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Meiji Seika Pharma Co., Ltd.

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Results of Phase III Study of Booster Vaccination of Kostaive™, Self-Amplifying mRNA Vaccine Against COVID-19, compared immunogenicity to COMIRNATY® was Published in *The Lancet Infectious Diseases*

Meiji Seika Pharma Co., Ltd. (Headquarters: Tokyo, Japan, President and Representative Director: Daikichiro Kobayashi) announced today that results of the phase III clinical study (jRCT2071220080) conducted in Japan for booster vaccination of Kostaive™ (ARCT-154), self-amplifying mRNA vaccine against COVID-19, were published in *The Lancet Infectious Diseases*.

The article describes the added value of this study, as follows; "To our knowledge, this is the first use of an saRNA (self-amplifying RNA) COVID-19 vaccine as a booster dose in adults who have previously received an mRNA vaccine. We show that a 5µg booster dose of ARCT-154 is safe, is well tolerated, and induces a robust immune response to the Wuhan-Hu1 strain of SARS-CoV-2 that is non-inferior to the response induced by a homologous 30µg booster dose of the BNT162b2 mRNA vaccine (COMIRNATY®). Additionally, ARCT-154 elicits a superior immune response against the tested omicron BA.4/5 subvariant to the homologous mRNA vaccine."

Kostaive™ is a vaccine against COVID-19 applying self-amplifying mRNA technology. It is designed to self-amplify* once delivered into cells, so that it generates a strong immune response and the potential for extended duration of protection while using lower doses of mRNA compared to existing mRNA vaccines. In the above Phase III clinical study, the authors compared immune responses to fourth doses of ARCT-154 or BNT162b2 in healthy Japanese adults aged 18 years or older previously immunized with two doses of mRNA COVID19 vaccine then a third dose of BNT162b2 at least 3 months beforehand. Four weeks after boosting in Per Protocol Set 1 (PPS-1), ARCT-154 induced non-inferior Wuhan-Hu-1 surrogate neutralizing antibody GMTs to BNT162b2 (5641 [95% CI: 4321–7363] vs. 3934 [2993–5169], respectively), a GMT ratio of 1·43 (95% CI: 1·26–1·63), with respective seroresponse rates (SRR) of 65.2% (60.2–69.9) vs. 51.6% (46.4–56.8), a 13.6% (95% CI: 6.8–20.5) difference. Anti-Omicron BA.4/5 GMTs were 2551 (1687–3859) vs. 1958 (1281–2993), a GMT ratio of 1·30 (95% CI: 1·07–1·58), with SRR of 69.9% (65.0–74.4) vs. 58.0% (52.8–63.1), a 12% (95% CI: 5-18) difference. ARCT-154 or BNT162b2 boosters were equally well-tolerated with no causally-associated severe or serious adverse events; 398/420 (95%) ARCT-154 and 395/408

(97%) BNT162B2 vaccinees reported local reactions and 276/420 (66%) and 255/408 (63%) had solicited systemic adverse events.

The results of this booster phase III clinical study conducted in Japan, together with the results of phase I/II/IIIa (in 1002 randomized subjects) and phase IIIb clinical studies (in 16,107 randomized subjects) conducted abroad (NCT05012943), were submitted as part of the materials for MHLW's Manufacturing and Marketing Approval for Kostaive™, which was approved in November 2023. The booster phase III 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. Meiji Seika Pharma is currently working for the vaccines against novel variants of COVID-19 virus, toward the goal of commercialization in 2024.

*: The results of pharmacokinetic studies showed that tissue RNA concentrations decreased significantly after 2 weeks to 1 month of intramuscular administration, regardless of the presence or absence of replicons. This suggests that encoding a replicon does not significantly extend its survival period in vivo compared to RNA that does not contain a replicon. (Review Report for Kostaive, PMDA, November 9, 2023. In Japanese)

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 by making copies of these instructions. 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.