CSL and Arcturus Therapeutics' ARCT-154 Demonstrates Non-Inferiority to Original Strain and Superior Immunogenicity to Omicron BA.4/5 Variant Compared to First-Generation mRNA Vaccine Booster

December 21, 2023

Study conducted by Meiji Seika Pharma in Japan

- *Data follow approval of the world's first Self-Amplifying messenger RNA (sa-mRNA) COVID-19 Vaccine for Adults by Japan Ministry of Health, Labor and Welfare*
- *The randomized, double-blind, active-controlled study, conducted at 11 sites in Japan, was designed to compare the immunogenicity and tolerability of the sa-mRNA vaccine ARCT-154 with Comirnaty®*
- *Phase 3 Study published in The Lancet Infectious Diseases*

KING OF PRUSSIA, Pa. & SAN DIEGO--(BUSINESS WIRE)--Dec. 21, 2023-- Global biotechnology leader CSL (ASX:CSL; USOTC:CSLLY) and Arcturus Therapeutics (Nasdaq: ARCT) today announced the publication in *Lancet Infectious Diseases* of a Phase 3 study showing that a booster dose of ARCT-154, a novel, self-amplifying messenger RNA (sa-mRNA) vaccine, elicited a numerically higher immune response (meeting the non-inferiority criteria) against the original Wuhan-Hu-1 virus strain, and a superior immune response against Omicron BA.4/5 subvariant of SARS-CoV-2 virus compared to a booster dose of the conventional mRNA vaccine Comirnaty®. ARCT-154 results were achieved with one sixth the dose of Comirnaty® (5 µg vs 30 µg).

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The study included healthy adults initially immunized with two doses of an mRNA vaccine (Comirnaty® or Spikevax™); and then a third dose of Comirnaty® at least three months prior to the booster dose of either ARCT-154 or Comirnaty® in the study. Both vaccines were well-tolerated, with no causally associated severe or serious adverse events. The study was conducted in partnership with Meiji Seika Pharma, a global health company based in Japan.

"The initial head-to-head results of the ARCT-154 study are exciting as they show that our sa-mRNA vaccine platform has the potential to produce immunogenicity against COVID-19 in previously vaccinated patients that is as good or better—and at a much lower dose—than first generation mRNA vaccines," said Jonathan Edelman, M.D., Senior Vice President, Vaccines Innovation Unit, CSL. "These results move CSL one step closer to delivering on our promise to develop and provide differentiated innovations that help protect the public against the ongoing burden of COVID-19. We look forward to sharing additional data from CSL's sa-mRNA programs as we continue to advance this exciting technology."

"These important study findings mark another major achievement in the development of our innovative sa-mRNA vaccine platform and a significant moment for Arcturus and CSL," said Pad Chivukula, Ph.D., Chief Scientific Officer of Arcturus Therapeutics. "This study represents the first phase of CSL and Arcturus' plans to launch this innovative vaccine platform globally."

The phase 3 study results with ARCT-154 were used to support the approval of ARCT-154 for primary immunization and as a booster dose in Japan in November of this year.

The ARCT-154 study is ongoing and will continue to collect safety data and assess durability of the immune response in participants at 3-, 6- and 12-months post-vaccination.

Study design and results

The randomized, double-blind, active-controlled study, conducted at 11 sites in Japan, was designed to compare the immunogenicity and tolerability of the sa-mRNA vaccine ARCT-154 with authorized mRNA COVID-19 vaccine Comirnaty.® Investigators compared immune responses to ARCT-154 and Comirnaty® booster doses in healthy Japanese adults 18 years of age or older initially immunized with two doses of mRNA COVID-19 vaccine (Comirnaty® or Spikevax®) and then a third dose of Comirnaty® at least three months prior to receiving a booster dose of one of the study vaccines. Neutralizing antibodies were measured before and 28 days after booster vaccination. The primary objective was to demonstrate immunological non-inferiority of ARCT-154 to Comirnaty®, as measured by neutralizing antibodies against Wuhan-Hu-1 SARS-CoV-2. Primary endpoints include geometric mean titer (GMT) ratios and seroresponse rates (SRR) differences of neutralizing antibodies. Key secondary objectives included the assessment of immunological non-inferiority and superiority against the Omicron BA.4/5 subvariant and vaccine tolerability assessed using participant-completed electronic diaries.

Between December 13, 2022, and February 25, 2023, 828 participants were enrolled and randomized 1:1 to receive ARCT-154 (n = 420) or Comirnaty® (n = 408) booster doses. Four weeks after boosting, ARCT-154 induced higher Wuhan-Hu-1 neutralizing antibodies GMTs than Comirnaty® (5641 [95% CI: 4321-7363] vs. 3934 [2993, 5169], respectively), a GMT ratio of 1·43 (95% CI: 1·26–1·63), with respective SRR of 65.2 (60.2–69.9) vs. 51.6% (46·4 – 56·8), a difference of 13.6 (95% CI: 6.8 – 20.5), meeting the pre-established non-inferiority criteria. Respective

anti-Omicron BA.4/5 GMTs were 2551 (1687–3859) and 1958 (1281–2993), a GMT ratio of 1·30 (95% CI: 1·07–1·58), with SRR of 69.97 (65.0–74.1) vs. 58.0% (52.8–63.1), meeting the superiority criteria for ARCT-154 over Comirnaty®.

The booster doses of ARCT-154 and Comirnaty® were equally well-tolerated in this adult population, with no causally associated severe or serious adverse events; 95% and 97% of ARCT-154 and Comirnaty® vaccinees respectively reported local reactions and 66% and 63% had solicited systemic adverse events. These were mainly mild, occurring and resolving within 3–4 days of vaccination.

About sa-mRNA

In contrast to standard messenger RNA vaccine technology, self-amplifying messenger RNA (sa-mRNA) vaccine technology helps protect against infectious diseases by not only instructing cells in the body to make a specific protein, but also to make copies of these instructions in the cell. The produced protein antigen stimulates the immune response and leaves a blueprint to recognize and fight future infection. Because of the self-amplifying element of the vaccine, more protein is produced compared to an equivalent amount of standard mRNA, allowing for lower doses of sa-mRNA to be used. sa-mRNA also has the potential to prompt a potent and durable cellular immune response in addition to producing effective antibodies against the targeted virus.

About CSL

CSL (ASX:CSL; USOTC:CSLLY) is a global biotechnology company with a dynamic portfolio of lifesaving medicines, including those that treat hemophilia and immune deficiencies, vaccines to prevent influenza, and therapies in iron deficiency and nephrology. Since our start in 1916, we have been driven by our promise to save lives using the latest technologies. Today, CSL – including our three businesses: CSL Behring, CSL Seqirus and CSL Vifor – provides lifesaving products to patients in more than 100 countries and employs 32,000 people. Our unique combination of commercial strength, R&D focus and operational excellence enables us to identify, develop and deliver innovations so our patients can live life to the fullest. For inspiring stories about the promise of biotechnology, visit CSLBehring.com/Vita and follow us on Twitter.com/CSL. For more information about CSL, visit www.CSL.com.

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. Arcturus developed 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 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.

About Meiji Seika Pharma Co., Ltd.

Meiji Seika Pharma, since it launched penicillin in 1946, has been providing efficacious and high-quality pharmaceutical products such as therapeutics and vaccines for infectious diseases, therapeutics for central nervous system diseases as well as generic drugs in response to various medical needs. As a leading company in the field of infectious diseases, we are strengthening our platform for infection control and prevention with vaccines and antimicrobial agents.

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