Arcturus Therapeutics Announces Initiation of Phase 1 H5N1 Flu Vaccine Trial

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LUNAR-H5N1 becomes the third STARR® mRNA vaccine candidate to enter clinic

First Phase 1 participant dosed December 2024

Interim Phase 1 data expected H2 2025

SAN DIEGO--(BUSINESS WIRE)--Jan. 10, 2025-- Arcturus Therapeutics Holdings Inc. (the “Company”, “Arcturus”, Nasdaq: ARCT), a commercial messenger RNA medicines company focused on the development of infectious disease vaccines and opportunities within liver and respiratory rare diseases, today announced the initiation of the Company’s Phase 1 study of ARCT-2304, a self-amplifying mRNA (sa-mRNA) vaccine candidate, also known as LUNAR-H5N1, for active immunization to prevent pandemic influenza disease caused by H5N1 virus.

The randomized placebo-controlled Phase 1 trial (NCT06602531) is being conducted at multiple sites in the U.S. and designed to enroll approximately 200 healthy adults (120 participants 18-59 years old; 80 participants 60-80 years old). Screening of study participants began November 2024, with the first participant inoculated in December 2024. The clinical study is fully funded by Biomedical Advanced Research and Development Authority (BARDA).

The primary objective of this initial clinical trial is to evaluate safety and immune responses of three different dose levels and two different vaccination schedules of ARCT-2304 vaccine. Immune responses are measured by hemagglutination inhibition (HAI), virus microneutralization (MN) and neuraminidase enzyme-linked lectin assays (ELLA).

ARCT-2304 (LUNAR-H5N1) utilizes clinically validated LUNAR® delivery and STARR® mRNA platform technologies. STARR® mRNA has demonstrated in multiple clinical trials its ability to elicit a robust immune response at very low dose levels, with extended persistence of neutralizing antibodies compared to approved conventional mRNA vaccines. The robust safety database of the LUNAR and STARR technologies have been established through multiple COVID-19 and seasonal influenza vaccine trials, which included more than 20,000 participants and dose ranges from 1 to 20 mcg of mRNA.

“Clinically validating our low-dose STARR® mRNA technology in H5N1 flu is a crucial step towards pandemic preparedness,” said Joseph Payne, President and CEO of Arcturus Therapeutics. “Our team is working diligently with our partners, BARDA and CSL, in the United States and globally in this effort.”

About H5N1 Influenza

H5N1 influenza is a significant concern in animal health. To date, H5N1 flu has affected over 10,000 wild birds, nearly a thousand dairy cows, and over 130 million poultry. Elevated H5N1 infections in animals have led to increasing numbers of human infections including two confirmed severe cases in the United States and one death. Most of the confirmed 67 human infections are due to exposure of U.S. dairy and poultry workers to infected dairy cows and poultry.

About sa-mRNA

mRNA vaccines help protect against infectious diseases by providing a blueprint for cells in the body to make a protein to help our immune systems recognize and fight the disease. Unlike conventional mRNA vaccines, self-amplifying mRNA vaccines instruct the body to make more mRNA and protein to boost the immune response.

About ARCT-2304 (LUNAR-H5N1)

ARCT-2304, also known as LUNAR-H5N1, is a sa-mRNA vaccine candidate formulated with Arcturus proprietary LUNAR® delivery technology. The sa-mRNA vaccine candidate is designed to make many copies of mRNA within the host cell after intramuscular injection to achieve enhanced expression of haemagglutinin (HA) and neuraminidase (NA) antigens, thereby enabling lower doses than conventional mRNA vaccines. Utilizing a mRNA-based platform for pandemic influenza vaccine development offers further options for meeting domestic vaccine manufacturing surge capacity goals. The technology may make vaccines available much sooner than egg- and cell-based technologies. The lyophilized vaccine formulation is stable in refrigerators, thereby simplifying cold-chain storage and reducing distribution risks.

About Arcturus

Founded in 2013 and based in San Diego, California, Arcturus Therapeutics Holdings Inc. (Nasdaq: ARCT) is a commercial mRNA medicines and vaccines company with enabling technologies: (i) LUNAR® lipid-mediated delivery, (ii) STARR® mRNA Technology (sa-mRNA) and (iii) mRNA drug substance along with drug product manufacturing expertise. Arcturus developed KOSTAIVE®, the first self-amplifying messenger RNA (sa-mRNA) COVID vaccine in the world to be approved. Arcturus has an ongoing global collaboration for innovative mRNA vaccines with CSL Seqirus, and a joint venture in Japan, ARCALIS, focused on the manufacture of mRNA vaccines and therapeutics. Arcturus’ pipeline includes RNA therapeutic candidates to potentially treat ornithine transcarbamylase (OTC) deficiency and cystic fibrosis (CF), along with its partnered mRNA vaccine programs for SARS-CoV-2 (COVID-19) and influenza. Arcturus’ versatile RNA therapeutics platforms can be applied toward multiple types of nucleic acid medicines

including messenger RNA, small interfering RNA, circular RNA, antisense RNA, self-amplifying RNA, DNA, and gene editing therapeutics. Arcturus' technologies are covered by its extensive patent portfolio (over 400 patents and patent applications in the U.S., Europe, Japan, China, and other countries). 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 the likelihood of success (including safety and efficacy) of ARCT-2304, the timing for the interim Phase 1 data, the targeted enrollment and continued conduct of the Phase 1 study of ARCT-2304, the likelihood that preclinical or clinical results received to date will be predictive of future results (including with respect to the safety data generated to date), the continued involvement and support of BARDA and collaboration with CSL, the likelihood of success of the Company's development and related efforts for an influenza vaccine candidate, the future activities under and fulfillment of the Company's contract with BARDA, the ability of the Company's influenza vaccine technologies to support U.S. government pandemic preparedness goals, 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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