



Arcturus Announces Self-amplifying COVID-19 mRNA Vaccine Candidate ARCT-154 Meets Primary Efficacy Endpoint in Phase 3 Study

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95% Efficacy overall for prevention of severe COVID-19 disease including related deaths

55% Efficacy overall for preventing symptomatic COVID-19 disease

Study conducted when Delta and Omicron variants were dominant in Vietnam

Incidence of unsolicited adverse events with ARCT-154 similar to placebo; No reported cases of myocarditis or pericarditis

ARCT-154 to advance into a pivotal booster trial in major markets

SAN DIEGO--(BUSINESS WIRE)--Apr. 20, 2022-- Arcturus Therapeutics Holdings Inc. (the "Company", "Arcturus", Nasdaq: ARCT), a leading clinical-stage messenger RNA medicines company focused on the development of infectious disease vaccines and significant opportunities within liver and respiratory rare diseases, today shared topline data from an ongoing Phase 1/2/3 trial evaluating ARCT-154, Arcturus' self-amplifying mRNA vaccine candidate against COVID-19 disease caused by the SARS-CoV-2 virus.

"We are very pleased with these results, and to see ARCT-154 providing protection against symptomatic COVID-19 and almost complete protection against severe disease in a placebo-controlled vaccine efficacy study. This represents a key milestone for the Company and provides significant clinical validation of our STARR™ platform. We believe self-amplifying mRNA combined with our LUNAR® delivery technology will create a path to better mRNA medicines," said Joseph Payne, President and CEO of Arcturus Therapeutics. "We are grateful to our collaborator Vinbiocare and to Vietstar, a leading CRO in Vietnam, for their extraordinary effort and efficiency in the sponsorship and analysis of this trial. We are also thankful to the study participants, investigators and clinical trial sites for their invaluable contributions to the study."

The ongoing Phase 1/2/3 registrational study, sponsored by Arcturus' collaborator Vinbiocare Biotechnology Joint Stock Company ("Vinbiocare"), a member of Vingroup Joint Stock Company, enrolled over 19,000 adult subjects in Vietnam, including individuals at higher risk of severe complications of COVID-19 disease. Results from the efficacy analysis of the study have been submitted to the Vietnam Ministry of Health by Vinbiocare on April 13, 2022 and shared with Arcturus in parallel with this filing. This additional efficacy data complements the data package under review by the Vietnam Ministry of Health for potential Emergency Use Authorization of ARCT-154. The Phase 3 placebo-controlled vaccine efficacy portion of this study enrolled over 16,000 participants. Evaluation of vaccine efficacy demonstrated that the study met its primary endpoint of prevention of virologically confirmed COVID-19 disease. Data provided by Vinbiocare show that, in an analysis of COVID-19 cases accrued between 7 days and 56 days after completion of a two-dose vaccination series, two 5-mcg doses of ARCT-154 demonstrated 55% vaccine efficacy for protection against COVID-19. The cases of COVID-19 disease in the study participants were detected in parallel with a SARS-CoV-2 outbreak in Vietnam in December 2021 to February 2022 where characterized SARS-CoV-2 variants Delta and Omicron have dominated*.

The key secondary endpoint of severe COVID-19 disease (including COVID-19 related deaths) was analyzed and included 43 severe cases in the analysis. Forty-one cases occurred in the placebo group and 2 occurred in the ARCT-154 vaccinated group, demonstrating point estimate of vaccine efficacy of 95% against severe (including fatal) COVID-19 disease. Nine COVID-19 related deaths were reported in the placebo group and 1 in the ARCT-154 vaccinated group. The single death in the ARCT-154 vaccination arm occurred in an older age group participant who was also at increased risk of severe COVID-19.

