April 15th, 2024

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 Present Data Supporting Development of Transformative Epigenome Editing Medicines for the Treatment of Muscular Dystrophy at the 4th Annual Next Generation Gene Therapy Vectors Summit

Modalis to present data to support the development of a treatment for Congenital Muscular Dystrophy.

- *Product concept and rationale for MDL-101, a differentiated precision medicine for LAMA2-congenital muscular dystrophy (LAMA2-CMD)*
- *Preclinical data supports efficacy in mouse and non-human primates (NHPs)*
- *Biodistribution and safety data of muscle tropic AAV vectors in NHPs*
- *Manufacturability of muscle tropic AAV vectors for use in clinical trials*

16-Apr-2024 TOKYO & Waltham, Mass – Modalis Therapeutics Corporation (Tokyo Stock Exchange: 4883), a pioneering company developing innovative products for the treatment of rare genetic diseases utilizing its proprietary CRISPR-GNDM® epigenome editing technology, announced that the company has been accepted for an Oral Presentation at the 4th Annual Next Generation Gene Therapy Vectors (June 12-14, 2024, Boston, USA), and the following research results will be presented by our CSO, Dr. Tetsuya Yamagata.

Modalis presentations at the 4th Annual Next Generation Gene Therapy Vectors will include preclinical data and muscle tropic AAV vector related data:

- In LAMA-2 knockout mice (dyW disease model mice) and non-human primates (NHPs), a CRISPR-GNDM® based molecule (MDL-101) targeting the LAMA-1 gene introduced using a muscle-specific AAV vector, raised LAMA-1 expression to levels that complement LAMA-2 function in the disease animals. This suggests that MDL-101 may have therapeutic potential in the clinic.

At 4th Annual Next Generation Gene Therapy Vectors, Modalis will present preclinical data from MDL-101 validating the efficacy and safety of our differentiated therapeutic strategy utilizing our CRISPR-GNDM® technology for the difficult-to-treat LAMA2-CMD. "Our proprietary and first-in-class CRISPR-based epigenome editing technology, CRISPR-GNDM®, controls the expression levels of disease-causing genes and provides a disease-modifying treatment for genetic disorders," said Dr. Tetsuya Yamagata, CSO of Modalis. "With the muscle tropic capsid, MDL-101 has raised the probability of technical success as a potentially life-changing gene therapy for the treatment of LAMA2-CMD and is currently on track for IND filing. At this meeting, we will share data from our mouse and NHP studies that demonstrate efficacy, safety, and manufacturability with muscle tropic AAV vectors, and discuss the potential implications for therapeutic efficacy in the clinic." stated.

The Modalis Therapeutics presentation will be at the 4th Annual Next Generation Gene Therapy Vectors（URL；https://next-gen-genetherapy-vectors.com/whats-on/speakers）

Oral Presentation:

Title: Epigenetic Editing with CRISPR-GNDM®: MDL-101 is a Novel Muscle-Tropic AAV Vectors for the Treatment of LAMA2-CMD
Date and Time: 6/14/2024, 11:15AM EST
Session Name: Beyond AAV: HIGHLIGHTING BOUNDARY-PUSHING VECTOR PLATFORMS

About The 4th Annual Next Generation Gene Therapy Vectors

Approximately 100 industry leaders will participate in a research-led discussion on the development of next-generation gene therapy and vectors to address vector safety, efficacious, and selectivity challenges presented by the first generation of gene therapy vectors. Participants will be across key players responsible for R&D, platform development, capsid engineering, payload optimization, business development, and external innovation. The 4th conference will focus on improving the specificity, targeting new cell types, expanding packing capacities, and reducing toxicity risks to create safer, cost-effective & efficacious gene therapies.

About MDL-101

MDL-101 is an experimental, epigenome modulation therapy under investigation for the treatment of LAMA2-Congenital Muscular Dystrophy (LAMA2-CMD). MDL-101 is comprised of guide nucleotide targeting LAMA-1 gene, a highly homologous sister gene of the disease-causing gene LAMA-2, enzyme-null Cas9 (dCas9) fused with trans-activating domain driven by a muscle-specific promoter and coded in a muscle-specific AAV vector. MDL-101 upregulates LAMA-1 gene products in patients' muscle tissue to compensate for

loss-of-function caused by mutation of LAMA-2, and therefore has the potential to provide a one-time, durable treatment benefit for people living with LAMA2-CMD.

About Modalis:

Modalis Therapeutics develops precision genetic medicines using epigenome editing technology. Modalis is pursuing therapies for orphan genetic diseases using its proprietary CRISPR-GNDM® technology which enables the gene/locus-specific modulation of gene expression or epigenetic editing without the need for DNA cleavage or altering DNA sequence. Headquartered in Tokyo with laboratories and facilities in Waltham Massachusetts, the company is listed on Tokyo Stock Exchange's Growth market. For additional information, visit www.modalistx.com.