December 25, 2025

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

Modalis Announces Publication in Human Gene Therapy of Study Demonstrating Efficient LAMA1 Gene Activation for the Treatment of LAMA2-CMD

- CRISPR-GNDM® platform achieves potent and specific activation of LAMA1 with therapeutic benefit in preclinical models
- Favorable safety and pharmacodynamics demonstrated in non-human primates

Tokyo, Japan & Waltham, Mass. – December 25, 2025 – Modalis Therapeutics Corporation (TSE: 4883) today announced that its research article titled "Efficient LAMA1 gene activation by epigenome editing as a therapeutic approach for LAMA2-CMD" has been published in the peer-reviewed journal *Human Gene Therapy*.

The publication highlights compelling preclinical evidence that Modalis' proprietary CRISPR-GNDM® epigenome editing technology can safely and robustly activate the *LAMA1* gene as a novel therapeutic strategy for LAMA2-related congenital muscular dystrophy (LAMA2-CMD), a severe pediatric neuromuscular disorder with no approved treatments.

Key findings include:

- Robust, muscle-specific activation of LAMA1 following a single administration of muscle-tropic AAV vectors encoding the GNDM activator
- Marked improvement in survival and muscle function in DyW mouse models, including dose-dependent increases in grip strength and normalization of muscle histology
- Favorable safety and pharmacodynamic profiles in non-human primates (NHPs), with strong LAMA1 induction observed even at half-doses in infant NHPs

“This work represents one of the first demonstrations of systemic, single-vector epigenome activation in large animals,” said Tetsuya Yamagata, MD, Ph.D. CSO of Modalis. “By enabling targeted activation of large genes that are not compatible with conventional AAV gene replacement approaches, this study opens the door to a new class of treatments for a wide range of genetic diseases.” Haru Morita, CEO, added: “The publication of this study demonstrates that the nonclinical results supporting our lead program MDL-101 have been recognized by the global scientific community as clear evidence of both efficacy and safety. These data form the scientific foundation for our planned clinical trials next year and significantly reinforce confidence in the broader CRISPR-GNDM® platform. Development of MDL-101 is progressing smoothly, with GLP toxicology studies and GMP manufacturing well underway. We intend to submit an investigational new drug application upon their completion, and remain committed to advancing this program to deliver a transformative, one-time treatment option for patients living with LAMA2-CMD.”

Publication Details

- **Title:** *Efficient LAMA1 gene activation by epigenome editing as a therapeutic approach for LAMA2-CMD*
- **Journal:** *Human Gene Therapy*
- **DOI:** https://doi.org/10.1177/10430342251401873
- **Authors:** Yuanbo Qin, Talha Akbulut, Rajakumar Mandraju, Keith Connolly, Seth Levy, Tetsuya Yamagata, et al. (Modalis Therapeutics)

About MDL-101

MDL-101 is an investigational epigenetic gene-activation therapy being developed for the treatment of LAMA2-Congenital Muscular Dystrophy (LAMA2-CMD).
The therapy utilizes:

- a guide RNA targeting LAMA1, a highly homologous compensatory gene to LAMA2
- a nuclease-null Cas9 (dCas9) fused to a transcriptional activator
- a muscle-specific promoter packaged within a muscle-tropic AAV vector

MDL-101 is designed to upregulate endogenous LAMA1 expression to compensate for loss-of-function caused by LAMA2 mutations. The program has the potential to be a one-time, durable treatment for individuals living with LAMA2-CMD.

About Modalis Therapeutics

Modalis Therapeutics (TSE: 4883) is a biotechnology company pioneering epigenetic gene modulation using its proprietary CRISPR-GNDM® platform, which enables precise control of gene expression without cutting DNA. The company is advancing a pipeline of novel therapeutics for genetic diseases with high unmet medical need, leveraging in vivo AAV delivery for safe, durable, and scalable treatment modalities.
For more information, please visit https://www.modalistx.com/en.

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