supplementary Data

The consolidated financial statements and related financial statement schedules required to be filed are listed in the Index to Consolidated Financial Statements and are incorporated herein and in Item 15 of Part IV of this Annual Report on Form 10-K.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our periodic and current reports that we file with the SEC is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our principal executive officer and our principal financial officer, as appropriate, to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable and not absolute assurance of achieving the desired control objectives. In reaching a reasonable level of assurance, management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures. In addition, the design of any system of controls is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions; over time, controls may become inadequate because of changes in conditions, or the degree of compliance with policies or procedures may

deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

As of December 31, 2021, our management, with the participation of our Chief Executive Officer, Chief Financial Officer and Principal Accounting Officer, has evaluated the effectiveness of the design and operation of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed in the reports we file or submit under the Exchange Act is accumulated and communicated to management, including our Chief Executive Officer, Chief Financial Officer and Principal Accounting Officer, as appropriate, to allow timely decisions regarding required disclosure. Based on this evaluation, our Chief Executive Officer, Chief Financial Officer and Principal Accounting Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2021.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Exchange Act Rules 13a-15(f) and 15(d) -15(f) as a process designed by, or under the supervision of, our Chief Executive Officer, Chief Financial Officer and Principal Accounting Officer to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with U.S. generally accepted accounting principles.

Because of inherent limitations, internal controls over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risks that controls may become inadequate because of changes in conditions or that the degree of compliance with the policies or procedures may deteriorate.

As of December 31, 2021, our management assessed the effectiveness of our internal control over financial reporting using the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control-Integrated Framework (2013). In adopting the 2013 Framework, management assessed the applicability of the principles within each component of internal control and determined whether or not they have been adequately addressed within the current system of internal control and adequately documented. Based on this assessment, management, under the supervision and with the participation of our Chief Executive Officer, Chief Financial Officer and Principal Accounting Officer, concluded that, as of December 31, 2021, our internal control over financial reporting was effective based on those criteria.

The effectiveness of our internal control over financial reporting as of December 31, 2021 has been audited by Ernst & Young LLP, an independent registered public accounting firm, as stated in its report, which is included herein.

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Arcturus Therapeutics Holdings Inc.

Opinion on Internal Control over Financial Reporting

We have audited Arcturus Therapeutics Holdings Inc. and its Subsidiaries' internal control over financial reporting as of December 31, 2021, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), (the COSO criteria). In our opinion, Arcturus Therapeutics Holdings Inc. and its Subsidiaries (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2021, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2021 and 2020, the related consolidated statements of operations and comprehensive loss, changes in stockholders' equity, and cash flows, for each of the three years in the period ended December 31, 2021, and the related notes and our report dated February 28, 2022 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Ernst & Young LLP

San Diego, California

February 28, 2022

Changes in Internal Control Over Financial Reporting.

An evaluation was also performed under the supervision and with the participation of our management, including our Chief Executive Officer, Chief Financial Officer and Principal Accounting Officer of any changes in our internal control over financial reporting that occurred during our last fiscal quarter and that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting. There were no changes in our internal control over financial reporting identified in management's evaluation pursuant to Rules 13a-15(d) or 15d-15(d) of the Exchange Act during the quarter ended December 31, 2021 that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

Information required by this item will be contained in our Definitive Proxy Statement for our 2022 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the Securities and Exchange Commission within 120 days of December 31, 2021. Such information is incorporated herein by reference.

Item 11. Executive Compensation

Information required by this item will be contained in our Definitive Proxy Statement for our 2022 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the Securities and Exchange Commission within 120 days of December 31, 2021. Such information is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

Information required by this item will be contained in our Definitive Proxy Statement for our 2022 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the Securities and Exchange Commission within 120 days of December 31, 2021. Such information is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence

Information required by this item will be contained in our Definitive Proxy Statement for our 2022 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the Securities and Exchange Commission within 120 days of December 31, 2021. Such information is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services

Information required by this item will be contained in our Definitive Proxy Statement for our 2022 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the Securities and Exchange Commission within 120 days of December 31, 2021. Such information is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules

(a)

(1) The information required by this item is included in Item 8 of Part II of this Annual Report.;

(2) Financial statement schedules not listed above have been omitted because information required to be set forth therein is not applicable, not required, or the information required by such schedules is shown in the consolidated financial statements or the notes thereto.

(3) See the exhibit index preceding the signature pages to this Annual Report, which is incorporated by reference herein.

(b) See the exhibit index preceding the signature pages to this Annual Report, which is incorporated by reference herein.

(c) Not applicable.

Item 16. Form 10-K Summary

None.

Exhibit Index

Exhibit Number	Description
1.1	Underwriting Agreement, dated December 7, 2020, by and among Arcturus Therapeutics Holdings Inc., Piper Sandler & Co., Guggenheim Securities, LLC and Wells Fargo Securities, LLC. Incorporated by reference to Exhibit 1.1 to Current Report on Form 8-K filed on December 8, 2020 (File No. 001-38942).
3.1	Certificate of Incorporation. Incorporated by reference to Annex B to the proxy statement/prospectus which forms part of the Registration Statement on Form S-4 filed on March 18, 2019 (File No. 333-230353).
3.2	Certificate of Amendment, dated November 25, 2020. Incorporated by reference to Exhibit 3.1 to Form 8-K filed on November 25, 2020 (File No. 001-38942).
3.3	Bylaws of Arcturus Therapeutics Holdings Inc. Incorporated by reference to Exhibit 3.2 to the Company's Registration Statement on Form S-3, filed with the SEC on May 8, 2020 (File No. 333-238139).
4.1*	Description of Registrant's Securities.
10.1†	Form of Indemnification Agreement. Incorporated by reference to Exhibit 10.1 to the Company's Annual Report on Form 10-K for the year ended December 31, 2019 filed on March 16, 2020 (File No. 001-38942).
10.2†	Amended and Restated 2019 Omnibus Equity Incentive Plan. Incorporated by reference Exhibit 4.3 to the Registration Statement on Form S-8 filed on August 5, 2020 (File No. 001-38942).
10.3†	Arcturus Therapeutics Ltd. Amended and Restated Compensation Policy for Company Office Holders. Incorporated by reference to Exhibit 99.2 to the Company's Report of Foreign Private Issuer on Form 6-K filed on July 27, 2018 (File No. 001-35932).
10.4**	Loan and Security Agreement, dated October 12, 2018, by and between Western Alliance Bank and Arcturus Therapeutics, Inc. Incorporated by reference to Exhibit 10.1 to the Company's Report of Foreign Private Issuer on Form 6-K filed on October 15, 2018 (File No. 001-35932).
10.5**	Amended and Restated Amendment to Development and Option Agreement, dated as of September 28, 2018, by and between CureVac AG and Arcturus Therapeutics Inc. Incorporated by reference to Exhibit 99.2 to the Company's Report of Foreign Private Issuer on Form 6-K filed on October 1, 2018 (File No. 001-35932).
10.6**	Research Collaboration and License Agreement, by and between Arcturus Therapeutics, Inc. and Janssen Pharmaceuticals, Inc., dated October 18, 2017. Incorporated by reference to Exhibit 4.7 to Form 20-F filed on May 14, 2018 (File No. 001-35932).
10.7**	Research and Exclusive License Agreement, by and between Arcturus Therapeutics, Inc. and Synthetic Genomics, Inc., effective October 24, 2017. Incorporated by reference to Exhibit 4.8 to Form 20-F filed on May 14, 2018 (File No. 001-35932).
10.8**	Research Agreement, by and between Arcturus Therapeutics, Inc. and Millennium Pharmaceuticals, Inc., a wholly-owned subsidiary of Takeda Pharmaceutical Company Limited, effective December 6, 2016, as amended December 21, 2017. Incorporated by reference to Exhibit 4.9 to Form 20-F filed on May 14, 2018 (File No. 001-35932).
10.9**	Research Collaboration and License Agreement, by and between Arcturus Therapeutics, Inc. and Ultragenyx Pharmaceutical Inc., entered into as of October 26, 2015, as amended October 17, 2017 and April 20, 2018. Incorporated by reference to Exhibit 4.10 to Form 20-F filed on May 14, 2018 (File No. 001-35932).

Exhibit Number	Description
10.10**	Third Amendment to Research Collaboration and License Agreement, by and between Arcturus Therapeutics, Inc. and Ultragenyx Pharmaceutical Inc., effective June 18, 2019. Incorporated by reference to Exhibit 10.2 to Form 8-K filed on June 20, 2019 (File No. 001- 38942).
10.11**	Letter Agreement, by and between Arcturus Therapeutics, Inc. and the Cystic Fibrosis Foundation, dated May 16, 2017. Incorporated by reference to Exhibit 4.11 to Form 20-F filed on May 14, 2018 (File No. 001-35932).
10.12**	Amendment No. 2 to Letter Agreement, by and between Arcturus Therapeutics, Inc. and the Cystic Fibrosis Foundation, dated August 1, 2019. Incorporated by reference to Exhibit 10.16 to Form 10-Q filed on August 14, 2019.
10.13**	Development and Option Agreement, by and between Arcturus Therapeutics, Inc. and CureVac AG, dated January 1, 2018, as amended May 3, 2018. Incorporated by reference to Exhibit 4.12 to Form 20-F filed on May 14, 2018 (File No. 001-35932).
10.14**	Third Amendment to Development and Option Agreement, by and between Arcturus Therapeutics, Inc. and CureVac AG, dated July 26, 2019. Incorporated by reference to Exhibit 10.20 to Form 10-Q filed on August 14, 2019 (File No. 001-38942).
10.15**	Co-Development and Co-Commercialization Agreement, by and between Arcturus Therapeutics, Inc. and CureVac AG, dated January 1, 2018. Incorporated by reference to Exhibit 4.13 to Form 20-F filed on May 14, 2018 (File No. 001-35932).
10.16	Termination Agreement, by and between Arcturus Therapeutics, Inc. and CureVac AG, dated July 26, 2019. Incorporated by reference to Exhibit 10.21 to Form 10-Q filed on August 14, 2019 (File No. 001-38942).
10.17**	License Agreement, by and between Arcturus Therapeutics, Inc., as successor-in-interest to Marina Biotech, Inc., and Protiva Biotherapeutics Inc., dated as of November 28, 2012. Incorporated by reference to Exhibit 4.14 to Form 20-F/A filed on July 10, 2018 (File No. 001-35932).
10.18**	Patent Assignment and License Agreement, by and between Arcturus Therapeutics, Inc. and Marina Biotech, Inc., dated as of August 9, 2013. Incorporated by reference to Exhibit 4.15 to Form 20-F filed on May 14, 2018 (File No. 001-35932).
10.19	Share Exchange Agreement, dated as of February 11, 2019, by and between Arcturus Therapeutics Ltd. and Arcturus Therapeutics Holdings Inc. Incorporated by reference to Exhibit 10.13 to the Company's Annual Report on Form 10-K for the year ended December 31, 2018 filed on March 18, 2019 (File No. 001-35932).
10.20**	Amended and Restated Joint Venture, Research Collaboration and License Agreement, dated as of July 14, 2018 by and between Arcturus Therapeutics, Inc. and Providence Therapeutics, Inc. Incorporated by reference to Exhibit 10.14 to the Company's Amendment No. 1 to Annual Report on Form 10-K for the year ended December 31, 2018 filed on April 10, 2019 (File No. 001-35932).
10.21**	Research Collaboration Agreement, dated as of March 8, 2019 by and between Arcturus Therapeutics, Inc. and Millennium Pharmaceuticals, Inc., a wholly-owned subsidiary of Takeda Pharmaceutical Company Limited. Incorporated by reference to Exhibit 10.15 to the Company's Annual Report on Form 10-K for the year ended December 31, 2018 filed on March 18, 2019 (File No. 001-35932).
10.22	Lease Agreement, by and between Arcturus Therapeutics, Inc. and ARE-SD Region No. 44, LLC, dated October 4, 2017. Incorporated by reference to Exhibit 4.6 to Form 20-F filed on May 14, 2018 (File No. 001-35932).

