Study Shows Novel sa-mRNA Vaccines Offer Robust, Broad, Enduring Protection Against COVID-19 Variants

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Late-breaking data presented at 9th ESWI Influenza Conference in Valencia

SAN DIEGO--(BUSINESS WIRE)--Sep. 19, 2023-- Arcturus Therapeutics Holdings Inc. (the “Company”, “Arcturus”, Nasdaq: ARCT), a global late-stage clinical messenger RNA medicines company focused on the development of infectious disease vaccines and opportunities within liver and respiratory rare diseases, today announced the results of a phase 1/2 study showing that a booster dose of a novel, self-amplifying messenger RNA (sa-mRNA) vaccine against COVID-19 induces a robust, broadly cross-reactive, and durable immune response in adults that remains elevated through 12 months after vaccination. Three sa-mRNA vaccines were used in the study, which was presented as a poster at the European Scientific Working Group on Influenza's 9th ESWI Influenza Conference in Valencia, Spain.

Messenger RNA (mRNA) vaccine technology protects against infectious diseases by instructing cells in the body to make a specific protein, stimulating the immune response, and leaving a blueprint to recognize and fight future infection. However, sa-mRNA also provides the body with instruction to make copies of the mRNA, amplifying the amount of protein made. This advanced technology has shown the potential to offer longer duration of immune response at considerably lower doses compared to conventional mRNA vaccines.

“Current mRNA technologies provide effective initial immunogenicity against COVID-19, but the results of this study show that our sa-mRNA vaccine platform can offer improvements in duration and breadth of protection against new and emerging variants,” said Igor Smolenov, Chief Development Officer, Arcturus. “We are proud of the role Arcturus has played, collaborating with CSL, in advancing sa-mRNA vaccine development.”

CSL’s vaccine business, CSL Seqirus, is Arcturus’ global exclusive partner for the development of novel mRNA vaccines against SARS-CoV-2 (COVID-19), influenza and pandemic preparedness. CSL has a dynamic portfolio of lifesaving medicines, including those that treat hemophilia, hereditary angioedema (HAE) and immune deficiencies, vaccines to prevent influenza, and therapies in iron deficiency and nephrology.

“We are encouraged by the findings of the study, indicating the sa-mRNA platform’s potential to solve the challenge of mRNA vaccine waning immunity over time, and thereby provide prolonged protection at lower doses,” said Esther Heijnen, M.D., Vice President, Clinical Development, Vaccines Innovation Unit, CSL. “Our collaboration with Arcturus on advanced mRNA vaccines is another example of CSL’s relentless pursuit of disruptive innovation when public health and patients can benefit.”

Study Design and Results

For this phase 1/2 randomized, observer-blind study conducted in the US and Singapore, 36 adults previously immunized with approved COVID-19 mRNA vaccines as a primary series were recruited. Participants were randomized 1:1:1 to receive one booster dose on Day 1 of either the ARCT-021, ARCT-154, or ARCT-165 vaccines, all of which encode the SARS-CoV-2 full-length S glycoprotein of, respectively, the ancestral strain in native conformation, a prefusion-stabilized B.1 variant including the D614G mutation, or the Beta variant. Immunogenicity was assessed as neutralizing antibody titers against the SARS-CoV-2 D614G strain, and a panel of SARS-CoV-2 variants measured by pseudoviral microneutralization assay on Days 1, 15, 29, 91, 181, 271, and 366. Solicited adverse events (AE) were assessed up to 7 days, unsolicited AEs up to 28 days, and serious AEs up to 366 days after vaccination.

All three vaccines induced robust neutralizing immune response against the D614G variant at Day 29 with geometric mean fold rises (GMFR) from pre-booster levels of 20.0, 36.7 and 23.5 after ARCT-021, ARCT-154, and ARCT-165, respectively. ARCT-154, a leading candidate, induced a broad, cross-neutralizing immune response, which persisted up to one-year post-booster with no further boosting. Similar trends were observed for other SARS-CoV-2 variants including Beta, Delta, Omicron BA.1, Omicron BA.2, and Omicron BA.4/5. Additional exploratory testing confirmed cross-neutralization against emergent BQ.1.1 and XBB.1.5 Omicron sub-lineages with GMFRs of 12.8 and 3.4, respectively, at Day 29 post-booster. Adverse events were mild or moderate and resolved quickly, and rates of related or severe AEs were low.

About Arcturus Therapeutics

Founded in 2013 and based in San Diego, California, Arcturus Therapeutics Holdings Inc. (Nasdaq: ARCT) is a global late-stage clinical 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. The Company has ongoing collaborations with CSL Seqirus and Meiji Seika Pharma, and a joint venture with ARCALIS. Arcturus’ pipeline includes RNA therapeutic candidates to potentially treat ornithine transcarbamylase deficiency and cystic fibrosis, 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 (patents and patent applications issued 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 Statement

This press release contains forward-looking statements that involve substantial risks and uncertainties for purposes of the safe harbor provided by the

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