Nature Communications Publishes Pivotal Data Demonstrating Efficacy and Tolerability of CSL and Arcturus Therapeutics' COVID-19 Vaccine

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- *Data follow the approval of the world's first self-amplifying (sa-mRNA) COVID-19 vaccine for adults in Japan.*
- *These results add to recently published data on ARCT-154 demonstrating superior immunogenicity to Omicron BA 4/5 compared to conventional mRNA COVID-19 vaccine booster and follow-up data demonstrating longer duration of immunity compared to traditional COVID-19 mRNA vaccine booster.*

KING OF PRUSSIA, Pa. & SAN DIEGO--(BUSINESS WIRE)--May 20, 2024-- Global biotechnology leader CSL (ASX:CSL; USOTC:CSLLY) and Arcturus Therapeutics (Nasdaq: ARCT) today announce *Nature Communications* has published results from an integrated phase 1/2/3a/3b study evaluating the safety, immunogenicity, and efficacy of ARCT-154, a novel self-amplifying (sa-mRNA) COVID-19 vaccine and the world's first approved sa-mRNA COVID-19 vaccine.

The results demonstrate that two 5 µg doses of ARCT-154, sa-mRNA vaccine, were well-tolerated, immunogenic and provided significant protection against multiple strains of COVID-19. The efficacy of ARCT-154 against severe COVID-19 was 100 percent in healthy persons aged 18-59 and more than 90 percent in persons at risk of severe consequences of the disease due to co-morbidities or older age.

"The results published in *Nature Communications* demonstrate the efficacy and tolerability of ARCT-154 and add to a growing body of evidence that our sa-mRNA vaccine has the potential to provide significant protection against the pervasive virus, reinforcing our promise to protect public health," said Jon Edelman, M.D., Senior Vice President, Vaccines Innovation Unit, CSL.

"We are thrilled that the results of the ARCT-154 study have been published in the highly respected journal *Nature Communications*," said Pad Chivukula, Ph.D., Chief Scientific Officer of Arcturus Therapeutics. "These data and the approval in Japan highlight the strength of our and CSL's commitment to delivering innovative technology that protects the public from COVID-19."

The *Nature Communications* article titled, "Safety, immunogenicity and efficacy of the self-amplifying mRNA ARCT-154 COVID-19 vaccine: pooled phase 1, 2, 3a and 3b randomized, controlled trials" was published online.

About the study

During the observer-blind, randomized, controlled phase 1, 2, 3a and 3b integrated study, adults ≥18 years old receive two 5 µg doses of ARCT-154 or saline placebo 28 days apart. Phase 2/3a/3b participants were stratified by age (< 60 or ≥ 60 years of age) and by risk of severe COVID-19 prior to being randomized 3:1 (phase 1/2/3a) or 1:1 (phase 3b) to vaccine or placebo groups. The primary endpoints were vaccine efficacy up to 2 months after dose 2, reactogenicity within up to 7 days of each dose, safety within up to 28 days after each dose, and immunogenicity measured 28 days after each dose. From August 15 to January 12, 2023, 1,001 participants were randomized (748 ARCT-154 and 253 placebo) in the integrated phase 1/2/3a study, and 16,100 participants (8,056 ARCT-154 and 8,044 placebo) in the phase 3b study.

In the phase 1/2/3a studies, ARCT-154 was safe and well tolerated. Most solicited adverse events were mild or moderate and resolved quickly, and rates of related or severe unsolicited adverse events were similar in the ARCT-154 and placebo groups. The phase 3b study confirmed these observations.

Four weeks after the second ARCT-154 dose in phase 3b, the neutralizing antibody seroconversion rate was 94.1% (95% CI: 92.1–95.8). There were 640 confirmed, protocol-defined COVID-19 cases, mainly of the Delta variant, that were determined to be eligible for analysis, including 43 severe cases and 10 deaths attributed to COVID-19. ARCT-154 absolute efficacy was 56.6% (95% CI: 48.7–63.3) against any COVID-19, 95.3% (80.5–98.9) against severe COVID-19 and 86.5% (-7.4–98.3) against death due to COVID-19. Efficacy against severe COVID-19 was 100% in healthy 18-59-year-olds and 91.9% (37.9–98.9) in participants in that age group with underlying co-morbidities, which put them at risk for severe disease. In adults aged 60 years or older, efficacy was 54.3% (28.2–70.9) against COVID-19 of any severity and 94.4% (58.2–99.3) against severe COVID-19.

The study was co-funded by Vinbiocare Biotechnology Joint Stock Company in Hanoi, Vietnam, and Arcturus Therapeutics.

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 standard mRNA vaccines, self-amplifying mRNA vaccines instruct the body to make more mRNA and protein to boost the immune response.

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 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 (Kostaive®) 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 (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.

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