Exhibit Number	Description
10.23	First Amendment to Lease Agreement, by and between Arcturus Therapeutics Holdings Inc. and ARE-SD Region No. 44, LLC dated February 1, 2020. Incorporated by reference to Exhibit 10.23 to the Company's Annual Report on Form 10-K for the year ended December 31, 2019 filed on March 16, 2020 (File No. 001-38942).
10.24**	Acceptance Letter, dated March 4, 2020, by and between Arcturus Therapeutics Holdings Inc. and the Economic Development Board of Singapore. Incorporated by reference to Exhibit 10.24 to the Company's Annual Report on Form 10-K for the year ended December 31, 2019 filed on March 16, 2020 (File No. 001-38942).
10.25**	Supply Agreement, dated August 17, 2020, by and between Arcturus Therapeutics, Inc. and the Israeli Ministry of Health. Incorporated by reference to Exhibit 10.32 to Quarterly Report on Form 10-Q filed on November 9, 2020 (File No. 001-38942).
10.26**	Manufacturing Support Agreement, dated November 7, 2020, by and between Arcturus Therapeutics Holdings Inc. and the Economic Development Board of Singapore. Incorporated by reference to Exhibit 10.33 to Quarterly Report on Form 10-Q filed on November 9, 2020 (File No. 001-38942).
10.27	Fourth Amendment to Loan and Security Agreement, dated December 1, 2020, by and between Arcturus Therapeutics, Inc. and Western Alliance Bank. Incorporated by reference to Exhibit 10.1 to Form 8-K filed on December 7, 2020 (File No. 001-38942).
10.28†	2020 Employee Stock Purchase Plan. Incorporated by reference to Exhibit 4.3 to Form S-8 filed on August 5, 2020 (File No. 001-38942).
10.29	Second Amendment to Lease, by and between Arcturus Therapeutics, Inc. and ARE-SD Region No. 44, LLC, dated November 13, 2020. Incorporated by reference to Exhibit 10.29 to the Company's Annual Report on Form 10-K for the year ended December 31, 2020 filed on March 1, 2020 (File No. 001-38942).
10.30	Third Amendment to Lease, by and between Arcturus Therapeutics, Inc. and ARE-SD Region No. 44, LLC, dated February 25, 2021. Incorporated by reference to Exhibit 10.30 to the Company's Annual Report on Form 10-K for the year ended December 31, 2020 filed on March 1, 2020 (File No. 001-38942).
10.31	Employment Agreement, dated as of June 13, 2019, between the Company and Joseph Payne. Incorporated by reference to Exhibit 10.1 to Form 8-K12B filed on June 14, 2019 (File No. 001-38942)
10.32	Employment Agreement, dated as of June 13, 2019, between the Company and Andy Sassine. Incorporated by reference to Exhibit 10.2 to Form 8-K12B filed on June 14, 2019 (File No. 001-38942)
10.33	Employment Agreement, dated as of June 13, 2019, between the Company and Dr. Padmanabh Chivukula. Incorporated by reference to Exhibit 10.3 to Form 8-K12B filed on June 14, 2019 (File No. 001-38942)
10.34	2021 Inducement Equity Incentive Plan. Incorporated by reference to Exhibit 4.1 to Form S-8 filed on October 20, 2021 (File No. 333-260391).
10.35	Fifth Amendment to Loan and Security Agreement, dated October 27, 2021, by and between Arcturus Therapeutics, Inc. and Western Alliance Bank. Incorporated by reference to Exhibit 10.34 to Form 10-Q filed on November 9, 2021 (File No. 001-38942).
10.36	Lease, by and between Arcturus Therapeutics, Inc. and TPSC IX, LLC, dated September 29, 2021. Incorporated by reference to Exhibit 10.35 to Form 10-Q filed on November 9, 2021 (File No. 001-38942).

Exhibit Number	Description
10.37	Third Amendment to Lease, by and between Arcturus Therapeutics, Inc. and ARE-SD Region No. 44, LLC, dated February 25, 2021. Incorporated by reference to Exhibit 10.30 to the Company's Annual Report on Form 10-K for the year ended December 31, 2020 filed on March 1, 2020 (File No. 001-38942).
10.38	Technology License and Technical Support Agreement, signed July 29, 2021 and effective July 30, 2021, by and between Arcturus Therapeutics, Inc. and Vinbiotech Research and Manufacture Joint Stock Company. Incorporated by reference to Exhibit 10.32 to Quarterly Report on Form 10-Q filed on August 10, 2021 (File No. 001-38942).
10.39	Framework Drug Substance Supply Agreement, signed July 29, 2021 and effective July 30, 2021, by and between Arcturus Therapeutics, Inc. and Vinbiotech Research and Manufacture Joint Stock Company. Incorporated by reference to Exhibit 10.33 to Quarterly Report on Form 10-Q filed on August 10, 2021 (File No. 001-38942).
10.40	Arcturus Therapeutics Holdings Inc. Severance Policy for Executives. Incorporated by reference to Exhibit 10.1 to Current Report on Form 8-K filed on April 26, 2021 (File No. 001-38942).
23.1*	Consent of Independent Registered Public Accounting Firm
24.1*	Power of Attorney (included on the signature page of this Annual Report).
31.1*	Certification by Principal Executive Officer pursuant to Rule 13a-14(a) or 15d-14(a) under the Securities Exchange Act of 1934, as amended.
31.2*	Certification by Principal Financial Officer pursuant to Rule 13a-14(a) or 15d-14(a) under the Securities Exchange Act of 1934, as amended.
31.3*	Certification by Principal Accounting Officer pursuant to Rule 13a-14(a) or 15d-14(a) under the Securities Exchange Act of 1934, as amended.
32.1*	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2*	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.3*	Certification of Principal Accounting Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101*	The following financial statements and footnotes from the Registrant's Annual Report on Form 10-K for the fiscal year ended December 31, 2021 formatted in Inline Extensible Business Reporting Language (Inline XBRL): 101.INS Inline XBRL Instance Document - the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document 101.SCH Inline XBRL Taxonomy Extension Schema
	101.CAL Inline XBRL Taxonomy Extension Calculation Linkbase
	101.DEF Inline XBRL Taxonomy Extension Definition Linkbase
	101.LAB Inline XBRL Taxonomy Extension Label Linkbase
	101.PRE Inline XBRL Taxonomy Extension Presentation Linkbase
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

* Filed herewith.

** Certain confidential portions of this exhibit have been redacted from the publicly filed document because such portions are (i) not material and (ii) would be competitively harmful if publicly disclosed.

Exhibit Number	Description

† Management compensatory plan, contract or arrangement.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

ARCTURUS THERAPEUTICS HOLDINGS INC.

Date: February 28, 2022

By: /s/ Joseph E. Payne
Name: Joseph E. Payne
Title: President, Chief Executive Officer and Director

The undersigned officers and directors of Arcturus Therapeutics Holdings Inc., hereby severally constitute and appoint Joseph E. Payne and Dr. Padmanabh Chivukula, and each of them individually, with full power of substitution and resubstitution, as their true and lawful attorneys and agents, to do any and all acts and things in their name and behalf in their capacities as directors and officers and to execute any and all instruments for them and in their names in the capacities indicated below, which said attorneys and agents, may deem necessary or advisable to enable said corporation to comply with the Securities Exchange Act of 1934, as amended, and any rules, regulations and requirements of the Securities and Exchange Commission, in connection with this Annual Report on Form 10-K, including specifically but without limitation, power and authority to sign for them or any of them in their names in the capacities indicated below, any and all amendments hereto, and they do hereby ratify and confirm all that said attorneys and agents, or either of them, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Annual Report has been signed below by the following persons on behalf of the Registrant and in the capacities and on the dates indicated.

Name	Title	Date
/s/ Joseph E. Payne **Joseph E. Payne**	President, Chief Executive Officer and Director *(principal executive officer)*	February 28, 2022
/s/ Dr. Peter Farrell **Dr. Peter Farrell**	Chairman of the Board	February 28, 2022
/s/ Andrew Sassine **Andrew Sassine**	Director and Chief Financial Officer *(principal financial officer)*	February 28, 2022
/s/ Dr. Magda Marquet **Dr. Magda Marquet**	Director	February 28, 2022
/s/ James Barlow **James Barlow**	Director	February 28, 2022
/s/ Edward Holmes **Edward Holmes**	Director	February 28, 2022
/s/ Jing Marantz **Jing Marantz**	Director	February 28, 2022
/s/ Keith C. Kummerfeld **Keith C. Kummerfeld**	Vice President of Finance and Corporate Controller *(principal accounting officer)*	February 28, 2022

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Arcturus Therapeutics Holdings Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Arcturus Therapeutics Holdings Inc. and its Subsidiaries (the Company) as of December 31, 2021 and 2020, the related consolidated statements of operations and comprehensive loss, changes in stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2021, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2021, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2021, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), and our report dated February 28, 2022 expressed an unqualified opinion thereon.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Accrued research and development expenses

Description of the Matter

At December 31, 2021, the Company incurred $173.8 million for research and development expenses and accrued $8.7 million for clinical trial expenses. As described in Note 2 to the consolidated financial statements, the Company records accruals for estimated costs of research and development activities, including contract services for clinical trials and related clinical manufacturing costs in connection with early discovery efforts. Clinical trial activities performed by third parties are accrued and expensed based upon estimates of the proportion of work completed over the life of the individual clinical trial and patient enrollment rates in accordance with agreements established with Clinical Research Organizations ("CROs") and clinical trial sites. Estimates are determined by reviewing contracts, vendor agreements and purchase orders, and through discussions with internal clinical personnel and external service providers as to the progress or stage of completion of trials or services and the agreed-upon fee to be paid for such services.

Auditing management's accounting for accrued research and development expenses, for which the Company has either not been invoiced or has not received information on the actual costs incurred, was especially challenging as evaluating the progress or stage of completion of the activities under the Company's research and development agreements is dependent upon information from internal clinical personnel and third party service providers and involves a high volume of data which is tracked in spreadsheets and other end user computing programs.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design and tested the operating effectiveness of controls over the accounting for accrued research and development expenses. For example, we tested controls over management's assessment and measurement of estimated accrued costs, including data inputs for study progress and remaining stages of completion under each study.

To test the Company's accrued research and development expenses, we obtained supporting evidence of the research and development activities performed for significant clinical trials. We attended internal clinical trial and project status meetings with accounting and clinical project managers to inspect the status of significant research and development activities. To assess the appropriate measurement of accrued research and development costs, our audit procedures included, among others, obtaining and inspecting significant agreements and agreement amendments, evaluating the Company's documentation of trial timelines, confirming amounts incurred to-date with third-party service providers, and testing a sample of transactions and comparing the costs against related invoices and contracts. We also tested a sample of subsequent payments to evaluate the completeness of the accrued expenses and compared the results to the current year accrual.

/s/ Ernst & Young, LLP

We have served as the Company's auditor since 2018.

San Diego, California

February 28, 2022

ARCTURUS THERAPEUTICS HOLDINGS INC. AND ITS SUBSIDIARIES
CONSOLIDATED BALANCE SHEETS
(in thousands, except par value information)

	As of December 31,	
	2021	**2020**
Assets		
Current assets:		
Cash and cash equivalents	$ 370,492	$ 462,895
Accounts receivable	3,367	2,125
Prepaid expenses and other current assets	5,102	2,769
Total current assets	378,961	467,789
Property and equipment, net	5,643	3,378
Operating lease right-of-use asset, net	5,618	5,182
Equity-method investment	515	—
Non-current restricted cash	2,077	107
Total assets	$ 392,814	$ 476,456
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 10,058	$ 10,774
Accrued liabilities	23,523	19,389
Current portion of long-term debt	22,474	1,250
Deferred revenue	43,482	18,108
Total current liabilities	99,537	49,521
Deferred revenue, net of current portion	19,931	12,512
Long-term debt, net of current portion	40,633	13,845
Operating lease liability, net of current portion	4,502	4,025
Total liabilities	164,603	79,903
Stockholders' equity:		
Common stock: $0.001 par value; 60,000 shares authorized; 26,372 shares issued and outstanding at December 31, 2021 and 26,192 shares issued and outstanding at December 31, 2020	26	26
Additional paid-in capital	575,675	540,343
Accumulated deficit	(347,490)	(143,816)
Total stockholders' equity	228,211	396,553
Total liabilities and stockholders' equity	$ 392,814	$ 476,456

The accompanying notes are an integral part of these consolidated financial statements.

