Self-Amplifying mRNA COVID-19 Vaccine Demonstrates Superior Immune Response Compared with mRNA Vaccine at 12 Months Post-Vaccination

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Head-to-head data, presented at OPTIONS XII for the Control of Influenza Conference, demonstrates advantage of sa-mRNA over conventional mRNA in duration of immune response; Results highlight CSL and Arcturus Therapeutics' commitment to advancing COVID-19 vaccine innovation to protect public health.

WALTHAM, Mass. & SAN DIEGO--(BUSINESS WIRE)--Global biotechnology leader CSL (ASX:CSL; USOTC:CSLLY) and self-amplifying messenger RNA (sa-mRNA) pioneer Arcturus Therapeutics (Nasdaq: ARCT) today announced the results of a head-to-head study demonstrating that self-amplifying (sa-mRNA) COVID-19 vaccine maintained superior immunogenicity compared to the conventional mRNA vaccine Comirnaty® for up to one year against Wuhan-Hu-1, Omicron BA.4-5 and certain other variants, and at one-sixth the dose of the comparator (5 µg vs 30 µg, respectively).

The data, presented as a poster at the OPTIONS XII for the Control of Influenza conference, highlights 12-month follow-up analysis of the Phase 3 trial conducted in Japan by Meiji Seika Pharma, evaluating a booster dose of ARCT-154, showing that the vaccine elicited superior immunogenicity and antibody persistence over Comirnaty® for up to 12 months postvaccination, against multiple SARS-CoV-2 strains and in both younger and older adult age groups.

“The 12-month results from the ARCT-154 study continue to establish the durability of immune response from this self-amplifying mRNA vaccine and reinforce the ability of this vaccine to provide protection against COVID-19 at lower doses compared to conventional mRNA vaccines,” said Jonathan Edelman, M.D., Senior Vice President, Vaccines Innovation Unit, CSL. “We are proud to showcase at the 2024 OPTIONS conference with these important data about the first sa-mRNA COVID-19 vaccine now approved in Japan.”

Additional data presented by CSL and Arcturus finds that the bivalent formula, ARCT-2301, developed on the same platform as ARCT-154, induces superior immunogenicity over conventional bivalent mRNA vaccine Comirnaty® that persists against key variants up to six months postvaccination.

“The recent surge in COVID-19 infections and the emerging new variants illustrate the critical need for vaccines that provide a longer duration of protection compared to conventional mRNA vaccines,” said Igor Smolenov, M.D., Ph.D. Chief Development Officer of Arcturus Therapeutics. "These compelling new studies reaffirm that these sa-mRNA vaccines have the potential to offer potent protection against COVID-19.”

The COVID-19 vaccine from this sa-mRNA platform targeted against the JN.1 variant is approved in Japan for immunization against COVID-19 in adults 18 years and older and is being sold under the trade name KOSTAIVE®.

ARCT-154 12-month Study Design and Results

The randomized, double-blind, active-controlled Phase 3 study was conducted at 11 clinical sites in Japan. The study enrolled 828 adults who had previously been fully immunized with three doses of mRNA vaccine(s). Participants were randomized equally to receive a booster dose of either ARCT-154 or Comirnaty®. Immune responses were measured as neutralizing antibodies against the Wuhan-Hu-1 and Omicron BA.4-5 strains in sera obtained at Day 1 before booster vaccination, and Days 29, 91, 181, and 361 after vaccination of participants who were seronegative for SARS-CoV-2 nucleocapsid protein (N-protein), considered to be an indicator of recent COVID-19 infection. At the same timepoints neutralizing antibodies against Delta, Omicron BA.2, Omicron BA.2.86, and Omicron XBB.1.5.6 variants were measured in subsets of participants (~30 per group). Responses are expressed as group geometric mean titers (GMT) with 95% confidence intervals, and geometric mean titer ratio (GMTR) between the two vaccine groups at each timepoint.

At Day 29, neutralizing antibodies (GMTs unadjusted) against the Wuhan-Hu-1 strain in ARCT-154 recipients (n = 378) were superior to those in the Comirnaty® group (n = 374): GMT = 5390 (95% CI: 4899–5931) vs. 3738 (3442–4060), a GMT ratio of 1.44 (1.27–1.64). This advantage persisted through all time points. At Day 361 (unadjusted) GMTs were 3396 (3019–3821) and 1771 (1532–2047) in ARCT-154 (n = 272) and Comirnaty® (n = 266) groups, a GMT ratio of 1.92 (1.59–2.31). Differences were also observed in responses against Omicron BA.4-5, with GMT ratios of 1.31 (1.07–1.59) at Day 29 and 1.89 (1.42– 2.50) at Day 361. A subset of subjects who were seronegative for N-protein displayed similar differences in immune responses between ARCT-154 and Comirnaty® against the Delta, Omicron BA.2, BA.2.86, and XBB.1.5.6 variants at Day 361. The GMT ratios were 1.88 (0.79–4.49) against Delta, 2.34 (1.06–5.17) against Omicron BA.2, 2.51 (1.00–6.31) against Omicron BA.2.86 and 2.81 (1.09–7.28) against Omicron XBB.1.5.6.

Bivalent 6-month Study Design and Results

In this randomized, multicenter, Phase 3, observer-blind, active-controlled trial in Japan, fully-immunized (3–5 doses of mRNA vaccine) adults were randomized 1:1 to receive a booster dose of ARCT-2301 or Comirnaty® Original/BA.4-5. The primary objective was to demonstrate non-inferiority of the immunogenicity of ARCT-2301 vs. Comirnaty® Original/BA.4-5 at Day 29 as neutralizing antibody GMT and seroresponse rates (SRR) against Omicron BA.4-5. Key secondary outcomes included titers of neutralizing antibodies against Wuhan-Hu-1 and Omicron XBB.1.5.

Between September and November 2023, 930 men and women (19–80 years) with at least three prior mRNA COVID-19 vaccinations were enrolled at

nine medical centers in Japan and administered ARCT-2301 (n = 465) or Comirnaty® Original/BA.4-5 (n = 465) boosters. At Day 29 ARCT-2301 (n = 398) induced superior neutralizing antibody responses vs. Comirnaty® (n = 405) against Omicron BA.4-5 (GMT ratio 1·49 [95% CI: 1.26–1.76], SRR difference 7.2% [95% CI: 0.6–13.7]), and against Wuhan-Hu-1 (GMT ratio 1.45 [1.28–1.63], SRR difference 12.5% [5.9–19.0]). The difference persisted through six months with GMT ratios of 2.17 (95% CI: 1.75-2.69) and 1.98 (95% CI: 1.69-2.31), respectively. Antibody responses against Omicron XBB.1.5 were also higher after ARCT-2301 vs. Comirnaty® (GMT ratio 1.63 [1.36–1.94], SRR difference 16.7% [10.1–23.2]).

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

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 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 strategy, future operations, the likelihood that KOSTAIVE will provide a longer duration of protection, the likelihood and timing of future approvals of KOSTAIVE anywhere in the world including Europe, the plans to submit additional regulatory filings and timing thereof, that preclinical or clinical data will be predictive of future clinical results, 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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