English translation for reference purposes only
In case of any discrepancy, the Japanese version shall prevail

The Third Quarter of 2025
Business and Financial report

(TSE：4883)

Modalis therapeutics Corporation

November 7, 2025

MODALIS

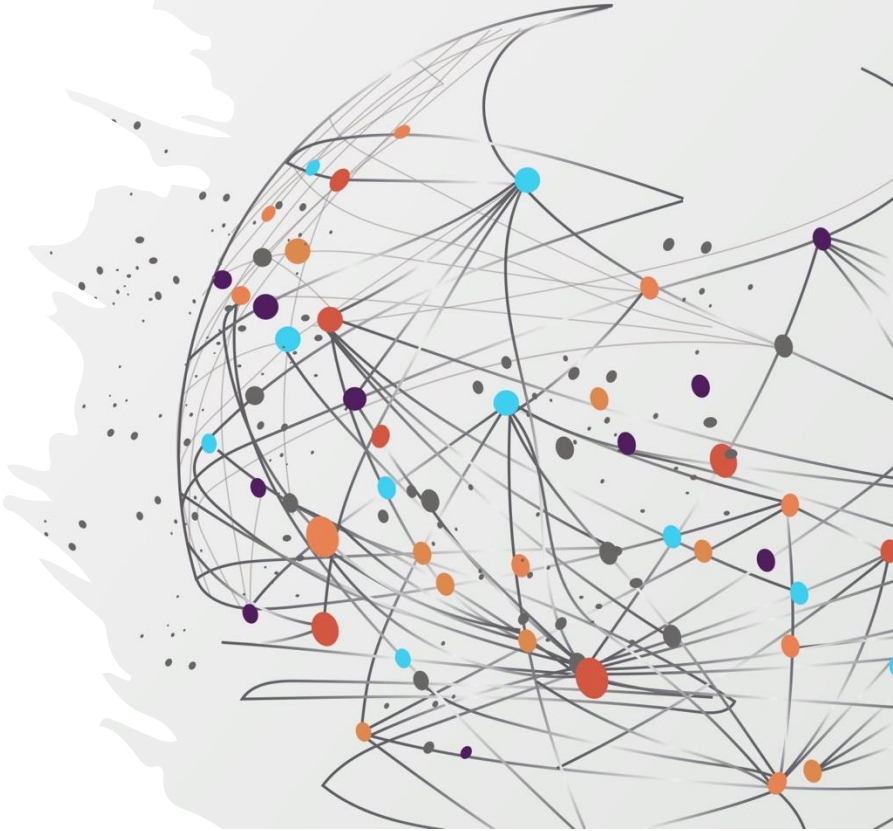
Disclaimer

This document has been prepared by Modalis Therapeutics corporation and Modalis Therapeutics Inc. (the "Companies") solely for information purpose only. This document does not constitute or form part of and should not be construed as, an offer to sell or issue or the solicitation of an offer to buy or acquire securities of the Companies in Japan, the United States or any other jurisdictions. The information contained herein is based on current economic, regulatory, market trends and other conditions. The Companies make no representation or guarantee with respect to the credibility, accuracy or completeness of the information herein. The information contained herein may change without prior notice. You may not publish or use this document and the contents thereof for any other purpose without a prior written consent of the Companies. Furthermore, the information on future business results are forward-looking statements. Forward-looking statements include but not limited to expressions such as "*believe*", "*expect*", "*plan*", "*strategic*", "*expect*", "*anticipate*", "*predict*" and "*possibility*", as well as other similar expressions to explain future business activities, achievements, events and future conditions. Forward-looking statements are predictions about the future that reflect management's judgment based on currently available information. As such, these forward-looking statements are subject to various risks and uncertainties that could cause actual results to differ materially from those expressed in or suggested by the forward-looking statements. Therefore, you may not rely entirely on forward-looking statements. The Companies do not assume any obligation to change or correct any forward-looking statements in light of new information, future events or other findings.