ARCTURUS THERAPEUTICS HOLDINGS INC. AND ITS SUBSIDIARIES
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(in thousands, except per share data)

	Year Ended December 31,		
	2021	2020	2019
Revenue	$ 12,359	$ 9,539	$ 20,789
Operating expenses:			
Research and development, net	173,760	57,846	33,640
General and administrative	41,451	23,217	12,662
Total operating expenses	215,211	81,063	46,302
Loss from operations	(202,852)	(71,524)	(25,513)
Gain (loss) from equity-method investment	515	(263)	(32)
Foreign currency transaction gain	584	—	—
Finance expense, net	(1,921)	(361)	(446)
Net loss	(203,674)	(72,148)	(25,991)
Net loss per share, basic and diluted	$ (7.74)	$ (3.55)	$ (2.15)
Weighted-average shares outstanding, basic and diluted	26,317	20,305	12,069
Comprehensive loss:			
Net loss	$ (203,674)	$ (72,148)	$ (25,991)
Comprehensive loss	$ (203,674)	$ (72,148)	$ (25,991)

The accompanying notes are an integral part of these consolidated financial statements.

ARCTURUS THERAPEUTICS HOLDINGS INC. AND ITS SUBSIDIARIES
CONSOLIDATED STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY
(in thousands)

	Common Stock		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount			
BALANCE – December 31, 2018	**10,762**	**$ 214**	**$ 58,302**	**$ (44,874)**	**$ 13,642**
Net loss	—	—	—	(25,991)	(25,991)
Share-based compensation	—	—	1,982	—	1,982
Redomiciliation share exchange	(43)	(203)	203	—	—
Issuance of common stock to Ultragenyx, net of issuance costs	2,400	2	15,543	—	15,545
Issuance of common stock, net of issuance costs	1,995	2	21,276	—	21,278
Issuance of common stock upon exercise of stock options	24	—	139	—	139
Effect of adoption of ASU 2014-09	—	—	—	(803)	(803)
BALANCE – December 31, 2019	**15,138**	**$ 15**	**$ 97,445**	**$ (71,668)**	**$ 25,792**
Net loss	—	—	—	(72,148)	(72,148)
Share-based compensation	—	—	6,764	—	6,764
Issuance of common stock to Ultragenyx on option exercise	600	1	9,599	—	9,600
Issuance of common stock, net of issuance costs	10,059	10	423,809	—	423,819
Issuance of common stock upon exercise of stock options	395	—	2,726	—	2,726
BALANCE – December 31, 2020	**26,192**	**$ 26**	**$ 540,343**	**$ (143,816)**	**$ 396,553**
Net loss	—	—	—	(203,674)	(203,674)
Share-based compensation	—	—	28,915	—	28,915
Issuance of common stock related to acquired in-process research and development	75	—	5,000	—	5,000
Issuance of common stock upon exercise of stock options	92	—	902	—	902
Issuance of common stock under equity plans	13	—	515	—	515
BALANCE – December 31, 2021	**26,372**	**$ 26**	**$ 575,675**	**$ (347,490)**	**$ 228,211**

The accompanying notes are an integral part of these consolidated financial statements.

ARCTURUS THERAPEUTICS HOLDINGS INC. AND ITS SUBSIDIARIES
CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Year Ended December 31,		
	2021	**2020**	**2019**
OPERATING ACTIVITIES:			
Net loss	$ (203,674)	$ (72,148)	$ (25,991)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	1,193	882	684
Share-based compensation expense	28,915	6,764	1,982
Acquired in-process research and development expense	5,000	—	—
(Gain) loss from equity-method investment	(515)	263	25
Foreign currency transaction gain	(577)	—	—
Other non-cash expenses	3,382	162	873
Changes in operating assets and liabilities:			
Accounts receivable	(1,242)	54	2,302
Prepaid expenses and other assets	(2,333)	(2,011)	(120)
Accounts payable	(769)	4,812	3,155
Accrued liabilities	2,783	11,320	1,675
Deferred revenue	32,794	7,041	8,970
Net cash used in operating activities	(135,043)	(42,861)	(6,445)
INVESTING ACTIVITIES:			
Acquisition of property and equipment	(3,406)	(1,742)	(818)
Net cash used in investing activities	(3,406)	(1,742)	(818)
FINANCING ACTIVITIES:			
Proceeds from long-term debt, net of lender fees	46,599	—	4,945
Proceeds from exercise of stock options	902	2,726	139
Proceeds from issuance of common stock under equity plans	515	—	—
Proceeds from exercise of stock option by Ultragenyx and issuance of common stock and option, net of issuance costs, to Ultragenyx	—	9,600	15,545
Proceeds from issuance of common stock, net of issuance costs	—	423,819	21,278
Net cash provided by financing activities	48,016	436,145	41,907
NET (DECREASE) INCREASE IN CASH, CASH EQUIVALENTS AND RESTRICTED CASH	(90,433)	391,542	34,644
Cash, cash equivalents and restricted cash at beginning of year	463,002	71,460	36,816
Cash, cash equivalents and restricted cash at end of year	$ 372,569	$ 463,002	$ 71,460

	Year Ended December 31,		
	2021	**2020**	**2019**
Supplemental disclosure of cash flow information:			
Cash paid for interest	$ 684	$ 751	$ 691
Non-cash investing activities			
Right-of-use asset obtained in exchange for lease liabilities	$ 1,828	$ 1,360	$ 5,868
Acquisition of in-process research and development through issuance of common stock	$ 5,000	$ —	$ —
Purchase of property and equipment in accounts payable	$ 53	$ 169	$ 240

The accompanying notes are an integral part of these consolidated financial statements.

Note 1. Organization

Description of Business

Arcturus Therapeutics Holdings Inc. (the "Company") is a late-stage global clinical messenger RNA medicines company focused on the development of infectious disease vaccines and significant opportunities within liver and respiratory rare diseases. The Company became a clinical stage company during 2020 when it announced that its Investigational New Drug ("IND") application for ornithine transcarbamylase ("OTC") deficiency and its Clinical Trial Application ("CTA") candidate LUNAR-COV19 were approved by applicable health authorities.

The financial statements for periods prior to June 17, 2019, the effective date of the Redomiciliation, relate to Arcturus Therapeutics Ltd. and for the periods from and after June 17, 2019 relate to Arcturus Therapeutics Holdings Inc.

Recent Developments

See *"Note 3 Revenue – Vinbiocare"* for further information on the agreements with Vinbiocare, a member of Vingroup Joint Stock Company ("Vinbiocare"), whereby the Company will provide technical expertise and support services to Vinbiocare to assist in the build out of a manufacturing facility in Vietnam.

Liquidity

The Company has incurred significant operating losses since its inception. As of December 31, 2021 and 2020, the Company had an accumulated deficit of $347.5 million and $143.8 million, respectively.

The Company's activities since inception have consisted principally of research and development activities, general and administrative activities, and raising capital. The Company's activities are subject to significant risks and uncertainties, including failing to secure additional funding before the Company achieves sustainable revenues and profit from operations. From the Company's inception through the year ended December 31, 2021, the Company has funded its operations principally with the proceeds from the sale of capital stock and funds received from collaboration agreements. During fiscal year 2021, the Company received a term loan of $46.6 million from Economic Development Board of the Republic of Singapore as well as an upfront payment of $40.0 million from Vinbiocare to assist with funding a phase 3 clinical trial in Vietnam. Through underwritten public offerings, the Company raised net proceeds of $423.8 million during fiscal year 2020, after deducting underwriting discounts, commissions, and offering expenses. At December 31, 2021, the Company's balance of cash and cash equivalents, including restricted cash, was $372.6 million.

Management believes that it has sufficient working capital on hand to fund operations through at least the next twelve months from the date these consolidated financial statements were available to be issued. There can be no assurance that the Company will be successful in acquiring additional funding, that the Company's projections of its future working capital needs will prove accurate, or that any additional funding would be sufficient to continue operations in future years.

Note 2. Summary of Significant Accounting Policies

Basis of Presentation and Principles of Consolidation

The accompanying consolidated financial statements include the accounts of Arcturus Therapeutics Holdings Inc. and its subsidiaries. All intercompany accounts and transactions have been eliminated in consolidation. These consolidated financial statements are prepared in conformity with accounting principles generally accepted in the United States (U.S. GAAP), which requires management to make estimates and assumptions regarding the valuation of certain debt and equity instruments, the equity method investment, share-based compensation, accruals for liabilities, income taxes, revenue and deferred revenue, leases, expense accruals, and other matters that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Although these estimates are based on management's knowledge of current events and actions the Company may undertake in the future, actual results could materially differ from those estimates.

Segment Information

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision-maker in making decisions regarding resource allocation and assessing performance. The Company and its chief operating decision-maker view the Company's operations and manage its business in one operating segment which is the research and development of medical applications for the Company's nucleic acid-focused technology.

Cash and Cash Equivalents

Cash equivalents are short-term highly liquid investments that are readily convertible to cash with original maturities of three months or less at the date of purchase.

Restricted cash

Restricted cash represents cash required to be set aside as security for lease payments and to maintain a letter of credit for the benefit of the landlord for the Company's offices. At December 31, 2021 and 2020, the Company had restricted cash of $2.1 million and $0.1 million in conjunction with property leases in San Diego, California, and such restriction is expected to be removed at the end of the lease term.

Fair Value Measurements

Fair value is defined as the exit price, or the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants as of the measurement date. A hierarchy has been established for inputs used in measuring fair value that maximizes the use of observable inputs and minimizes the use of unobservable inputs by requiring that the most observable inputs be used when available.

Observable inputs are inputs that market participants would use in valuing the asset or liability developed based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the factors market participants would use in valuing the asset or liability developed based upon the best information available under the circumstances. The hierarchy consists of three levels. Level 1 inputs are quoted prices (unadjusted) in active markets for identical assets or liabilities. Level 2 inputs include quoted prices for similar assets or liabilities in active markets, quoted prices for identical or similar assets or liabilities in markets that are not active, and inputs (other than quoted prices) that are observable for the asset or liability, either directly or indirectly. Level 3 inputs are unobservable inputs for the asset or liability. Categorization within the valuation hierarchy is based upon the lowest level of input that is significant to the fair value measurement.

Accounts Receivable

Accounts receivable are recorded at the net invoice value and are non-interest bearing. The Company considers receivables past due based on the contractual payment terms. The Company reserves for specific receivables if collectability is no longer reasonably assured. Estimates for allowances for doubtful accounts are determined based on existing contractual obligations, historical payment patterns, and individual customer circumstances. The Company reevaluates such reserves on a regular basis and adjusts its reserves as needed. Once a

receivable is deemed to be uncollectible, such balance is charged against the reserve. No reserves have been recorded as of December 31, 2021 or 2020.

Concentration of Credit Risk and Significant Customers

Financial instruments, which potentially subject the Company to concentrations of credit risk, consist of cash and cash equivalents. The Company limits its exposure to credit loss by placing its cash and cash equivalents with high credit quality financial institutions in instruments with short maturities.

There were two customers that comprised 100% of the total accounts receivable balance at December 31, 2021 and one customer that comprised 100% of the total accounts receivable balance at December 31, 2020.

For the year ended December 31, 2021, the Company's top four customers collectively represented 99% of the Company's total revenue. For the year ended December 31, 2020, there were four customers that collectively represented 94% of the Company's total revenue.

Joint Ventures, Equity Method Investments and Variable Interest Entities

Investments for which the Company exercises significant influence but does not have control are accounted for under the equity method. Equity method investment activity is related to a 49% joint venture with Axcelead, Inc. (see the following paragraph for further details) and a 12% ownership in Vallon Pharmaceuticals, Inc. (see "*Note 12, Related Party Transactions"* for further details). The Company's share of the investees results is presented as either income or loss from equity method investees in the accompanying consolidated statements of operations and comprehensive loss.

In April 2021, Arcturus and Axcelead, Inc., a company existing under the laws of Japan ("Axcelead"), formed a joint venture entity, named Arcalis, Inc. ("JV Entity"), which operates as a corporation under the laws of Japan. Axcelead is an integrated drug discovery solutions provider to the pharmaceutical industry in Japan. On July 1, 2017, Axcelead became the successor to a portion of the drug discovery research department of Takeda Pharmaceutical Company Limited. The goal of the JV Entity is to be a contract development and manufacturing organization focused on mRNA manufacturing that would provide manufacturing services to the Company and also to third parties. The joint venture includes a shareholders agreement setting forth initial funding of the JV Entity and rights of the shareholders, including certain approval rights of Arcturus. As part of the joint venture, the Company entered into a License and Technology Transfer Agreement with the JV Entity, pursuant to which Arcturus grants to JV Entity a nonexclusive license to certain intellectual property for use at the JV Entity's facilities, and obligates Arcturus to conduct certain technology transfer activities.

