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Stock exchange listing: Tokyo Stock Exchange
Code number: 4883
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FDA Grants Rare Pediatric Disease Designation to MDL-101 for the treatment of congenital muscular dystrophy type 1a (LAMA2-CMD)

30-Sep-2024 TOKYO & Waltham, Mass – Modalis Therapeutics Corporation (Modalis: Tokyo Stock Exchange: 4883, Chief Executive Officer: Haruhiko Morita), a pioneering company developing innovative drugs for the treatment of rare genetic diseases, utilizing its proprietary CRISPR-based epigenome editing technology CRISPR-GNDM®, announced the U.S. Food and Drug Administration (FDA) has granted Rare Pediatric Disease (RPD) designation to MDL-101, which is being developed for the treatment of congenital muscular dystrophy type 1a (LAMA2-CMD).

FDA grants RPD for serious and life-threatening diseases that primarily affect children ages 18 years or younger and fewer than 200,000 people in the United States. When the product that has received this designation obtains marketing approval from the FDA, Modalis will be eligible to receive priority review voucher for another product from the FDA. The Orphan Drug application that was submitted at the same time is being reviewed separately by the FDA.

LAMA2-CMD is a severe, early onset congenital muscular dystrophy caused by the absence of the LAMA2 protein, which is made up of more than 3,000 amino acids. Because it cannot be loaded onto an AAV vector, it is thought that the conventional approach to gene therapy development is difficult. For this reason, there is currently no treatment, including gene therapy, that addresses the underlying cause of LAMA2-CMD.

Modalis' proprietary CRISPR-GNDM®, is capable of specific modulation of the expression of disease-relevant genes, without introducing double-strand DNA breaks, and our MDL-101 is potentially the first-in-class therapeutics to solve the challenge and provide life-changing

therapeutics for the patients of LAMA2-CMD by inducing expression of the sister gene LAMA1 across muscle tissues to compensate for the deficient function of LAMA2.

Having the company mission "*Every life deserves attention*" Modalis has been working actively for the treatment to patients suffering from diseases for which there is no cure.

About MDL-101

MDL-101 is an experimental, epigenetic editing therapy that is being developed for the treatment of LAMA2-Congenital Muscular Dystrophy (LAMA2-CMD). MDL-101 is comprised of a guide nucleotide targeting LAMA1 gene, a highly homologous sister gene of the disease-causing gene LAMA2, 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 LAMA1 gene products in patients' muscle tissue to compensate for loss-of-function caused by mutation of LAMA2, and therefore has the potential to provide a one-time, durable treatment to benefit 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 epigenome editing without the need for DNA cleavage or altering DNA sequence. Headquartered in Tokyo with all research and development operations in Waltham Massachusetts, the company is listed on the Tokyo Stock Exchange's Growth market. For additional information, visit www.modalistx.com.