This document and its contents are confidential and are being provided to you solely for your information and may not be retransmitted. This presentation is being furnished to you solely for your information and may not be reproduced or redistributed to any other person. In giving this presentation, the Companies do not undertake any obligation to provide the recipient with access to any additional information or to update this presentation or any additional information or to correct any inaccuracies in any such information which may become apparent.

Information on companies other than the Companies and information provided from third parties are based on public information or sources. The Companies have not independently verified the accuracy and appropriateness of such data and indicators used herein, nor assume any responsibility for the accuracy and appropriateness of such data and indicators presented in this document.

About Modalis



MODALIS Value Highlights

Established the first robust **epigenetic platform** for activation and inhibition of endogenous genes using CRISPR-GNDM® platform

Demonstrated sustained modulation of gene expression across species resulting in functional **efficacy without serious toxicities**

Pipelines in **muscular dystrophies**, additional programs in CNS, cardiovascular and unlimited therapeutic potential in other areas

Manufacturing process established for challenging AAV capsids to enable tissue tropic delivery for programs

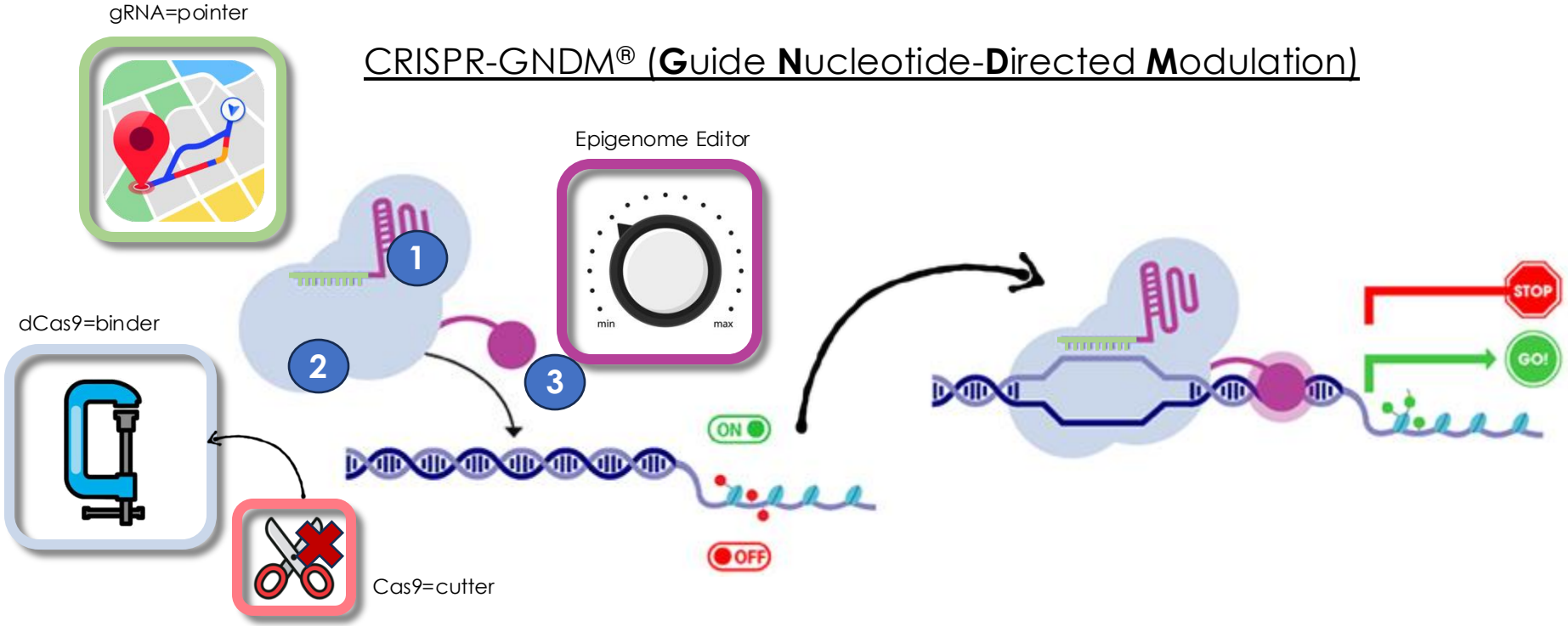
Experienced team with deep knowledge of platform