The Company consolidates variable interest entities ("VIEs") where it has been determined that the Company is the primary beneficiary of those entities' operations. Management believes that power is shared between Arcturus and Axcelead, as unrelated parties. The consent of each of the parties is substantive and is required to make the decisions about the JV Entity's significant activities. Management does not believe that Arcturus has the power to direct the activities of the JV Entity that most significantly impact the JV Entity's economic performance. Therefore, the Company concluded it is not required to consolidate the JV Entity under the VIE model.

The equity method of accounting is applicable for the JV Entity as the Company does not own more than 50% of voting power, but has influence over the operation and financial policies of the investee. The Company accounts for its investment in the JV Entity using the equity method of accounting as specified in ASC 323, *Investments — Equity Method and Joint Ventures*. Under ASC 323, equity method investments are recorded initially at cost. The Company's initial investment in the JV Entity totaled $9.2 million. However, the JV Entity paid the Company back the initial investment of $9.2 million as an upfront fee/consideration for the License and Technology Transfer Agreement. In substance, there was no cash consideration paid by the Company for its 49% equity interest in the JV Entity.

Property and Equipment, net

Property and equipment are stated at cost, net of accumulated depreciation and amortization. The cost of property and equipment is depreciated or amortized using the straight-line method over the respective useful lives of the assets, ranging from three to five years. Leasehold improvements are amortized using the straight-line method over the shorter of the estimated useful life of the asset or the lease term. Long-lived assets, including property and equipment are reviewed for impairment whenever events or circumstances indicate that the carrying amount of these assets may not be recoverable. The determinants used for this evaluation include management's estimate of an asset's ability to generate positive income from operations and positive cash flow in future periods, as well as the strategic significance of the assets to the Company's business objectives. The Company did not recognize any impairment losses for the years ended December 31, 2021, 2020 and 2019.

Comprehensive Income/Loss

Comprehensive income/loss is defined as the change in stockholders' equity during a period from transactions and other events and circumstances from non-owner sources. There was no other comprehensive loss in the years ended December 31, 2021, 2020 or 2019. There was no income tax effect related to unrealized losses for the years ended December 31, 2021, 2020 or 2019.

Revenue Recognition

Effective January 1, 2019, the Company adopted *Accounting Standards Update ("ASU") 2014-09, Revenue from Contracts with Customers (Topic 606)* ("Topic 606"), using the modified retrospective transition method. Topic 606 provides a unified model to determine how revenue is recognized and the Company applied the standard to collaborative research and technology agreements that were in progress as of the effective date, January 1, 2019. The Company determines revenue recognition for arrangements within the scope of Topic 606 by performing the following five steps: (i) identify the contract; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when, or as, the company satisfies a performance obligation.

The terms of the Company's revenue agreements include license fees, upfront payments, milestone payments, reimbursement for research and development activities, option exercise fees, consulting and related technology transfer fees and royalties on sales of commercialized products. Arrangements that include upfront payments are recorded as deferred revenue upon receipt or when due and may require deferral of revenue recognition to a future period until the Company performs obligations under these arrangements. The event-based milestone payments represent variable consideration, and the Company uses the most likely amount method to estimate this variable consideration because the Company will either receive the milestone payment or will not, which makes the potential milestone payment a binary event. The most likely amount method requires the Company to determine the likelihood of earning the milestone payment. Given the high degree of uncertainty around achievement of these milestones, the Company determines the milestone amounts to be fully constrained and does not recognize revenue until the uncertainty associated with these payments is resolved. The Company will recognize revenue from sales-based royalty payments when or as the sales occur. The Company will re-evaluate the transaction price in each reporting period as uncertain events are resolved and other changes in circumstances occur.

A performance obligation is a promise in a contract to transfer a distinct good or service to the collaborative partner and is the unit of account in Topic 606. A contract's transaction price is allocated to each distinct performance obligation based on relative standalone selling price and recognized as revenue when, or as, the performance obligation is satisfied.

See *"Note 3, Revenue"* for specific details surrounding the Company's arrangements.

Leases

See *"Note 11, Commitments and Contingences"* for specific details surrounding the Company's leases.

Research and Development Costs, net

All research and development costs are expensed as incurred. Research and development costs consist primarily of salaries, employee benefits, costs associated with preclinical studies and clinical trials (including amounts paid to clinical research organizations and other professional services), in process research and development expenses and license agreement expenses, net of any grants and prelaunch inventory. Payments made

prior to the receipt of goods or services to be used in research and development are capitalized until the goods or services are received.

The Company records accruals for estimated research and development costs, comprising payments for work performed by third party contractors, laboratories, participating clinical trial sites, and others. Some of these contractors bill monthly based on actual services performed, while others bill periodically based upon achieving certain contractual milestones. For the latter, the Company accrues the expenses as goods or services are used or rendered. Clinical trial site costs related to patient enrollment are accrued as patients enter and progress through the trial.

Share-Based Compensation

The Company recognizes share-based compensation for equity awards granted to employees, consultants, officers and directors as an expense on the statements of operations and comprehensive loss. Share-based compensation is recognized over the requisite service period of the individual awards using the straight-line attribution method, which generally equals the vesting period. Employees and officers' stock options have a ten-year life and generally vest 25% on the first anniversary of the grant and in 1/36th equal installments on each monthly anniversary thereafter, such that options are fully vested on the four-year anniversary of the date of grant. The exercisability and vesting periods of options granted to consultants and directors vary.

The fair value of stock options is estimated using a Black-Scholes valuation model on the date of grant. This method requires certain assumptions be used as inputs, such as the fair value of the underlying common stock, expected term of the option before exercise, expected volatility of the Company's common stock, expected dividend yield, and a risk-free interest rate. The Company has limited historical stock option activity and therefore estimates the expected term of stock options granted using the simplified method, which represents the average of the contractual term of the stock option and its weighted-average vesting period. The expected volatility of stock options is based upon the historical volatility of a peer group of publicly traded companies. The Company has not declared or paid any dividends and does not currently expect to do so in the foreseeable future. The risk-free interest rates used are based on the implied yield currently available in United States Treasury securities at maturity with a term equivalent to the expected term of the stock options. The effect of forfeited awards is recorded when the forfeiture occurs.

Pre-Launch Inventory

Prior to obtaining initial regulatory approval for an investigational product candidate, the Company expenses costs relating to production of inventory as research and development expense in its consolidated statements of operations and comprehensive loss, in the period incurred. When the Company believes regulatory approval and subsequent commercialization of an investigational product candidate is probable, and the Company also expects future economic benefit from the sales of the investigational product candidate to be realized, it will then capitalize the costs of production as inventory.

Statement of Cash Flows

The following table provides a reconciliation of cash and cash equivalents and restricted cash reported within the consolidated balance sheets to the total of such amounts shown in the consolidated statement of cash flows:

	As of December 31,		
(in thousands)	**2021**	**2020**	**2019**
Cash and cash equivalents	$ 370,492	$ 462,895	$ 71,353
Non-current restricted cash	2,077	107	107
Total cash, cash equivalents and restricted cash shown in the statement of cash flows	$ 372,569	$ 463,002	$ 71,460

Income Tax Expense

Income taxes are accounted for using an asset and liability approach that requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of temporary differences between the financial reporting basis and the tax basis of the Company's assets and liabilities at the applicable tax rates, along with net operating loss and tax credit carryovers. The Company records a valuation allowance against its deferred tax assets

to reduce the net carrying value to an amount that it believes is more likely than not to be realized. Management has considered estimated taxable income and ongoing prudent and feasible tax planning strategies in assessing the amount of the valuation allowance. Based upon the weight of available evidence, which includes the Company's historical operating performance and limited potential to utilize tax credit carryforwards, the Company has determined that total deferred tax assets should be fully offset by a valuation allowance. When the Company establishes or reduces the valuation allowance against its deferred tax assets, its provision for income taxes will increase or decrease, respectively, in the period such determination is made.

The Company is required to file federal and state income tax returns in the United States and various other state jurisdictions. The Company also files income tax returns in the foreign countries in which it operates. The preparation of these income tax returns requires the Company to interpret the applicable tax laws and regulations in effect in such jurisdictions, which could affect the amount of tax paid by the Company.

Additionally, the Company follows an accounting standard addressing the accounting for uncertainty in income taxes that prescribes rules for recognition, measurement, and classification in the consolidated financial statements of tax positions taken or expected to be taken in a tax return.

In December 2019, the FASB issued an ASU 2019-12 that simplifies the accounting for income taxes by eliminating certain exceptions to the guidance in ASC 740 related to the approach for intraperiod tax allocation, the methodology for calculating income taxes in an interim period and the recognition of deferred tax liabilities for outside basis differences. This ASU is effective for annual periods and interim periods for those annual periods beginning after December 15, 2020, with early adoption permitted. The Company adopted this standard effective January 1, 2021. The adoption of this standard did not have an impact on the Company's Consolidated Financial Statements.

Net Loss per Share

Basic net loss per share is calculated by dividing the net loss by the weighted-average number of shares of common stock outstanding for the period, without consideration for common stock equivalents. Diluted net loss per share is calculated by dividing the net loss by the weighted-average number of shares of common stock and dilutive common stock equivalents outstanding for the period determined using the treasury-stock method. Dilutive shares of common stock for the years ended December 31, 2021, 2020 and 2019 are comprised of stock options.

No dividends were declared or paid during the reporting periods.

NOTE 3. Revenue

The Company has entered into license agreements and collaborative research and development arrangements with pharmaceutical and biotechnology companies, as well as consulting, related technology transfer and product revenue agreements. Under these arrangements, the Company is entitled to receive license fees, consulting fees, product fees, technological transfer fees, upfront payments, milestone payments if and when certain research and development milestones or technology transfer milestones are achieved, royalties on approved product sales and reimbursement for research and development activities. The Company's costs of performing these services are included within research and development expenses. The Company's milestone payments are typically defined by achievement of certain preclinical, clinical, and commercial success criteria. Preclinical milestones may include *in vivo* proof of concept in disease animal models, lead candidate identification, and completion of IND-enabling toxicology studies. Clinical milestones may, for example, include successful enrollment of the first patient in or completion of Phase 1, 2 and 3 clinical trials, and commercial milestones are often tiered based on net or aggregate sale amounts. The Company cannot guarantee the achievement of these milestones due to risks associated with preclinical and clinical activities required for development of nucleic acid medicine-based therapeutics and vaccines.

The following table presents changes during the year ended December 31, 2021 in the balances of contract assets, including receivables from collaborative partners, consulting and related technology transfer partners, and contract liabilities, including deferred revenue.

(in thousands)	Contract Assets
BALANCE - December 31, 2020	$ 2,125
Additions for revenue recognized from billings	35,152
Deductions for cash collections	(33,910)
BALANCE - December 31, 2021	$ 3,367

(in thousands)	Contract Liabilities
BALANCE - December 31, 2020	$ 30,620
Additions for advanced billings	45,152
Deductions for promised services provided in current period	(12,359)
BALANCE – December 31, 2021	$ 63,413

The following table summarizes the Company's revenue for the periods indicated (in thousands). Approximately $5.0 million, $1.0 million and $7.0 million of total revenue represents revenue derived from foreign countries for the years ended December 31, 2021, 2020 and 2019, respectively.

	For the Year Ended December 31,		
(in thousands)	2021	2020	2019
Vinbiocare	$ 4,364	$ —	$ —
Janssen	3,129	2,964	2,912
Ultragenyx	3,700	3,983	5,862
CureVac	1,019	1,006	6,611
SGI	—	256	3,518
Other	147	1,330	1,886
Total revenue	$ 12,359	$ 9,539	$ 20,789

The following paragraphs provide information regarding the nature and purpose of the Company's most significant revenue arrangements.

Vinbiocare

From June 11, 2021 through August 2, 2021, the Company entered into a series of agreements with Vinbiocare, a member of Vingroup Joint Stock Company (collectively the "Vinbiocare Agreement"), whereby the Company will provide technical expertise and support services to Vinbiocare to assist in the build out of a mRNA drug product manufacturing facility in Vietnam. Such expertise shall include a specified level of access to the Company's personnel and drug substance necessary to validate the successful set up of the facility. Under the terms of the arrangements, the Company will also provide a specified number of doses of ARCT-154 for use by Vinbiocare in a phase 3 clinical study within Vietnam. The Company received an upfront payment in aggregate of $40.0 million and subsequent to achieving emergency use authorization, the Company will receive low single digit payments per dose for drug substance and related royalties.

