

January 6, 2020

Ono and Seikagaku Submit a New Drug Application for Manufacturing and Marketing Approval for ONO-5704/SI-613 for the Treatment of Osteoarthritis in Japan

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; “Ono”) and Seikagaku Corporation (Tokyo, Japan; “Seikagaku”) announced today that the companies have submitted a new drug application (“NDA”) for manufacturing and marketing approval for ONO-5704/SI-613 (“the Product”) in Japan, for the treatment of osteoarthritis (knee joint, hip joint and ankle joint). The Product is being jointly developed by the companies in Japan.

The NDA is based on the results of three Phase III clinical studies*¹ conducted with the Product in Japan. As announced in the press release issued on February 19, 2019, in a confirmatory study in 440 patients with knee osteoarthritis, the Product demonstrated a statistically significant improvement in WOMAC (a knee pain evaluation index) scores at twelve weeks after the initial injection (three injections every four weeks), a primary endpoint of the study, compared with a placebo.

Also, in a clinical study in 290 patients with osteoarthritis at four joint sites of the shoulder, elbow, hip or ankle, the Product met a primary endpoint, a change in pain score of a patient diary at twelve weeks after the initial injection (three injections every four weeks) in patients with osteoarthritis of the hip joint and ankle joint, among the four joint sites studied.

In a long-term study in 166 patients with osteoarthritis, evaluating long-term safety of the Product by repeated injections every 4 weeks for 52 weeks, no major safety concerns were identified in any osteoarthritis patients.

Osteoarthritis is a disease caused by the articular cartilage damage, leading to inflammation and pain, which result in deterioration of quality of life (QOL). Osteoarthritis of the knee and ankle are mainly caused by aging factor, and osteoarthritis of the hip is often caused by congenital factors. The number of symptomatic patients with knee osteoarthritis in Japan is estimated to be about 7.8 million, particularly common in women, of whom approximately 70% in their 70s are reported to suffer from knee osteoarthritis.*² Also, it has been reported that the prevalence rate of osteoarthritis of the hip based on X-ray diagnosis is in the range of 1.0 - 4.3% of the population, 0.0 - 2.0% in men and 2.0 - 7.5% in women.*³

Ono and Seikagaku aim to contribute to improvement of QOL in patients by providing a new treatment option for osteoarthritis (of the knee joint, hip joint and ankle joint) and will work to obtain an approval of the Product as soon as possible.

There is no change in the forecast of consolidated financial results for the fiscal year ending March 31, 2020 for either Ono or Seikagaku in connection with this matter.

- *1: 1) Confirmatory study in patients with knee osteoarthritis
- 2) Clinical study in patients with osteoarthritis (four joint sites: shoulder, elbow, hip, and ankle)
- 3) Long-term study in patients with osteoarthritis, primarily for safety evaluation (five joint sites: knee, shoulder, elbow, hip, and ankle)

*2: Yoshimura N et al., *J Bone Miner Metab*, 2009;27:620-8

*3: *Clinical Practice Guideline on the Management of Osteoarthritis of the Hip* (2016). 2nd Edition. Tokyo: Nankodo Co., Ltd.; 2016: 10-13.

About ONO-5704/SI-613

ONO-5704/SI-613 is a formulation in which hyaluronic acid and diclofenac (an anti-inflammatory drug) are chemically bound using Seikagaku's own proprietary technology. The product combines the pain relief and anti-inflammatory effect of diclofenac designed for sustained release*⁴ using a drug delivery system*⁵ with the joint function improving effect of hyaluronic acid. It is expected to provide prompt and long-lasting relief of the pain and inflammation associated with osteoarthritis (of the knee joint, hip joint, and ankle joint). Further, since the product is administered directly into the joint cavity as an injectable treatment, systemic exposure to diclofenac is low, and the risk of systemic adverse drug reaction is thought to be low.

*4: Drug delivery system (DDS) is a technology for the controlled release, targeting, and absorption improvement of drugs.

*5: Sustained release is the gradual release of the active pharmaceutical ingredients of a drug to achieve a sustained therapeutic effect.

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