Strong **IP portfolio and strategy** that includes granted and licensed patents

Clear regulatory and clinical path in place based on recent FDA guidance and commnnuications

CRISPR-GNDM®

GNDM controls the expression of target proteins through epigenetic regulation

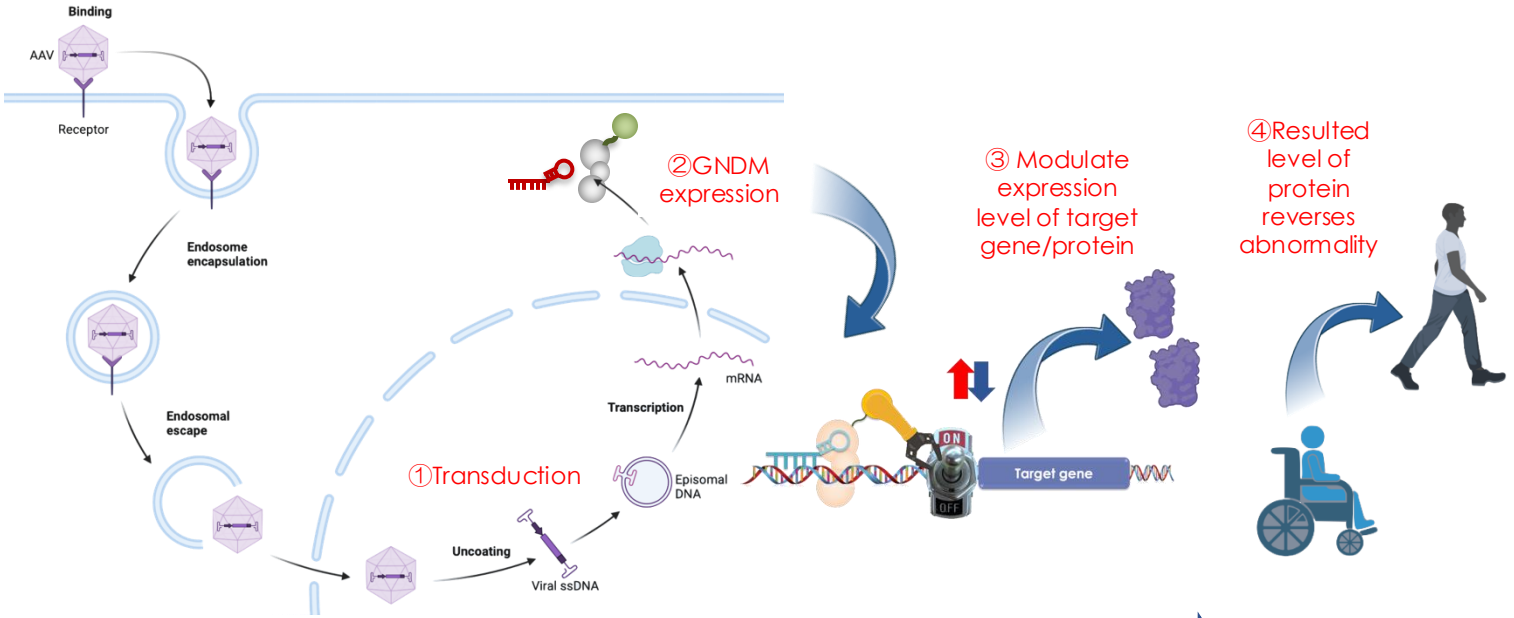


CRISPR-GNDM® consists of: ① a "guide RNA (gRNA)" for positioning, ② 'dCas9' as the binding device to DNA, ③ an "editor" for editing the epigenome, enabling precise control over gene expression on and off.