In evaluating the Vinbiocare Agreement in accordance with Accounting Standards Codification ("ASC") Topic 606, the Company concluded that Vinbiocare is a customer. The Company identified all promised goods/services within the Vinbiocare Agreement, and when combining certain promised goods/services, the Company concluded that there are four distinct performance obligations. The four performance obligations include (i) consulting to support the build out of the manufacturing facility and technical transfer, (ii) shipment of 80 grams of drug substance to validate the manufacturing facility, (iii) the sale of 2,500 vials of drug product to support the phase 3 clinical trial and (iv) consulting to support the phase 3 clinical trial and related regulatory filings. For each performance obligation, the Company estimated the standalone selling price based on cost plus margin for drug substance and drug product as well as estimated headcount and full-time equivalent ("FTE") rates for consulting services to support the phase 3 clinical trial, the build out of the manufacturing facility and the technology transfer.

As of December 31, 2021, the transaction price consists of upfront consideration received and budgeted reimbursable out-of-pocket costs to support the build out of the manufacturing facility and technology transfer. The Company allocated the transaction price to the performance obligations in proportion to their standalone selling price, the relative standalone selling price basis. The drug substance and drug product performance obligations are recognized at the point in time the goods are transferred. The consulting performance obligations are recognized over a period of time based on the percentage of services rendered, meaning actual costs incurred divided by total costs budgeted to satisfy the performance obligation. Any consideration related to sales-based royalties will be recognized when the drug product is manufactured as they are constrained. The revenue recognized in 2021 relates to consulting to support the build out of the manufacturing facility and technical transfer, the sale of 2,500 vials of drug product to support the phase 3 clinical trial and consulting to support the phase 3 clinical trial.

Total deferred revenue as of December 31, 2021 for the Vinbiocare agreement was $37.2 million.

For Janssen Pharmaceuticals, Inc. ("Janssen"), Ultragenyx Pharmaceutical Inc. ("Ultragenyx") and CureVac AG ("CureVac"), the Company evaluated the respective agreement in accordance with Accounting Standards Codification ("ASC") Topic 606. The Company concluded that the contract counterparty is a customer. The Company identified all promised goods/services within each agreement, and concluded that the promised goods/services are incapable of being distinct and consequently do not have any value on a standalone basis. Accordingly, the promised goods/services within each agreement were determined to represent a single performance obligation. Lastly, the Company concluded that any options to select additional collaboration targets and to license rights to selected targets were not priced at a discount and therefore do not represent performance obligations for which the transaction price would be allocated.

Janssen

In October 2017, the Company entered into a research collaboration and license agreement with Janssen (the "2017 Agreement") to collaborate on developing candidates for treating HBV with RNA therapeutics. The 2017 Agreement allocated discovery, development, funding obligations, and ownership of related intellectual property among the Company and Janssen. The Company received an upfront payment of $7.7 million and may receive preclinical, development and sales milestone payments of up to $56.5 million, as well as royalty payments on any future licensed product sales. In October 2021, the LUNAR-HBV program reached an incremental milestone based on demonstration of in vivo efficacy and safety for which Janssen paid the Company $1.0 million. Janssen began reimbursing the Company for research costs during the first quarter of 2019 upon the completion of the first of three research periods. Janssen will pay royalties of a low to mid-single digit percentage of net sales of licensed products, subject to reduction on a country-by-country and licensed-product-by-licensed-product basis and subject to certain events, such as expiration of program patents.

As of December 31, 2021, the remaining transaction price consisting of upfront consideration received and budgeted reimbursable out-of-pocket costs, is expected to be recognized using an input method over the remaining research period of 12 months. None of the development and commercialization milestones were included in the transaction price as they are outside the control of the Company and contingent upon success in future clinical trials and the collaborator's efforts. The development milestone achieved in October 2021 was included in the transaction price during the fourth quarter of 2021. Any consideration related to sales-based royalties will be recognized when the related sales occur, provided that the reported sales are reliably measurable, and the Company has no remaining promised goods/services, as such sales were determined to relate predominantly to the license granted to Janssen and therefore have also been excluded from the transaction price.

Total deferred revenue as of December 31, 2021 and 2020 for Janssen was $6.3 million and $5.9 million, respectively.

Ultragenyx

In October 2015 the Company entered into a research collaboration and license agreement with Ultragenyx (the "Ultragenyx Agreement"), whereby Arcturus granted to Ultragenyx a co-exclusive license to certain Arcturus technology, which is in effect only during the reserve target exclusivity term as discussed in the following paragraphs. This collaboration agreement was amended in 2017, 2018 and during the second quarter of 2019. During the initial phase of the collaboration, the Company will design and optimize therapeutics for certain rare disease targets. Ultragenyx has the option under the Ultragenyx Agreement to add additional rare disease targets during the collaborative development period. Additionally, during the collaborative development period, the Company will participate with Ultragenyx in a joint steering committee.

As part of the Ultragenyx Agreement and related amendments, Ultragenyx has paid $27.9 million in upfront fees, exclusivity extension fees and additional consideration. Ultragenyx also reimburses the Company for all internal and external development costs incurred. Pursuant to the Ultragenyx Agreement, Ultragenyx is required to make additional payments upon exercise of the Ultragenyx expansion option or exclusivity extension (if any) and if Ultragenyx achieves certain, clinical, regulatory and sales milestones, then the Company is eligible to receive royalty payments. For each development target for which Ultragenyx exercises its option, Ultragenyx will pay the Company a one-time option exercise fee that increases based upon the number of development targets selected by Ultragenyx and ranges from $0.5 million to $1.5 million. During the fourth quarter of 2020, Ultragenyx exercised its option to move forward with Preclinical Candidate Designation for its development target, Glycogen Storage Disease III, and paid an option fee to the Company of $0.5 million.

The current potential development, regulatory and commercial milestone payments for the existing development targets as of December 31, 2021 are $138.0 million. Ultragenyx will pay royalties as a single-digit percentage of net sales on a product-by-product and country-by-country basis during the applicable royalty term. As of December 31, 2021, Ultragenyx is working to identify and enroll patients in a Phase 1/2 study.

On June 18, 2019, Arcturus and Ultragenyx amended the collaboration agreement for a third time ("Amendment 3"). As part of Amendment 3, the total number of targets was increased from 10 to 12, and reserve targets will be exclusively reserved for Ultragenyx with no fees for four years after execution of the amendment. An equity component was also added as part of Amendment 3 wherein Ultragenyx purchased 2.4 million shares of common stock at a premium price. Along with the equity purchase, Ultragenyx received an option to purchase 0.6 million additional shares of common stock at $16.00 per share. In May 2020, the option was exercised.

The consideration received from Ultragenyx as a result of Amendment 3 was equal to $30.0 million and was comprised of a $24.0 million common stock purchase and a $6.0 million upfront payment. Specifically for

Amendment 3, management determined the transaction price to be $14.4 million. Management determined the fair value of the premium received by using the opening stock price subsequent to execution of Amendment 3 and applying a lack of marketability discount, as the shares received by Ultragenyx were initially restricted for up to two years. These restrictions have since expired.

As of December 31, 2021, the transaction price included the upfront consideration received, option payments, exclusivity extension payments and additional consideration received pursuant to Amendment 3. The Company recognizes the reimbursement of labor and expenses as costs are incurred and none of the development and commercialization milestones were included in the transaction price, as all milestone amounts were fully constrained. As part of its evaluation of the constraint, the Company considered numerous factors, including that the consideration is outside the control of the Company and contingent upon success in future clinical trials, approval from the FDA and the collaborator's efforts. Any consideration related to sales-based royalties will be recognized when the related sales occur as they are constrained, provided that the reported sales are reliably measurable and the Company has no remaining promised goods/services, as such sales were determined to relate predominantly to the license granted to Ultragenyx and therefore have also been excluded from the transaction price.

Amendment 3 was deemed a contract modification and accounted for as part of the original Ultragenyx Agreement. The transaction price is recognized to revenue on a straight-line basis using an input method over the 4-year reserve target exclusivity period. The reserve target exclusivity period represents the timing over which promised goods/services will be provided. Total deferred revenue at December 31, 2021 and December 31, 2020 from Ultragenyx was $5.5 million and $9.2 million, respectively.

CureVac

In January 2018, the Company entered into a Development and Option Agreement (the "Development and Option Agreement") with CureVac. Under the terms of the Development and Option Agreement, the parties agreed to conduct joint preclinical development programs once CureVac makes a payment to pull down a target on the basis of which CureVac is granted options for taking a license on pre-agreed license terms to develop and commercialize certain products incorporating the Company's patents and know-how related to LUNAR delivery technology (the "Arcturus Delivery Technology"), and CureVac patents and know-how related to mRNA technology.

Prior to expiration of the initial term of eight years (which was subsequently amended, as discussed below), the Development and Option Agreement also includes an option to extend the term on an annual basis for up to three years, subject to payment by CureVac to Arcturus of a non-refundable annual extension fee. The Development and Option Agreement includes potential milestone payments from CureVac to the Company for selected targets. The current potential milestone payments for the remaining targets as of December 31, 2021 are $14.0 million for rare disease targets and $23.0 million for non-rare disease targets. CureVac will pay royalties as a percentage of net sales on a product-by-product and country-by-country basis during the applicable royalty term in the low single-digit range. As of December 31, 2021, CureVac has not yet reached the clinical phase of the contract. Pursuant to a May 2018 amendment to the Development and Option Agreement (and as amended and restated on September 28, 2018), the Company increased the number of targets available to CureVac under the Development and Option Agreement and agreed upon the license forms to be executed upon selection of the targets by CureVac.

On July 26, 2019, the Company entered into an amendment ("CureVac Amendment") to its Development and Option Agreement with CureVac (as amended, the "Development and Option Agreement"), pursuant to which the Company and CureVac agreed to shorten the time period during which CureVac may select potential targets to be licensed from the Company from eight years to four years, and to reduce the overall number of maximum targets that may be reserved and licensed. In connection with the July 2019 CureVac Amendment, the Company and CureVac also entered into a Termination Agreement (the "Termination Agreement") terminating the January 1, 2018 Co-Development Agreement between the Company and CureVac.

As of December 31, 2021, the transaction price included the upfront consideration received. The Company recognizes the reimbursement of labor and expenses as costs are incurred and none of the development and commercialization milestones were included in the transaction price, as all milestone amounts were fully constrained. As part of its evaluation of the constraint, the Company considered numerous factors, including that receipt of the milestones is outside the control of the Company and contingent upon success in future clinical trials and the collaborator's efforts. Any consideration related to sales-based royalties will be recognized when the related sales occur as they are constrained, provided that the reported sales are reliably measurable and the Company has no remaining promised goods/services, as such sales were determined to relate predominantly to the license granted to CureVac and therefore have also been excluded from the transaction price. As of December 31, 2021, no adjustments were made to the transaction price.

The upfront consideration of $5.0 million was recorded as deferred revenue in the Company's balance sheet upon receipt and is currently being recognized as revenue on a straight-line basis using an input method over the remaining 19 month contractual term as of December 31, 2021. Total deferred revenue as of December 31, 2021 and December 31, 2020 for CureVac was $1.4 million and $2.3 million, respectively.

Other Agreements

Subsequent to December 31, 2021, the Company entered into an agreement with a pharmaceutical company, whereby the pharmaceutical company agreed to fund up to $25 million for a clinical trial for a LUNAR-COV19 vaccine candidate as a booster.

Israeli Ministry of Health

On August 17, 2020, the Company entered into an agreement with the Israeli Ministry of Health ("MOH") to supply the Company's COVID-19 vaccine candidate to Israel (the "Israel Supply Agreement") subject to certain conditions, including applicable regulatory approvals. In October 2020, and in association with the Israel Supply Agreement, the Company received a non-refundable payment of $12.5 million from the MOH which is included in deferred revenue as of December 31, 2021. This payment of $12.5 million is associated with a specified clinical trial milestone and serves as an initial reserve payment for a specified number of doses of the LUNAR-COV19 vaccine candidate pursuant to the Israel Supply Agreement. As a result of the making of this payment, the MOH became bound to purchase an initial quantity of 500,000 reserved vaccine doses, as set forth in and subject to the terms and conditions of the Israel Supply Agreement.

NOTE 4. Fair Value Measurements

The Company establishes the fair value of its assets and liabilities using the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. The Company established a fair value hierarchy based on the inputs used to measure fair value.

The three levels of the fair value hierarchy are as follows:

Level 1: Quoted prices in active markets for identical assets or liabilities.

Level 2: Inputs, other than the quoted prices in active markets, that are observable either directly or indirectly.

Level 3: Unobservable inputs in which little or no market data exists and are therefore determined using estimates and assumptions developed by the Company, which reflect those that a market participant would use.

