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Chugai Files Elevidys (SRP-9001) as a Gene Therapy Product for Duchenne Muscular Dystrophy in Japan

- The filing is based on the results from a global phase III study in Duchenne muscular dystrophy, a rare, genetic and difficult-to-treat muscle-wasting disease
- The application will be reviewed under priority review in Japan
- If approved, Elevidys will be the first gene therapy product for Duchenne muscular dystrophy in Japan

TOKYO, August 14, 2024 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced today that it filed a regulatory application with the Ministry of Health, Labour and Welfare (MHLW) for delandistrogene moxeparvovec, a gene therapy product under development (development code: SRP-9001, overseas product name: Elevidys), for the treatment of Duchenne muscular dystrophy (DMD). Its target population aims to include ambulatory boys aged 3-7 years with DMD who do not have any deletion in exons 8 and/or 9 in the DMD gene and do not have a pre-existing immunity against AAVrh74. Delandistrogene moxeparvovec received orphan regenerative medical product designation from the MHLW, and the applications will be reviewed under priority review. For the confirmation of anti-AAVrh74 antibody negativity prior to administration, Roche Diagnostics K.K. has filed a regulatory application for Elecsys Anti-AAVrh74 (overseas product name) assay as an *in vitro* diagnostic, intended for an aid in identifying DMD patients eligible for delandistrogene moxeparvovec on June 18, 2024.

“DMD is a refractory muscular disease with a poor life prognosis that develops in early childhood and rapidly progresses during childhood. While it causes a significant decline in the ability to live independently and quality of life due to muscle weakness, there is no fundamental treatment. Delandistrogene moxeparvovec is designed to compensate for the expression of dystrophin, the cause of DMD, with a single administration, and has the potential to become the first gene therapy product for this disease in Japan. We will continue to work for approval to deliver delandistrogene moxeparvovec, as a new therapy for DMD to patients as soon as possible,” said Chugai’s President and CEO, Dr. Osamu Okuda.

The application is based on the results from the global Phase III clinical study (EMBARK), which evaluated the efficacy and safety of delandistrogene moxeparvovec in ambulatory boys aged 4-7 years with DMD. While the primary endpoint of motor function assessed by the North Star Ambulatory Assessment (NSAA) did not show statistical significance compared to placebo, clinically meaningful improvements were observed in key secondary endpoints (time to rise from the floor, 10-meter walk time, next to stride velocity 95th centile [SV95C] and time to ascend 4-steps). Based on the results of all clinical trials conducted to date and comparisons with the natural history of DMD, Chugai believes that the benefit-risk balance of this therapy is positive, leading to this regulatory application. Chugai will continue working with health authorities towards the approval of this therapy.

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[Reference]
Roche announces EMBARK trial in Duchenne muscular dystrophy (DMD) did not reach primary endpoint, but shows positive efficacy outcomes on all timed functional key endpoints (Roche's Media Release on October 31, 2023)
https://www.roche.com/media/releases/med-cor-2023-10-30

About Duchenne muscular dystrophy (DMD)
DMD is a rare, genetic, muscle-wasting disease that progresses rapidly from early childhood. Approximately one in 5,000 boys worldwide are born with DMD, while DMD in girls is very rare.[1] Everyone who has DMD will lose the ability to walk, upper limb, lung and cardiac function,[1-3] and mean life expectancy is 28 years.[4] A diagnosis of DMD will require full-time caregiving which is most often provided by parents,[1-3] the majority of whom will find it difficult to carry out usual work or household activities and suffer from depression, physical pain and discomfort.

DMD is caused by mutations of the DMD gene, which affects the production of the muscle protein, dystrophin. Dystrophin is a critical component of a protein complex that strengthens muscle fibers and protects them from injury during muscle contraction. Due to a genetic mutation in the DMD gene, people with DMD do not make functional dystrophin; their muscle cells are more sensitive to injury and muscle tissue is progressively replaced with scar tissue and fat.[2,3]

About delandistrogene moxeparvovec (SRP-9001)
Delandistrogene moxeparvovec (SRP-9001) is the gene therapy product under development for Duchenne muscular dystrophy (DMD) and is designed to address the underlying cause of Duchenne through targeted skeletal, respiratory and cardiac muscle expression of shortened dystrophin produced by delandistrogene moxeparvovec. Delandistrogene moxeparvovec received an orphan regenerative medical product designation for DMD in Japan. It received approval as the first gene therapy product for DMD in the US in June 2023 and was filed in EU on May 2024.

Sources
1. Salvatore Crisafulli et al, Global epidemiology of Duchenne muscular dystrophy: an updated systematic review and meta-analysis. Orphanet J Rare Dis. 2020 Jun 5;15(1):141
2. David J Birnkrant et al, Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and neuromuscular, rehabilitation, endocrine, and gastrointestinal and nutritional management. Lancet Neurol. 2018 Mar;17(3):251-267
3. The Japan Neurosurgical Society, General Incorporated Association. Clinical Practice Guidelines for Duchenne muscular dystrophy. https://neurology-jp.org/guidelinem/dmd.html (Accessed August, 2024) (Japanese only)
4. Broomfield J, et al. Life expectancy in Duchenne muscular dystrophy: reproduced individual patient data meta-analysis. Neurology. 2021. Dec 7;97(23):e2304–2314.

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