September 17th, 2024

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

DMPK Patent Granted in Japan

- The patent application "Method for treating muscular dystrophy by targeting DMPK gene" developed and applied for by MODALIS was granted in Japan.
- The patent is for MDL-202, a gene therapy drug for Myotonic Dystrophy Type 1(DM1) using our company's proprietary CRISPR-GNDM® epigenome editing* technology.

September 17, 2024, Modalis Therapeutics Corporation TSE 4883.T (Modalis) announced it has received a notice from the Japan Patent Office that our patent (JP-2022-518586) for our CRISPR-GNDM® based DM1 treating gene therapy concerning MDL-202 has been granted in Japan.

Myotonic dystrophy type 1 is the most common form of muscular dystrophy in adults, with an incidence rate of approximately 5 cases per 100,000 people in Japan, and is characterized by myotonia and muscle atrophy. The pathogenesis of DM1 is attributed to the abnormal expansion of CTG repeat sequences in the 3' untranslated region of the DMPK gene. This expansion results in the sequestration of proteins, such as MBNL1, that are involved in RNA splicings, thereby disrupting normal splicing processes in muscle cells.

To address this, we have developed MDL-202, which is based on CRISPR-GNDM® technology and specifically designed to silence the DMPK gene along with its CTG repeats under the control of a muscle-specific promoter. This construct is delivered via an adeno-associated virus (AAV). Although other modalities, such as antisense oligonucleotides (ASOs), are also being developed for DM1, it is challenging to achieve effective concentrations for silencing DMPK in target tissues without affecting other organs due to the non-selective nature of ASOs. In contrast, MDL-202 utilizes AAV vectors and promoters that selectively target muscle tissue, enabling efficient suppression of the DMPK gene with high specificity.

The patent application primarily claims a GNDM molecule containing guide RNAs that are highly optimized for the DMPK gene. We believe that the novelty and inventive steps of this approach were crucial factors in granting this patent. This patent has already been issued in China (CN 202080032034.2), and the fact that it has been granted in Japan, an important market for our company, has allowed us to establish strong intellectual property rights that will protect our business from competition with biosimilars after the launch of MDL-202. We also expect that patents will be granted in other major countries following Japan.

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*Epigenome editing: The control of gene expression through modification of DNA, histones, non-coding RNA, etc., to turn genes on or off while leaving the gene sequence intact.
dCas9: An enzyme from which the cleavage activity of Cas9, a genome-editing cleavage enzyme, has been removed. It can be used for base substitution and epigenome editing by linking with transcription factors and other elements.