COVID-19 Cases	Vaccine Efficacy for 2-dose (5 mcg/dose) ARCT-154
<i>Severe (including fatal) COVID-19 cases</i>	95.3% (95% CI; 80.4% - 98.9%)
<i>Overall COVID-19 cases</i>	55.0% (95% CI; 46.9% - 61.9%)

Table: Vaccine efficacy data provided by Vinbiocare and submitted to Vietnam Ministry of Health

The analysis performed by Vinbiocare included a review of the available safety data from over 17,000 participants enrolled in the Phase 1, 2 and 3 portions of the study through one month after second dose of ARCT-154. An independent Data Safety Monitoring Board has performed ongoing review of the safety data and has agreed with the continuation of the study without modification. The safety data show:

- The incidence of unsolicited adverse events in the ARCT-154 group and placebo group are comparable. No cases of myocarditis or pericarditis have been reported; however, the study is not large enough to reliably observe these events given their extremely rare frequency of occurrence.
- Adverse events collected in diaries of study participants (solicited adverse events) for seven days following each vaccination with ARCT-154 demonstrate that the majority of these events were mild or moderate in severity. In general, the frequency and severity of solicited adverse events did not increase with second dose administration. The majority of solicited adverse events resolved within the 7-day window of observation.

Additional data provided by Vinbiocare show that the study also met the immunogenicity primary endpoint, with 98.4% 4-fold seroconversion for ancestral (Wuhan) strain, measured by surrogate virus neutralization test (sVNT) 28 days after the second dose of ARCT-154. This analysis was conducted in the first approximately 1,000 participants enrolled in the Phase 1/2/3 study and was provided earlier by Vinbiocare to the Vietnam Ministry of Health as part of the filing for EUA. More comprehensive immunogenicity, efficacy and safety data from the study will be disclosed in a publication.

Arcturus has advanced ARCT-154 (5 mcg) toward a pivotal booster study which will involve approximately 2,400 participants. A clinical research organization to conduct the trial has been engaged and the Company has received constructive feedback from several regulatory agencies, including the U.S. Food and Drug Administration (FDA), the UK Medicines and Healthcare products Regulatory Agency (MHRA) and the European Medicines Agency (EMA), regarding the trial design.

* References: <https://covariants.org/per-country> (Accessed 04/20/2022); <https://covid19.who.int/region/wpro/country/vn> (Accessed 04/20/2022); <https://ourworldindata.org> COVID-19 Data Explorer ([Vietnam Link](#))

About Arcturus Therapeutics

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

Forward Looking Statements

This press release contains forward-looking statements that involve substantial risks and uncertainties for purposes of the safe harbor provided by the Private Securities Litigation Reform Act of 1995. Any statements, other than statements of historical fact included in this press release, are forward-looking statements, including those regarding strategy, future operations, the expectations for or likelihood of success of any collaborations, the likelihood of success (including safety and efficacy) of the Company's pipeline (including ARCT-154), the promise of the company's STARR platform or LUNAR delivery technology with self-amplifying mRNA, the likelihood that any independent verification by Arcturus, or any regulatory body's assessment of, of the data will be consistent with the information shared by Vinbiocare, the likelihood that clinical data will be predictive of future clinical results, the likelihood that clinical results will be predictive of results against future COVID variants, the likelihood of regulatory clearance to proceed with, and the planned initiation, design or completion of any clinical trials (including with respect to planned pivotal booster trial for ARCT-154), the timing or completion of any regulatory submissions including by Vinbiocare for submissions regarding ARCT-154, the ability to enroll, planned enrollment and timing for enrollment of, subjects in the planned pivotal booster trial for ARCT-154, the likelihood that clinical data will be sufficient for an EUA in Vietnam or for any other regulatory approval, the likelihood or timing of an EUA in Vietnam for ARCT-154 or for any regulatory approval, the timing and anticipated capacity of the manufacturing facility in Hanoi, Vietnam, the likelihood that a patent will issue from any patent application, and the impact of general business and economic conditions. Arcturus may not actually achieve the plans, carry out the intentions or meet the expectations or projections disclosed in any forward-looking statements such as the foregoing and you should not place undue reliance on such forward-looking statements. These statements are only current predictions or expectations, 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, including those discussed under the heading "Risk Factors" in Arcturus' most recent Annual Report on Form 10-K, and in subsequent filings with, or submissions to, the SEC, which are available on the SEC's website at www.sec.gov. Except as otherwise required by law, Arcturus disclaims any intention or obligation to update or revise any forward-looking statements, which speak only as of the date they were made, whether as a result of new information, future events or circumstances or otherwise.

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