September 15, 2022

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

Notice of transition of MDL-101 to an improved version

Modalis Therapeutics Corporation (hereafter, "the Company") hereby announces that by the resolution of the Board of Directors dated as of September 15, 2022, the Company decided to transit MDL-101 to an improved version.

The Company are announcing that the company has decided to modify components of MDL-101, which is being developed for the treatment of CMD1A. This will delay the project timeline by approximately one year. At the same time, MDL-104, which is being developed for the treatment of tauopathy, will be given higher priority and developed in parallel with MDL-101.

The Company's method of administering therapeutics is envisioned to deliver our proprietary CRISPR-GNDM® in an adeno-associated virus (AAV) vector to target cells in the body, but in this decision, the Company is transiting to an improved version of the AAV as a delivery method tool.

While gene therapies using systemically delivered AAV for the treatment of muscle diseases have shown promising results in recent clinical trials by various groups, there are growing safety concerns associated with high-dose administration of AAV, and the improved version of AAVs have shown excellent target tissue tropism(specificity) and high transduction efficiency. Given these recent developments, the Company believes that switching to an improved AAV will be a strong industry imperative from all perspectives, including efficacy, safety, cost, and, most of all, ethics. The pace of recent technological innovation in the field of gene therapy has been very rapid, and it is imperative for our program to adapt to these developments, which is why the Company has decided to improve MDL-101 now rather than later. This will delay the development timeline by approximately one year, but the Company believes it will bring greater value in total considering the advantages of the product.

On the other hand, MDL-104, which is planned to be administered via the ICM (intra cisterna magna) route, will be locally injected into the brain, and not be prevented by the blood-brain barrier (BBB), thus is avoiding the problems of large systemic doses and tissue specificity. Therefore, the issues with systemic administration are not relevant, and the Company believes that we can maintain our efforts with the existing development molecule. Taking the approximately one-year delay of MDL-101 and recent advancement of MDL-104 in account, the Company believes MDL-104 can reach clinical trials around the same time as MDL-101.

As a result, both MDL-101 and MDL-104 are expected to be filed for Pre-IND in mid-2023 and IND in 2024. Meanwhile, the Company continue to work on partnering of the both programs.

This matter has no impact on our business performance for the fiscal year ending December 2022. The Company shall promptly announce all future matters that require disclosure.