MODALIS

Delivery of GNDM to the target

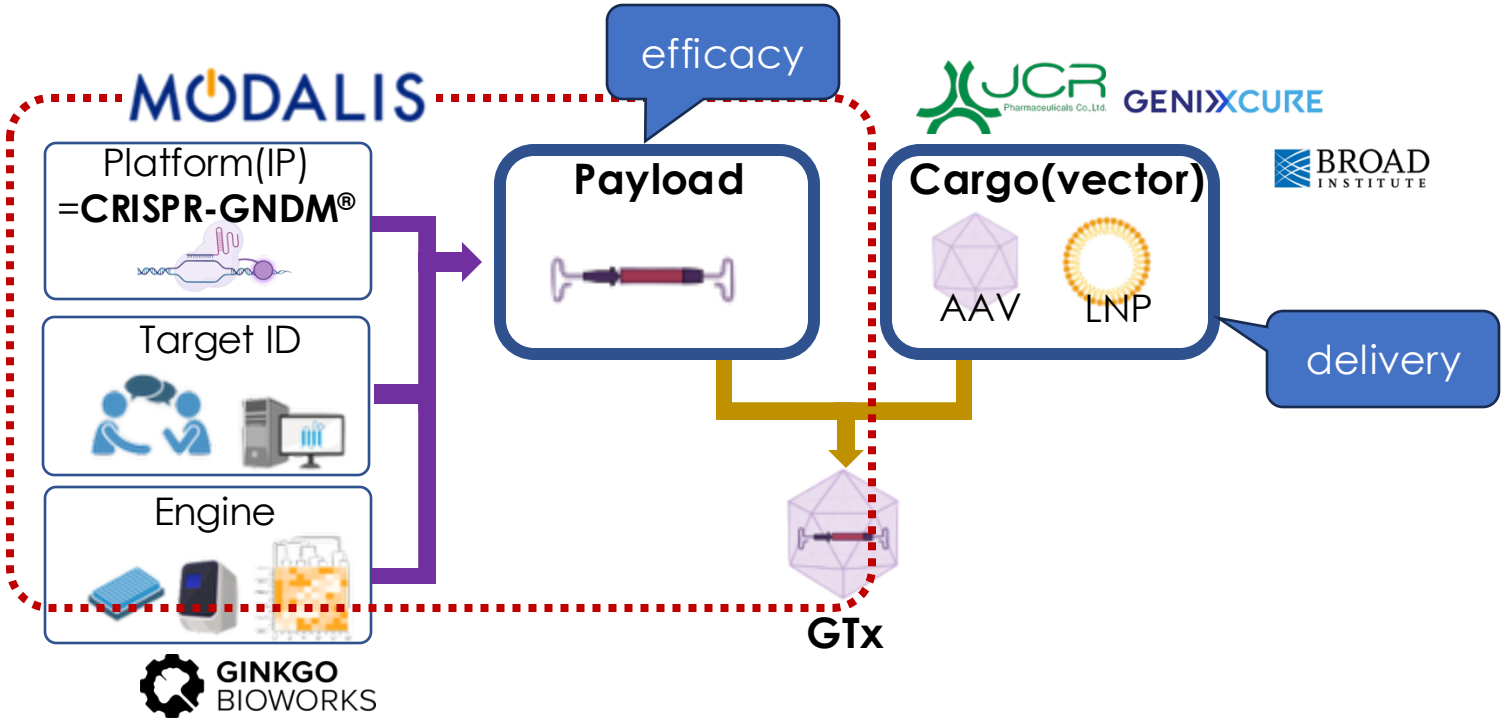
Packed in a vector, GNDM is delivered to target cells and selectively controls the expression of the target gene



Updated

MODALIS' core competence and collaboration

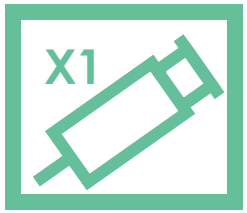
For GTx, the payload—the active component—and the cargo (vector) that delivers it to the target tissue are crucial



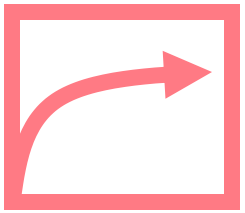
CRISPR-GNDM®'s advantages

A single injection provides long term disease modifying effect

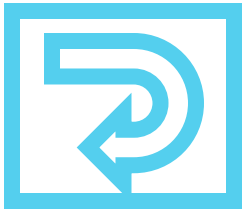
Potential benefits of CRISPR-GNDM® Technology