The carrying value of cash, restricted cash, accounts receivable, accounts payable, accrued liabilities and the Singapore loan approximate their respective fair values due to their relative short maturities. The carrying amounts of long-term debt for the amount drawn on the Company's debt facility approximates fair value as the interest rate is variable and reflects current market rates.

As of December 31, 2021 and 2020, all assets measured at fair value on a recurring basis consisted of cash equivalents, money market funds, which were classified within Level 1 of the fair value hierarchy. The fair value of these financial instruments was measured based on quoted prices.

NOTE 5. Balance Sheet Details

Accrued liabilities consisted of the following:

(in thousands)	December 31, 2021	December 31, 2020
Accrued compensation	$ 3,578	$ 2,097
Cystic Fibrosis Foundation liability	2,777	6,585
Singapore Economic Development Board liability	—	1,761
Current portion of operating lease liability	1,537	1,630
Clinical accruals	8,675	4,067
Other accrued research and development expenses	6,956	3,249
Total	$ 23,523	$ 19,389

NOTE 6. Property and Equipment, Net

Property and equipment, net consisted of the following:

(in thousands)	December 31, 2021	December 31, 2020
Research equipment	$ 6,735	$ 5,539
Computers and software	488	284
Office equipment and furniture	574	574
Leasehold improvements	44	44
Construction in progress	2,058	—
Total	$ 9,899	$ 6,441
Less accumulated depreciation and amortization	(4,256)	(3,063)
Property and equipment, net	$ 5,643	$ 3,378

Depreciation and amortization expense was $1.2 million , $0.9 million and $0.7 million for the years ended December 31, 2021, 2020 and 2019, respectively.

NOTE 7. Debt

Manufacturing Supply Agreement

On November 7, 2020, the Company's wholly-owned subsidiary, Arcturus Therapeutics, Inc., entered into a Manufacturing Support Agreement (the "Support Agreement") with the Economic Development Board of the Republic of Singapore (the "EDB"). Pursuant to the Support Agreement, the EDB agreed to make a term loan (the "Singapore Loan") of S$62.1 million to the Company, subject to the satisfaction of customary deliveries, to support the manufacture of the LUNAR-COV19 vaccine candidate (ARCT-021). The EDB has agreed to an extension of the reconciliation period to March 31, 2022 with unused funds as of such date to be subsequently returned within thirty days, subject to any further agreed upon extension of the reconciliation date. The parties are in continued negotiations with respect to amendments of the Singapore Loan terms. Under current terms, (i) the Company will provide a quarterly reconciliation report within forty-five days of each financial quarter end, (ii) the Company will provide a projection of expenditures through March 31, 2022 followed by an audited statement of actual expenditures through March 31, 2022 by June 30, 2022, (iii) the Company will provide EDB with a right of first refusal on GMP manufacturing slots of the LUNAR-COV19 vaccine candidate up to an agreed-upon maximum amount, (iv) and the obligation to repay the Singapore Loan will be secured by an interest in the raw materials and manufacturing equipment purchased by the Company with the funds from the Singapore Loan in form and substance satisfactory to the EDB in its sole discretion. The Company elected to borrow the full amount available under the Support Agreement of S$62.1 million ($46.6 million) on January 29, 2021. As of December 31, 2021, the Company has reported a portion of the Singapore Loan as current to reflect a potential principal repayment of approximately 20.9 million Singapore dollars (US $15.2 million) in fiscal year 2022 based on amounts not used toward the manufacture of ARCT-021.

The Singapore Loan accrues interest at a rate of 4.5% per annum calculated on a daily basis. Subject to certain exceptions, the Singapore Loan is intended to be a limited recourse loan that will be repaid solely through a royalty

payment of 10% of net sales proceeds of the LUNAR-COV19 vaccine candidate, up to the amount of the outstanding principal and interest under the Singapore Loan. However, all unpaid principal and interest under the Singapore Loan will be due and payable five years after draw date, if net sales of the LUNAR-COV19 vaccine exceed a certain minimum threshold during this five year period or the Company obtains clearance to sell the vaccine in specified jurisdictions. Unpaid principal and interest under the Singapore Loan will also become due and payable upon an event of default under the Support Agreement. The first vaccine sales, including the amount of net sales, shall be reported to EDB within 10 days of delivery and quarterly reports of aggregate vaccine sales, including net sales proceeds shall be provided within 30 days after quarter end.

The Singapore Loan is forgivable if the Company has not obtained regulatory approval by the final repayment date and net sales of the LUNAR-COV19 vaccine candidate are less than $100 million. If, any portion of the Singapore Loan is required to be forgiven pursuant to the terms of the Support Agreement, the EDB has the right to take ownership of certain raw materials and equipment that were purchased by the Company with proceeds of the Singapore Loan (the “Specified Assets”). The Company entered into a security agreement (the “Security Agreement”) for the benefit of the EDB to provide that repayment of the Singapore Loan and related obligations are secured by a lien on the Specified Assets.

In connection with the entry into the Support Agreement, the Company entered into a consent agreement with Western Alliance Bank (the “Bank”) and an amendment to the Loan and Security Agreement, dated as of October 12, 2018, between Western Alliance Bank and the Company (the “Loan Agreement”), to exclude the Specified Assets from Western Alliance Bank’s lien on certain assets of the Company.

The Singapore Loan was initially recorded as long-term debt at $46.6 million, the amount of cash proceeds at the time the Company received the funding. As of December 31, 2021, the debt balance was adjusted to reflect the current exchange rate resulting in a debt balance of $46.0 million and a net foreign currency transaction gain of $0.6 million for the year ended December 31, 2021. The Company also recorded interest expense of $1.9 million for the year ended December 31, 2021. Lastly, the Company was in compliance with all covenants under the Singapore Loan and related commitments.

Long-term debt with Western Alliance Bank

On October 12, 2018, Arcturus Therapeutics, Inc. entered into the Loan with the Bank, whereby it received $10.0 million.

The Loan is collateralized by all of the assets of Arcturus Therapeutics, Inc., excluding intellectual property, which is subject to a negative pledge. The Loan contains customary conditions of borrowing, events of default and covenants, including covenants that restrict Arcturus Therapeutics, Inc.’s ability to dispose of assets, merge with or acquire other entities, incur indebtedness and make distributions to holders of its capital stock. In addition, Arcturus Therapeutics, Inc. is required to maintain at least 100% of its consolidated, unrestricted cash, or $15.0 million, whichever is lower, with the Bank.

On October 30, 2019, Arcturus Therapeutics, Inc. and the Bank entered into a Third Amendment (the “Third Amendment”) to the Loan (as amended, the “Loan Agreement”).

Pursuant to the amendment, the Bank agreed to make a term loan to Arcturus Therapeutics, Inc. on October 30, 2019, in the amount of $15.0 million (the “Term Loan”). The resulting net increase in the indebtedness of Arcturus Therapeutics, Inc. was $5.0 million. The Term Loan bears interest at a floating rate ranging from 1.25% to 2.75% above the prime rate. The amendment further provides that the Term Loan has a maturity date of October 30, 2023. Arcturus Therapeutics, Inc. will make monthly payments of interest only until October 1, 2021. The Fourth Amendment was executed in connection with the Singapore Loan. In October of 2021, the Company and the Bank entered into a Fifth Amendment to Loan Agreement that provides for a six month extension to the interest only period which moves the first principal payment to May 1, 2022.

Arcturus Therapeutics, Inc. paid a loan origination fee of $54,000 which was recorded as a debt discount along with the remaining loan origination fee from the Loan and is being accreted over the term of the Term Loan. In addition, Arcturus Therapeutics, Inc. is required to pay a fee of $525,000 upon certain change of control events.

The Term Loan may be prepaid in full at any time, subject to a prepayment fee ranging from 0.50% to 2.00% of the prepaid principal amount depending upon the date of the prepayment.

Upon maturity or prepayment (as previously discussed), Arcturus Therapeutics, Inc. will be required to pay a 2% fee as a result of the FDA’s approval to proceed with the Company’s LUNAR-OTC program based on its IND submission. Such fee is accreted to the long-term debt balance using the effective interest method over the term of the Loan Agreement.

Should an event of default occur, including the occurrence of a material adverse effect, the Company could be liable for immediate repayment of all obligations under the Loan Agreement. As of December 31, 2021, the Company was in compliance with all covenants under the Loan Agreement.

Principal payments, including the final payment due at repayment, on the long-term debt are as follows:

Year Ending December 31,		
2022	$	6,666,667
2023		8,633,333
Total	$	15,300,000

The Company recognized interest expense related to its long-term debt of $2.7 million, $0.9 million and $0.9 million during the years ended December 31, 2021, 2020 and 2019, respectively.

NOTE 8. Stockholders' Equity

Alexion Pharmaceuticals License Agreement

On February 17, 2021, the Company entered into an exclusive license agreement with Alexion Pharmaceuticals, Inc. ("Alexion") pursuant to which Alexion granted to the Company an exclusive, worldwide license to exploit certain specified Alexion patent applications. In accordance with the terms of the license agreement, and in exchange for the license, the Company issued 74,713 shares of its common stock to Alexion on February 19, 2021 valued at approximately $5.0 million. The number of shares issued under the agreement was calculated by dividing (i) five million dollars ($5.0 million) by (ii) the volume-weighted average price per share of the Company's common stock on the Nasdaq Global Market for the thirty (30) trading days immediately preceding the Effective Date (rounded to the nearest whole share). The Company recorded the transaction as an asset purchase as management concluded that all of the value received was related to a single identifiable asset. Further, the Company concluded that there was no alternative future use for the asset and recorded a charge at the closing of the transaction for the full $5.0 million value assigned to the shares issued in connection with the license agreement. This non-cash charge was recorded as acquired in-process research and development expense in the statements of operations and comprehensive loss.

Net Loss per Share

Dilutive securities that were not included in the calculation of diluted net loss per share for the years ended December 31, 2021, 2020 and 2019 as they were anti-dilutive totaled 1,261,112, 1,157,175 and 138,377, respectively.

For the year ended December 31, 2019, the calculation of the weighted-average number of shares outstanding excludes 622,667 unvested restricted common shares held by founders of the Company. During the year ended 2020, the remaining milestones under the founder share agreements were achieved and the related restricted common shares fully vested.

NOTE 9. Share-Based Compensation

In October 2021, the Company adopted the 2021 Inducement Equity Incentive Plan which covers the award of up to 1,000,000 shares of common stock (the "2021 Plan") effective as of October 15, 2021. Approval of the Company's stockholders will not be required as a condition to the effectiveness of the 2021 Plan for so long as the plan is in compliance with Nasdaq inducement plan rules. On October 20, 2021, the Company filed a Form S-8 with the United States Securities and Exchange Commission to register 1,000,000 awards. As of December 31, 2021, a total of 756,300 shares remain available for future issuance under the 2021 Plan, subject to the terms of the 2021 Plan.

In June 2020, the stockholders of the Company approved an increase to the number of shares authorized for use in making awards under the 2019 Omnibus Equity Incentive Plan (the "2019 Plan") by 2,400,000 shares to 5,000,000. Accordingly, as of December 31, 2021, a total of 78,840 shares remain available for future issuance under the 2019 Plan, subject to the terms of the 2019 Plan. stock

Employee Stock Purchase Plan

In June 2020, the stockholders of the Company approved the 2020 Employee Stock Purchase Plan ("2020 Plan") which provides for 600,000 shares of Company common stock reserved for future issuance. The first accumulation period under the 2020 Plan commenced on August 17, 2020 and ended on the purchase date, August 13, 2021, at which point 12,601 shares of common stock were purchased. The next accumulation period commenced on August 16, 2021.

Under the 2020 Plan, eligible employees may purchase shares of the Company's common stock at a discount annually, subject to a maximum of $25,000 per year. The discounted purchase price is equal to the lower of 85% of (i) the market value per share of the common stock on the first day of the accumulation period or (ii) the market value per share of common stock on the purchase date. Share-based compensation expense recognized under the 2020 Plan was $0.3 million and $0.1 million for 2021 and 2020, respectively.

