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December 22th, 2023

Company name: Modalis Therapeutics Corporation

Stock exchange listing: Tokyo Stock Exchange

Code number: 4883

URL: <https://www.modalistx.com/en/>

Representative: Haruhiko Morita

Engineered “Mini Cas9” Patent Granted in Japan

- A proprietary engineered Cas9 Patent, "Modified Cas9 protein and its applications" has been granted in Japan and China.
- Mini dCas9 enables epigenome editing using MODALIS' proprietary CRISPR technology, overcoming size limitations for promoters and transgenes when used with AAV and other vectors.

December 22, 2023, Modalis Therapeutics Corporation TSE 4883.T (Modalis) announced it has received notification from the Japan Patent Office and China National Intellectual Property Administration that our patent for our “Mini Cas9” (JP-A2020-523211 or 201880050453.1(PCT/JP2018/021068)) has been granted in Japan and China, respectively.

When Cas9 is used for epigenome editing, vectors such as adeno-associated virus (AAV) are frequently employed to target specific organs, tissues, or cell types in the body. AAVs have been shown to selectively target neurological and muscle diseases, where LNPs and mRNAs may lack the required tissue or target specificity. However, AAVs have a maximum transgene size limit of 4.9 kb, which restricts the ability to deliver large transgenes such as Cas9.

The Mini Cas9, derived from *Staphylococcus aureus*, covered by our patent is a shortened version of Cas9 that was engineered by deleting sequences that are not required to maintain binding function, as revealed by structural analysis. This provides capacity within the AAV capsid to carry transcription factors linked to Cas9, along with other components such as promoters and gRNAs.

The Mini Cas9 technology strengthens our technology portfolio and differentiates Modalis from the other epigenetic technologies while enabling disease-modifying therapeutics for genetic conditions that are not addressed by current therapies.

Epigenome editing: The control of gene expression through modification of DNA, histones, non-coding RNA, etc., to turn genes on or off while leaving the gene sequence intact.

dCas9: An enzyme from which the cleavage activity of Cas9, a genome-editing cleavage enzyme, has been removed. It can be used for base substitution and epigenome editing by linking with transcription factors and other elements.