Single dose
Doesn't require
Repeated dosing



Long-lasting
Sustained effect
for years or decades



Disease Modifying
Not just to reduces
symptoms but
gives cure

Epigenome editing competitive landscape

While the field is gaining more traction, MODALIS is uniquely differentiated from the other epigenome companies

Company	Year Founded	Funding	Platform	Pipeline/Target indication	Stage of Development
MODALIS	2016	Public	CRISPR-GNDM x AAV	• MDL-101/LAMA2-CMD • MDL-201/DMD **Gene activation**	IND enabling
Tune Therapeutics	2020	Series B ($175M, 2025)	DNMT-KRAB fusion dCas9 x LNP	Une-401 for HBV **Gene suppression**	**CTA approval from Hongkong, NZ and Moldova on HBV**
nChroma	2021	Merged into nChroma (Dec 2024)	DNMT-KRAB fusion dCas9 x LNP	CRMA-1001 for PCSK9 **Gene suppression**	Unclear
Epicrispr	2022	Series B ($68M, 2025)	Cas12f-fused with demethylation enzyme x AAVrh74	EPI-321/FSHD **Gene suppression**	IND clearance of EPI-321 from FDA. Starting FPFD in 2025
Epigenic	2022	**Series B ($60M, 2025)**	dCas+editor x LNP	EPI-001 PCSK9 for hypercholesteremia **Gene suppression**	**Chinese IIT**