Share Options

The following table presents the weighted-average assumptions used in the Black-Scholes valuation model by the Company in calculating the fair value of stock options granted:

	For the Year Ended December 31,		
	2021	2020	2019
Expected life (in years)	6.03	6.04	5.92
Expected volatility	73.7%	72.4%	73.9%
Expected dividend yield	—%	—%	—%
Risk-free interest rate	1.13%	0.74%	1.82%
Grant date weighted average fair value	$ 26.71	$ 42.33	$ 6.39

The following table summarizes the Company's stock option activity for the year ended December 31, 2021:

	Number of Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (in thousands)
Outstanding – December 31, 2020	3,324,713	$ 46.03		
Granted	1,699,559	$ 41.87		
Exercised	(93,165)	$ 9.68		
Forfeited/cancelled	(277,540)	$ 56.37		
Outstanding – December 31, 2021	4,653,567	$ 44.62	8.05	$ 47,111
Exercisable – December 31, 2021	1,613,438	$ 29.48	7.28	$ 31,322
Exercisable and expected to vest – December 31, 2021	4,653,567	$ 44.62	8.05	$ 47,111

At December 31, 2021, the total unrecognized compensation cost of $97.5 million will be recognized over the weighted-average remaining service period of approximately 3.0 years. The fair value of the options vested during the years ended December 31, 2021, 2020 and 2019 was $28.4 million, $4.2 million and $1.9 million, respectively. The total intrinsic value of options exercised during the years ended December 31, 2021, 2020 and 2019 was $3.6 million, $20.2 million and $0.1 million, respectively.

Share-based compensation expenses included in the Company's statements of operations and comprehensive loss for the years ended December 31, 2021, 2020 and 2019 were:

	For the Year Ended December 31,		
(in thousands)	2021	2020	2019
Research and development	$ 14,101	$ 2,670	$ 654
General and administrative	14,814	4,094	1,328
Total	$ 28,915	$ 6,764	$ 1,982

NOTE 10. Income Taxes

A reconciliation of loss before income taxes for domestic and foreign locations is as follows:

(In thousands)	For the Year Ended December 31, 2021	2020	2019
United States	$ (203,674)	$ (72,148)	$ (25,922)
Foreign	—	—	(69)
Total loss before income taxes	$ (203,674)	$ (72,148)	$ (25,991)

The Company accounts for income taxes in accordance with ASC 740-10, *Accounting for Uncertainty in Income Taxes*. The impact of an uncertain income tax position on the income tax return must be recognized at the largest amount that is more likely than not to be sustained upon audit by the relevant taxing authority. An uncertain tax position will not be recognized if it has less than 50% likelihood of being sustained.

A reconciliation of unrecognized tax benefits is as follows (in millions):

	December 31, 2021	2020	2019
Beginning balance of unrecognized tax benefits	$ 1.5	$ 0.4	$ 0.4
Settlement of prior period tax positions	—	—	—
(Decrease) increase for prior period tax positions	(0.1)	0.3	—
Increase for current period tax positions	1.0	0.8	—
Ending balance of unrecognized tax benefits	$ 2.4	$ 1.5	$ 0.4

Amounts in the summary rollforward would not impact our effective tax rate as the Company maintains a full valuation on its net deferred tax assets. The Company is subject to taxation and files income tax returns in the United States, California and Israel. The Company's tax years from 2014 to date are subject to examination by the Israeli, U.S., and state taxing authorities due to the carryforward of unutilized net operating losses and research and development credits. The Company's policy is to recognize interest expense and penalties related to income tax matters as income tax expense. As of December 31, 2021, 2020 and 2019, there are unrecognized tax benefits of $2.4 million, $1.5 million and $0.4 million, respectively, for both the United States and California. There was no tax related interest or penalties recognized for the years ended December 31, 2021, 2020 and 2019.

The Company does not anticipate any material changes to its unrecognized tax benefits within the next twelve months.

The significant components of deferred income taxes are as follows:

(in thousands)	December 31, 2021	December 31, 2020
Deferred tax assets:		
Net operating loss	$ 69,761	$ 33,896
Tax credits	11,020	6,278
Accrued liabilities	910	535
Deferred revenue	5,098	3,230
Inventory	5,850	—
Basis difference in equity investments	1,957	—
Depreciation and amortization	960	—
Lease liability	1,360	1,274
Share-based compensation	3,971	1,338
Total gross deferred tax assets	100,887	46,551
Deferred tax liabilities:		
Depreciation and amortization	—	(69)
Right-of-use asset	(1,265)	(1,168)
Valuation allowance	(99,622)	(45,314)
Net deferred tax asset	$ —	$ —

The Company has established a valuation allowance against net deferred tax assets due to the uncertainty that such assets will be realized. The Company periodically evaluates the recoverability of the deferred tax assets. At such time as it is determined that it is more likely than not that deferred tax assets will be realizable, the valuation allowance will be reduced.

At December 31, 2021, the Company had federal and state net operating losses (“NOL”) carryforwards of approximately $258.0 million and $226.8 million, respectively. The federal NOL carryforwards begin to expire in 2034, and the state NOL carryforwards begin to expire in 2034. The federal net operating loss carryover includes $242.2 million of net operating losses generated in 2018 and after. Federal net operating losses generated in 2018 and after carryover indefinitely and may generally be used to offset up to 80% of future taxable income.

At December 31, 2021, the Company has federal and state research and development credit carryforwards of approximately $6.5 million and $4.6 million, respectively. The federal credit carryforwards begin to expire in 2033, and the state credits carry forward indefinitely. Additionally, the Company has an Orphan Drug Credit of $3.1 million as of December 31, 2021 which will begin to expire in 2039 unless previously utilized.

Pursuant to Internal Revenue Code (IRC) Sections 382 and 383, annual use of the Company’s federal and California net operating loss and research and development credit carryforwards may be limited in the event a cumulative change in ownership of more than 50% occurs within a three-year period. The Company has not completed an IRC Section 382 analysis regarding the limitation of net operating loss carryforwards and other tax attributes. There is a risk that changes in ownership have occurred since Company's formation. If a change in ownership were to have occurred, the NOL carryforwards and other tax attributes could be limited or restricted. If limited, the related asset would be removed from the deferred tax asset schedule with a corresponding reduction in the valuation allowance. Due to the existence of the valuation allowance, limitations created by future ownership changes, if any, related to the Company’s operations in the U.S. will not impact the Company’s effective tax rate.

A reconciliation of the federal statutory income tax rate to the Company's effective income tax rate is as follows:

	For the Year Ended December 31,		
	2021	2020	2019
Federal statutory income tax rate	21.0%	21.0%	21.0%
State income taxes, net of federal benefit	6.2%	6.8%	4.6%
Foreign rate differential	—%	—%	0.3%
Share-based compensation	(0.4%)	5.5%	(0.1%)
Officers compensation	(1.1%)	—%	—%
Research and development credits	2.9%	8.7%	—%
Uncertain tax position	(0.4%)	(1.5%)	—%
Change in tax rate	(1.7%)	(1.5%)	(0.1%)
Foreign net operating losses	—%	28.5%	—%
Change in valuation allowance	(26.7%)	(67.4%)	(25.1%)
Other	0.2%	(0.1%)	0.1%
Permanent differences	—%	—%	(0.7%)
Provision for income taxes	—%	—%	—%

NOTE 11. Commitments and Contingencies

COVID-19 Vaccine Development

On March 4, 2020, the Company was awarded a grant ("Grant 1") from the Singapore EDB to support the co-development of a potential COVID-19 vaccine with the Duke-NUS Medical School. The Grant provides for up to S$14.0 million (approximately US$10.0 million using the exchange rate at the time the grant contract was entered into) in grants to support the development of the vaccine. The Grant has been paid in full by the EDB as a result of the achievement of certain milestones related to the progress of the development of the vaccine, as set forth in the award agreement. The funds received have been recognized as contra research and development expense. The parties are in continued negotiations with respect to amendments of Grant 1. Currently, the Company is liable for certain expenses during the program and is also subject to certain conditions including the requirement to pay an agreed upon royalty rate to Duke-NUS on future net sales of the LUNAR-COV19 vaccine candidate developed with Duke-NUS in markets or jurisdictions outside of Singapore. For the year ended December 31, 2021 and 2020, the Company recognized $1.3 million and $8.7 million, respectively, of contra expense for Grant 1. At December 31, 2021, no amount remained in accrued expenses. At December 31, 2020, $1.3 million remained in accrued expenses.

On October 2, 2020, the Company was awarded another grant ("Grant 2") from the Singapore EDB to support the clinical development of a potential COVID-19 vaccine (ARCT-021). The grant provides for up to S$9.3 million (approximately US$6.7 million) to support the clinical development of the vaccine candidate for costs incurred in Singapore subject to certain conditions. The grant is paid in two installments upon the achievement of certain milestones related to the progress of the development of the vaccine candidate. The Company received the first installment of $3.6 million in the fourth quarter of 2020. The funds received are recognized as contra research and development expense as costs are incurred. As of the year ended December 31, 2021, the Company recognized the remaining amount of the first installment as contra research and development expense for Grant 2. The parties are in continued negotiations with respect to amendments of Grant 2.

Cystic Fibrosis Foundation Therapeutics Funding agreement

On August 1, 2019, the Company amended its Development Program Letter Agreement, dated May 16, 2017 and as amended July 13, 2018, with the Cystic Fibrosis Foundation ("CFF"). Pursuant to the amendment, (i) CFF increased the amount it will award to advance LUNAR-CF to $15.0 million from approximately $3.2 million, (ii) the Company will provide $5.0 million in matching funds for remaining budgeted costs, (iii) the related disbursement schedule from CFF to Arcturus will be modified such that (a) $4.0 million will be disbursed upon execution of the CFF Amendment, (b) $2.0 million will be disbursed within 30 days of the first day of each of January, April, July and October 2020 upon Arcturus invoicing CFF to meet project goals, and (c) the last payment of $3.0 million less the prior award previously paid out, equaling approximately $2.3 million, will be disbursed upon Arcturus Sub invoicing CFF to meet good manufacturing practices and opening an Investigational New Drug ("IND") application. The funds received from CFF are recognized as contra research and development expense in proportion to the percentage covered by CFF of the overall budget. For the years ended December 31, 2021 and 2020, the Company recognized $3.8 million and $3.4 million of contra expense with $2.8 million and $6.6 million remaining in accrued expenses, respectively.

Leases

In October 2017, the Company entered into a non-cancellable operating lease agreement for office space adjacent to its previously occupied headquarters. The commencement of the lease began in March 2018 and extends for approximately 84 months from the commencement date with a remaining lease term through March 2025. Monthly rental payments are due under the lease and there are escalating rent payments during the term of the lease. The Company is also responsible for its proportional share of operating expenses of the building and common areas. In conjunction with the new lease, the Company received free rent for four months and received a tenant improvement allowance of $74,000. The lease may be extended for one five-year period at the then current market rate with annual escalations; however, the Company deemed the extension option not reasonably certain to be exercised and therefore excluded the option from the lease terms. The Company entered into an irrevocable standby letter of credit with the landlord for a security deposit of $96,000 upon executing the lease which is included (along with additional funds required to secure the letter of credit) in the balance of non-current restricted cash.

In February 2020, the Company entered into a non-cancellable operating lease agreement for office space near its current headquarters. The lease extends for 13 months from the commencement date and included a right to extend the lease for one twelve-month period. In February 2021, the Company opted to extend the lease through March 2025 to coincide with the Company's headquarters.

In February 2021, the Company entered into a third non-cancellable operating lease agreement for office space near its current headquarters. The lease extends for 12 months from the commencement date with monthly base rent of approximately $11,000. During the year ended 2021, the Company opted to extend the lease for an additional 12 months.

In September 2021, the Company entered into a non-cancellable lease agreement for office, research and development, engineering and laboratory space near its current headquarters. The initial term of the lease will extend ten years and eight months from the date of possession, and the Company will have the right to extend the term of the lease for an additional five-year period. The lease has a monthly base rent ranging from $268,000 to $360,000 which escalates over the lease term. The Company is expecting that it will gain access to the space in the second quarter of 2022.

Operating lease right-of-use asset and liability on the consolidated balance sheets represent the present value of remaining lease payments over the remaining lease terms. The Company does not allocate lease payments to non-lease components; therefore, payments for common-area-maintenance and administrative services are not included in the operating lease right-of-use asset and liability. The Company uses its incremental borrowing rate to calculate the present value of the lease payments, as the implicit rate in the lease is not readily determinable.

As of December 31, 2021, the payments of the operating lease liability were as follows:

(in thousands)	Remaining Lease Payments
2022	$ 1,987
2023	2,185
2024	2,251
Thereafter	522
Total remaining lease payments	6,945
Less: imputed interest	(906)
Total operating lease liabilities	$ 6,039
Weighted-average remaining lease term	3.25 years
Weighted-average discount rate	8.4%

Operating lease costs consist of the fixed lease payments included in operating lease liability and are recorded on a straight-line basis over the lease terms. Operating lease costs were $1.9 million, $1.9 million and $1.2 million for the years ended December 31, 2021, 2020 and 2019, respectively.

