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Company name: Modalis Therapeutics Corporation
Stock exchange listing: Tokyo Stock Exchange
Code number: 4883
URL: https://www.modalistx.com/en/
Representative: Haruhiko Morita

Modalis Therapeutics to Regain Full Rights to DM1 and DMD Programs

Modalis Therapeutics Corporation (TSE: 4883) today announced it will regain full development and commercial rights to MDL-201 and MDL-202 from Astellas Pharma Inc. It also reveals that target indications for the products are Duchene Muscular Dystrophy (DMD) and Myotonic Dystrophy type 1 (DM1), respectively.

"We are grateful to Astellas for their investment in MDL-201 and -202 over the years and are pleased to be regaining full rights to the programs," said Haru Morita, President and CEO of Modalis Therapeutics. " Recent data generated by Modalis for MDL-101 employing muscle tropic capsids, warrant a promising future of the muscular disease programs. This is a perfect opportunity for us to leverage our preclinical expertise and assets accumulated in the development of MDL-101 to advance development in relatively large indications in the neuromuscular disease area. We are also enthusiastic about initiating discussions with potential pharmaceutical partners around partnering of the acquired assets, MDL-201 and MDL-202."

MDL-201 is a unique molecule whose mechanism of action is to activate the expression of the Utrophin gene, a fetal version of Dystrophin, for the treatment of DMD patients who have mutated Dystrophin. In contrast, the mechanism of MDL-202 is a silencing of the DMPK gene, which is associated with the expression of toxic CTG repeats from its 3'UTR. "We are excited to regain the full rights of the two differentiated molecules, which have demonstrated robust preclinical data" Dr. Tetsuya Yamagata, CSO of Modalis Therapeutics commented. "We are very pleased to have the opportunity to advance these products, whose value has been enhanced by the collaboration, and we expect to have improved potency and safety through the adoption of new capsid technologies."

Modalis is also announcing a sharpened strategic focus, to prioritize its investments in the most promising programs: MDL-101, the lead program in its pipeline which has completed preIND and is moving forward to the clinic for LAMA2-CMD, and MDL-202 for DM1.

This matter shall have a minor impact on our cost compared with that of the whole R&D for the fiscal year ending December 31, 2023, and the following years.

About Myotonic Dystrophy Type 1 (DM1)

- DM1 is the most prevalent form of adult-onset muscular dystrophy and arises from an abnormal expansion of the DNA sequence (CTG repeats) within the 3' noncoding region of the DMPK gene on chromosome 19. This expansion leads to the production of a modified protein, giving rise to the characteristic symptoms and complications associated with DM1. Normal individuals have between 5 and 37 repeats, but symptomatic patients typically have > 50 repeats.
- At the core of DM1 is myotonia, a condition characterized by prolonged muscle contractions, resulting in muscle stiffness and difficulty relaxing after contraction. This myotonia affects various muscle groups, including those in the face, hands, arms, and legs. Individuals with DM1 may encounter challenges with fine motor skills, such as gripping objects or releasing their grip. The severity and progression of myotonia can vary among affected individuals, with some experiencing mild symptoms and others facing more pronounced difficulties.
- The prevalence varies by region and is most common in individuals of European descent. Based on a most recent unbiased analysis of genetic prevalence of expansion of CTG repeats (>50) CTG expansion was measured as 1:2,100 (4.8 per 10,000). In contrast to the prevalence number of patients diagnosed with clinical onset (5–20 per 100,000) individuals) this suggests that significant numbers of patients remain undiagnosed.

About Duchenne Muscular Dystrophy (DMD)

- Muscular Dystrophy (DMD), a genetic disorder that affects a significant number of individuals worldwide. DMD is a progressive neuromuscular condition that profoundly impacts the lives of affected individuals and their families.
- The hallmark characteristic of DMD is progressive muscle weakness, which typically begins in early childhood. Children with DMD often exhibit delayed motor milestones, such as difficulty walking or getting up from the floor. As the condition progresses, individuals may require assistive devices like wheelchairs to aid in mobility. The muscle weakness primarily affects the proximal muscles, including those in the hips, thighs, and shoulders.
- DMD predominantly affects males, as the dystrophin gene is located on the X chromosome. However, in rare cases, females can also be affected, though typically with milder symptoms due to the presence of a second X chromosome. According to reports, it affects about one in 3,500 to 6,000 males at birth.
- During fetal muscle development, utrophin is expressed beneath the sarcolemma before dystrophin. When dystrophin expression starts, utrophin expression begins to be down-regulated. Dystrophin and utrophin are highly homologous and can recruit dystrophin-glycoprotein complex (DGC)-related proteins. Regardless of the genetic mutation that causes Duchenne muscular dystrophy (DMD), utrophin can compensate for dystrophin deficiency.

The notes above provide a general explanation of DMD and DM1 but does not constitute medical advice. For specific information regarding the condition and treatment options, individuals should consult their healthcare professionals.