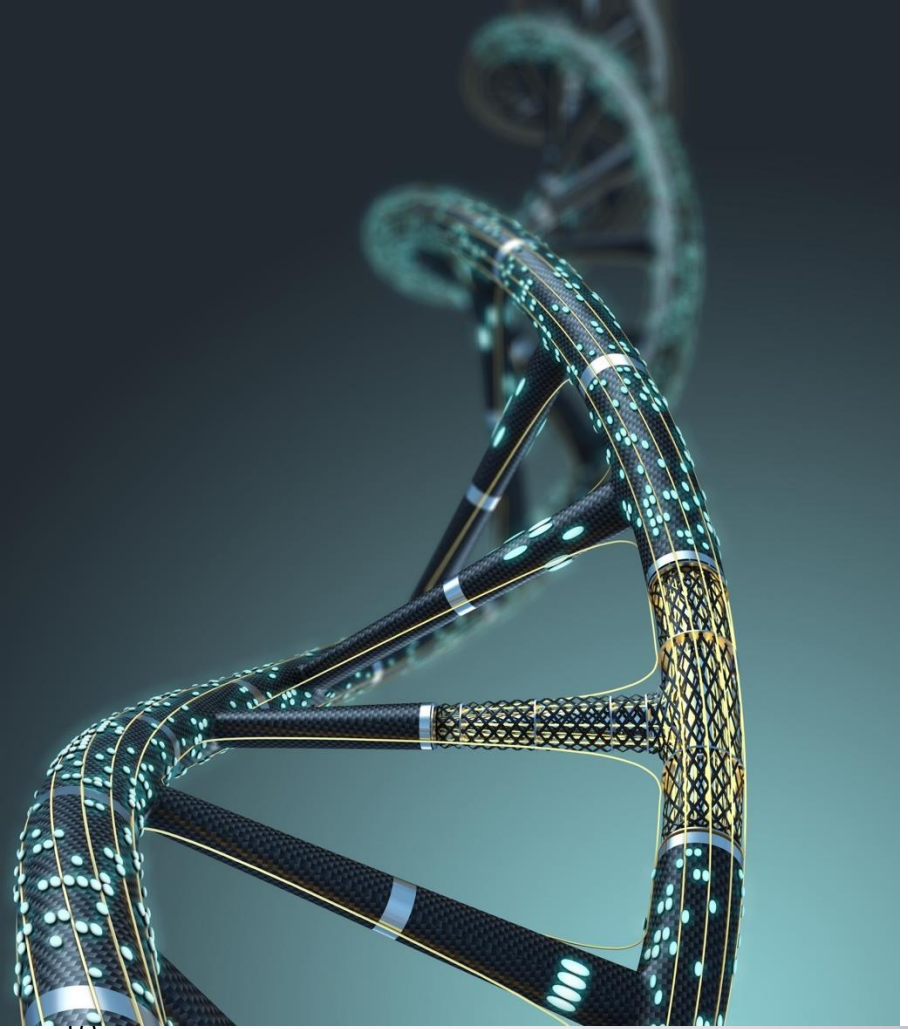


Table of contents

1. Business Highlights of the 3Q/2025

01
Status of MDL-101 (LAMA2-CMD)

02
Progress in MDL-201 (DMD)

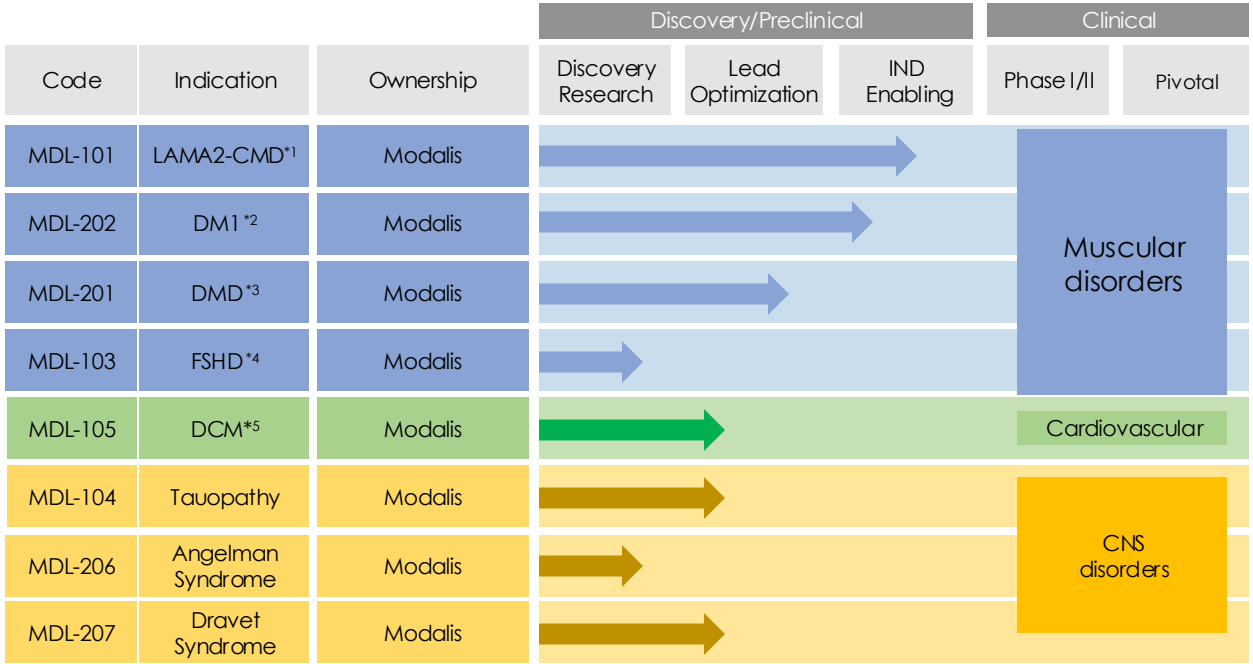
03
Progress in MDL-103 (FSHD)

04
Progress in IPs

05
Finance and Others

The current pipeline of MODALIS

Taking muscular disease-centered strategy with focus on MDL-101



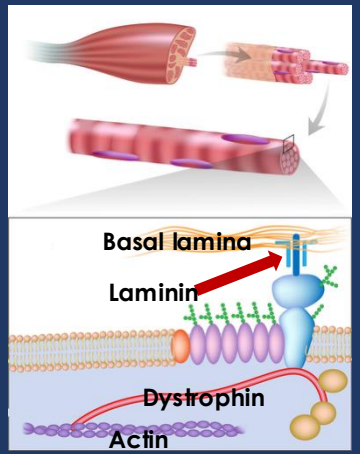
*1: LAMA2-related congenital muscular dystrophy
*2: Myotonic Dystrophy Type 1
*3: Duchene Muscular Dystrophy
*4: facioscapulohumeral muscular dystrophy
*5: Dilated Cardiomyopathy

