June 26th, 2023

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

Modalis Receives Positive FDA Response for Pre-IND Review For MDL-101 Clinical Development

We are pleased to announce that on June 23rd, 2023 (U.S. time), we received Pre-IND (Type B) response from the U.S. regulatory agency, the FDA for our MDL-101 program.

After positive animal proof-of-concept results in rodent and target engagement in non-human primate studies and pilot manufacturing, Modalis submitted a Pre-IND meeting request and briefing package with the FDA's Center for Biologics Evaluation and Research (CBER) earlier this year to further advance development toward clinical trials. The Pre-IND review request is a critical step in the US regulatory approval process, as it affords an opportunity for study sponsor companies to seek clarification from the FDA on preclinical and clinical trial design, clinical materials manufacturing, quality controls, etc.

"The Type B response from the FDA on Friday further strengthens our confidence in our plans to enter the clinic during the second half of 2024 with IND filing followed by trial initiation without major changes in the development plan," said Haru Morita, Chief Executive Officer of Modalis Therapeutics. "Based on preclinical studies, we have growing confidence in the performance of MDL-101 and the FDA's response provided us with an opportunity to clarify our path to our IND and to confirm that our original plan was largely consistent with the authorities. Our planned clinical trial should provide important insights into LAMA2-CMD therapy, along with the safety of our approach with CRISPR-GNDM® technology. Furthermore, we believe that the response contains many suggestions that can be extrapolated to other pipelines that share the same technology platform, especially the muscle disease pipelines, allowing subsequent programs to proceed more smoothly. For the anticipated phase 1/2 clinical trial, we look forward to moving forward with a program that could have a significant impact on patient care."

This matter has no impact on our business performance for the fiscal year ending December 2023. The Company shall promptly announce all future matters that require disclosure.

Pre-IND: https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/otat-pre-ind-meetings

About MDL-101
MDL-101 is a gene therapy being developed for the treatment of congenital muscular dystrophy type 1A (LAMA2-CMD) by complementing the mutated LAMA2 gene in patients with its sister gene, LAMA1, by inducing its expression using CRISPR-GNDM®. The LAMA2 gene encodes a protein involved in muscle function, and mutations in this gene cause muscle dysfunction, resulting in severe disability from early

childhood. Both LAMA1 and LAMA2 gene are large genes, exceeding 9 kb in size, and cannot be treated by conventional gene therapy because it is far larger than the packing capacity of AAV. It is also difficult to be targeted by a single gene editing therapy because the mutations vary from patient to patient and exist across the gene. Therefore, we believe that CRISPR-GNDM® based therapy is the only feasible method, and the advantages of the technology will be most useful.