Note 12. Related Party Transactions

Ultragenyx

On June 17, 2019, Arcturus and Ultragenyx executed Amendment 3 to the Ultragenyx Agreement. Pursuant to the amended Ultragenyx Agreement, the Company granted Ultragenyx a two-year option to purchase up to 600,000 additional shares of common stock at a price of $16.00 per share, and in May 2020 Ultragenyx exercised the option. During 2021, Ultragenyx sold 1,800,000 shares of common stock resulting in an ownership of 4.6% of the outstanding common stock of Arcturus as of December 31, 2021. For the years ended December 31, 2021, 2020 and 2019, the Company has recognized revenue of $3.7 million, $4.0 million and $5.9 million, respectively, related to the Ultragenyx Agreement. As of December 31, 2021 and 2020, the Company holds accounts receivable balances of negligible amounts related to the Ultragenyx Agreement.

Equity-Method Investment

In June 2018, the Company completed the sale of its intangible asset related to the ADAIR technology. Pursuant to the asset purchase agreement for ADAIR, the Company received a 30% ownership interest in the common stock of Vallon Pharmaceuticals, Inc. ("Vallon") in consideration for the sale of the ADAIR technology. The Company has no requirement to invest further in Vallon. Vallon completed an initial public offering and began trading on The Nasdaq Stock Market under the ticker "VLON" in February 2021. Immediately after this offering, Arcturus owned 843,750 shares of Vallon, or approximately 12%. Based on the Company's ownership and the Vallon board of directors seat held by an executive of Arcturus, the Company has the ability to exercise significant influence over the operating and financial policies of Vallon; therefore, the Company accounts for this investment as an equity-method investment. The Company accounts for its share of the earnings or losses of the investee with a reporting lag of three months, as the financial statements of the investee are not completed on a basis that is sufficient for the Company to apply the equity method on a current basis. The offering was at a share price of $8.00, greater than the initial investment which resulted in the Company recording a gain in its equity-method investment. Using a three month lag, the gain has been offset by losses incurred by Vallon through September 30, 2021.

Note 13. Subsequent Events

None.

Note 14. Selected Quarterly Financial Data (Unaudited)

A summary of our quarterly results is as follows:

(in thousands, except per share data)	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Year Ended December 31, 2021:				
Revenue	$ 2,127	$ 2,001	$ 2,437	$ 5,794
Research and development expenses, net	50,050	45,679	45,398	32,633
General and administrative expenses	9,743	10,042	10,860	10,806
Loss from operations	(57,666)	(53,720)	(53,821)	(37,645)
Net loss	(56,346)	(54,581)	(54,084)	(38,663)
Net loss per share, basic and diluted	$ (2.15)	$ (2.07)	$ (2.05)	$ (1.47)
Weighted average shares outstanding, basic and diluted	26,243	26,323	26,338	26,359
Year Ended December 31, 2020:				
Revenue	$ 2,646	$ 2,322	$ 2,333	$ 2,238
Research and development expenses, net	7,917	7,944	17,699	24,286
General and administrative expenses	4,191	4,420	5,572	9,034
Loss from operations	(9,462)	(10,042)	(20,938)	(31,082)
Net loss	(9,777)	(10,263)	(21,004)	(31,104)
Net loss per share, basic and diluted	$ (0.67)	$ (0.55)	$ (0.92)	$ (1.25)
Weighted average shares outstanding, basic and diluted	14,521	18,794	22,938	24,886

Common Stock

As of February 23, 2022, there were 26,375,002 shares of common stock outstanding. The holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders. The holders of common stock are not entitled to cumulative voting rights with respect to the election of directors, and as a consequence, minority stockholders will not be able to elect directors on the basis of their votes alone. Subject to preferences that may be applicable to any then outstanding shares of preferred stock, holders of common stock are entitled to receive ratably such dividends as may be declared by the board of directors out of funds legally available therefor. In the event of a liquidation, dissolution or winding up of us, holders of the common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preferences of any then outstanding shares of preferred stock. Holders of common stock have no preemptive rights and no right to convert their common stock into any other securities. There are no redemption or sinking fund provisions applicable to our common stock. All outstanding shares of common stock are fully paid and non-assessable. The rights, preferences and privileges of holders of our common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any of our outstanding preferred stock.

Listing

Our common stock is listed under the symbol “ARCT” on the NASDAQ.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Continental Stock Transfer & Trust.

Dividends

We have not declared any cash dividends on our common stock since inception and we do not anticipate paying any cash dividends on our common stock in the foreseeable future.

Possible Anti-Takeover Effects of Delaware Law and our Charter Documents

Provisions of the Delaware General Corporation Law, or DGCL, our certificate of incorporation, and our bylaws, could make it more difficult to acquire us by means of a tender offer, a proxy contest or otherwise, or to remove incumbent officers and directors. These provisions, summarized below, are expected to discourage certain types of coercive takeover practices and takeover bids that our board of directors may consider inadequate and to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of increased protection of our ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure us outweigh the disadvantages of discouraging takeover or acquisition proposals because, among other things, negotiation of these proposals could result in an improvement of their terms.

Delaware Anti-Takeover Statute

We are subject to Section 203 of the DGCL, an anti-takeover statute. In general, Section 203 of the DGCL prohibits a publicly held Delaware corporation from engaging in a “business combination” with an “interested stockholder” for a period of three years following the time the person became an interested stockholder, unless the business combination or the acquisition of shares that resulted in a stockholder becoming an interested stockholder is approved in a prescribed manner. Generally, a “business combination” includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. Generally, an “interested stockholder” is a person who, together with affiliates and associates, owns (or within three years prior to the determination of interested stockholder status did own) 15% or more of a corporation’s voting stock. The existence of this provision would be expected to have an anti-takeover effect with respect to transactions not approved in advance by our board of directors, including discouraging attempts that might result in a premium over the market price for the shares of common stock held by our stockholders.

Election and Removal of Directors

Our board of directors is elected annually by all holders of our capital stock. The stockholders may nominate one or more persons for election as directors at an annual meeting of stockholders, but only if written notice of such stockholder’s intent to make such nomination or nominations has been received by the Secretary of the Company not less than forty-five (45) nor more than seventy-five (75) days prior to the first anniversary of the preceding year’s annual meeting of stockholders. Any vacancy on the board of directors resulting from death, resignation,

removal or otherwise or newly created directorships may be filled by the vote of the majority of directors then in office, although less than a quorum, or by a sole remaining director.

Amendment
The affirmative vote of a majority of the entire board of directors may amend and repeal the bylaws. The bylaws may be altered, amended or repealed, and new bylaws may be adopted, at any annual meeting of the stockholders (or at any special meeting thereof duly called for that purpose) by a majority of the combined voting power of the then outstanding shares of capital stock of all classes and series of the Company entitled to vote generally in the election of directors, voting as a single class, provided that, in the notice of any such special meeting, notice of such purpose shall be given.

Size of Board and Vacancies
Pursuant to our certificate of incorporation, and our bylaws, the number of directors constituting the board shall be at least one and no more than nine and our board of directors has the exclusive right to fix the size of the board and to fill any vacancies resulting from death, resignation, disqualification or removal as well as any newly created directorships arising from an increase in the size of the board.

Special Stockholder Meetings
Our bylaws provide that special meetings of stockholders can be called only by the board of directors, the chairman of the board of directors or the chief executive officer. Stockholders are not permitted to call a special meeting and cannot require the board of directors to call a special meeting. There is no right of stockholders to act by written consent without a meeting.

Requirements for Advance Notification of Stockholder Nominations and Proposals
Our bylaws establish advance notice procedures with respect to stockholder proposals and nomination of candidates for election as directors other than nominations made by or at the direction of our board of directors or a committee of our board of directors.

No Cumulative Voting
The DGCL provides that stockholders are denied the right to cumulate votes in the election of directors unless our certificate of incorporation provides otherwise. Our amended and certificate of incorporation does not provide for cumulative voting.

Authorized but Unissued Shares
Our authorized but unissued shares of common stock and preferred stock will be available for future issuance without stockholder approval. We may use additional shares for a variety of purposes, including future public offerings to raise additional capital, to fund acquisitions and as employee compensation. The existence of authorized but unissued shares of undesignated preferred stock may enable our board of directors to render more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of us or our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer, stockholder or stockholder group. The rights of holders of our common stock described above will be subject to, and may be adversely affected by, the rights of any preferred stock that we may designate and issue in the future. The issuance of shares of undesignated preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Director Liability
Our bylaws limit the extent to which our directors are personally liable to us and our stockholders, to the fullest extent permitted by the DGCL. The inclusion of this provision in our bylaws may reduce the likelihood of derivative litigation against directors and may discourage or deter stockholders or management from bringing a lawsuit against directors for breach of their duty of care.

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-4 No. 333-230353) of Arcturus Therapeutics Holdings Inc.,
(2) Registration Statement (Form S-8 No. 333-232272) pertaining to the Arcturus Therapeutics Holdings Inc. 2019 Omnibus Equity Incentive Plan,
(3) Registration Statement (Form S-8 No. 333-240397) pertaining to the Arcturus Therapeutics Holdings Inc. Amended and Restated 2019 Omnibus Equity Incentive Plan,
(4) Registration Statement (Form S-8 No. 333-240392) pertaining to the Arcturus Therapeutics Holdings Inc. 2020 Employee Stock Purchase Plan,
(5) Registration Statement (Form S-8 No. 333-260391) pertaining to the Arcturus Therapeutics Holdings Inc. 2021 Inducement Equity Incentive Plan, and
(6) Registration Statements (Form S-3 Nos. 333-232281, 333-235475, 333-237703, 333-238139, 333-235475 and 333-251175) of Arcturus Therapeutics Holdings Inc.

of our reports dated February 28, 2022, with respect to the consolidated financial statements of Arcturus Therapeutics Holdings Inc., and the effectiveness of internal control over financial reporting of Arcturus Therapeutics Holdings Inc. included in this Annual Report (Form 10-K) for the year ended December 31, 2021.

/s/ Ernst & Young LLP

San Diego, California
February 28, 2022

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a)

I, Joseph E. Payne, certify that:

1. I have reviewed this Annual Report on Form 10-K of Arcturus Therapeutics Holdings Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 28, 2022

By: /s/ Joseph E. Payne

Joseph E. Payne
President, Chief Executive Officer and Director
(principal executive officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO
RULES 13a-14(a)

I, Andrew Sassine, certify that:

1. I have reviewed this Annual Report on Form 10-K of Arcturus Therapeutics Holdings Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 28, 2022

By: /s/ Andrew Sassine

Andrew Sassine
Director and Chief Financial Officer
(principal financial officer)

Exhibit 31.3

CERTIFICATION PURSUANT TO
RULES 13a-14(a)

I, Keith C. Kummerfeld, certify that:

1. I have reviewed this Annual Report on Form 10-K of Arcturus Therapeutics Holdings Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 28, 2022

By: /s/ Keith C. Kummerfeld

Keith C. Kummerfeld
Vice President of Finance and Corporate Controller
(principal accounting officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350

In connection with the Annual Report of Arcturus Therapeutics Holdings Inc. (the "Company") on Form 10-K for the fiscal year ended December 31, 2021 (the "Report"), I, Joseph E. Payne, President, Chief Executive Officer and Director of the Company, hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to my knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 28, 2022

By: /s/ Joseph E. Payne

Joseph E. Payne
President, Chief Executive Officer and Director
(principal executive officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350

In connection with the Annual Report of Arcturus Therapeutics Holdings Inc. (the "Company") on Form 10-K for the fiscal year ended December 31, 2021 (the "Report"), I, Andrew Sassine, Chief Financial Officer and Director of the Company, hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to my knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 28, 2022

By: /s/ Andrew Sassine

Andrew Sassine
Director and Chief Financial Officer
(principal financial officer)

Exhibit 32.3

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350

In connection with the Annual Report of Arcturus Therapeutics Holdings Inc. (the "Company") on Form 10-K for the fiscal year ended December 31, 2021 (the "Report"), I, Keith C. Kummerfeld, Vice President of Finance and Corporate Controller of the Company, hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to my knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 28, 2022

By: /s/ Keith C. Kummerfeld

Keith C. Kummerfeld
Vice President of Finance and Corporate Controller
(principal accounting officer)