LAMA2-CMD (aka CMD1a)

Severe muscular dystrophy caused by loss of function mutation in LAMA2 gene

MDL-101

Potential to be the first LAMA2-CMD gene activation therapy



Prevalence	**8.3 in 1 million*** 2,500 in US	
Disease Onset	Apparent at birth or within a few months after birth	
Disease Burden	Patients do not survive past adolescence	• Severe muscle weakness • Lack of muscle tone (hypotonia) • Little spontaneous movement • Joint deformities (contractures) • Heart problems and seizures
Disease Causing Gene	**LAMA2 mutation**	
Commercial opportunity	**$500M+**	

Source: *Estimating the Prevalence of LAMA2 Congenital Muscular Dystrophy using Population Genetic Databases (2023)

MODALIS

Status of manufacturing

Following process development, GMP manufacturing is currently underway

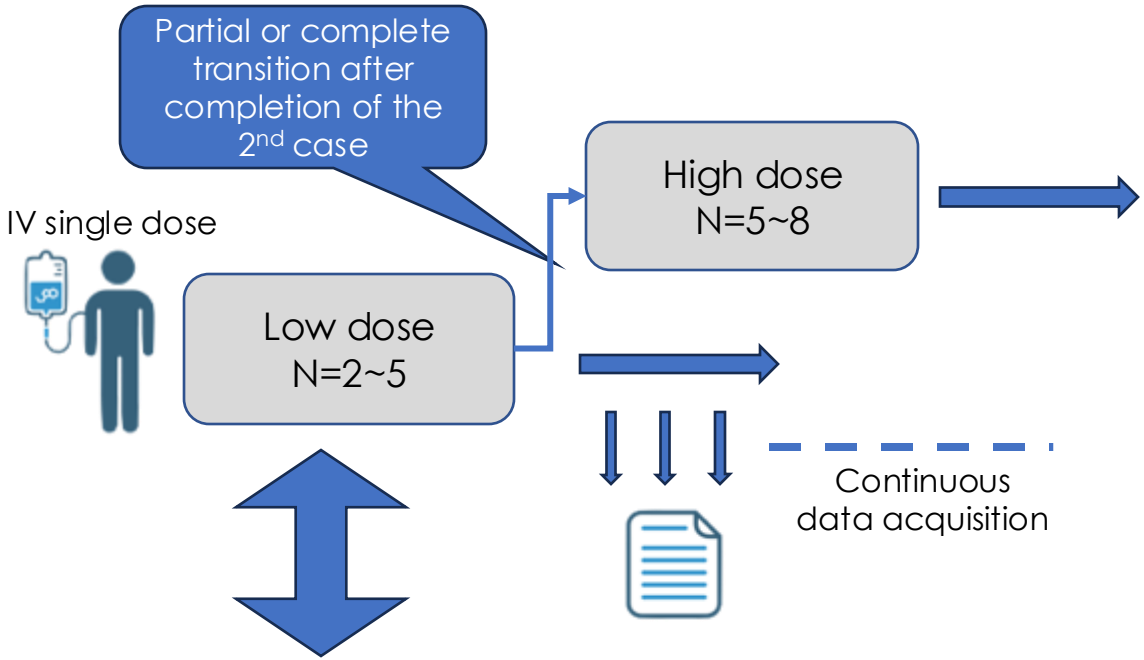
- Established manufacturing processes adapted for modified capsids
  - Achieved rational production efficiency, yield, and quality
  - Concurrently established analytical methods
- Engineering run of AAV successfully completed with feasible quality and productivity.
- Completed GMP manufacturing of plasmids for AAV vectors
- Significantly reduced per patient CoGs through lower dosage x improved production efficiency

MDL-101-001 Trial design

Open-label trial with two doses. Efficacy evaluated in comparison with natural history observation trial.

- Patients aged 36 months or younger (male or female)
- Clinical condition and/or significant reduction in LAMA2 protein levels in muscles associated with Lama2 gene mutations
- Stable condition during treatment
- Difficulty with independent walking or sitting

Phase1/2 Open-label dose escalating trial



Compare with Natural History Study
(NCT06354790, NCT04299321, NCT06132750)

Preparations for the clinical trial

Selection of clinical trial sites is underway

- Conducted interviews at candidate clinical trial sites in two countries, including the US
- Proceeded with site selection while adjusting the clinical trial design
- Currently building a framework for preparing the application package

Summary of MDL-101

undergoing GMP and IND-enabling activities in preparation for clinical trials

Updated

- **Manufacturing**
  - ✓ **Completed engineering run of AAV**
  - ✓ **Completed plasmid GMP**
  - ● **Preparing for GMP campaign**
- **GLP Tox Study**
  - **Mouse IND enabling initiated**
  - **NHP GLP tox initiated**
- **Coordinating with patient groups for the clinical trial**
- **Site selection and preparation**

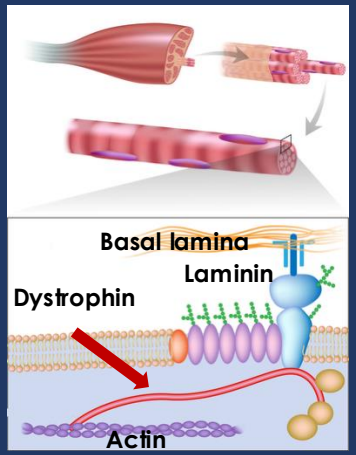
MODALIS

Duchenne Muscular Dystrophy (DMD)

A type of muscular dystrophy caused by mutation in Dystrophin gene

MDL-201

Potentially best-in-class molecule by rebooting UTRN gene expression by GNDM



Prevalence	**1 in 3,500 to 5,000 male newborns**	Relatively high in genetic disorders
Disease onset	most commonly appears **between 3 and 6 years old**	
Disease Burden	Most severe clinical symptoms of all the muscular dystrophies including muscles weakness and atrophy	Motor development begins to slow in early childhood and muscle weakness progresses, followed by cardiomyopathy, scoliosis, and respiratory complications
Cause of disease	Disruption or mutation in Dystrophin gene	Loss of dystrophin and abnormal histological development of muscle necrosis and regeneration
Market size	**$1.1BM** 2022	Expected to grow at CAGR=42.5% with approval of new therapeutics

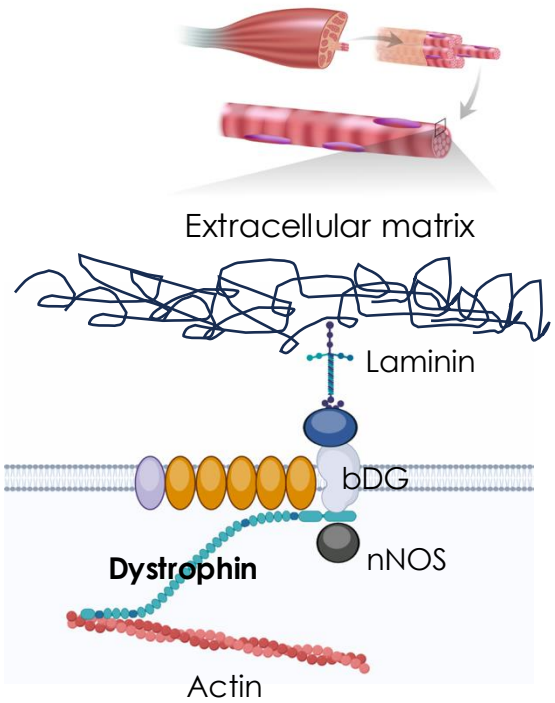
*Source: https://doi.org/10.1212/WNL.0000000000011425

MODALIS

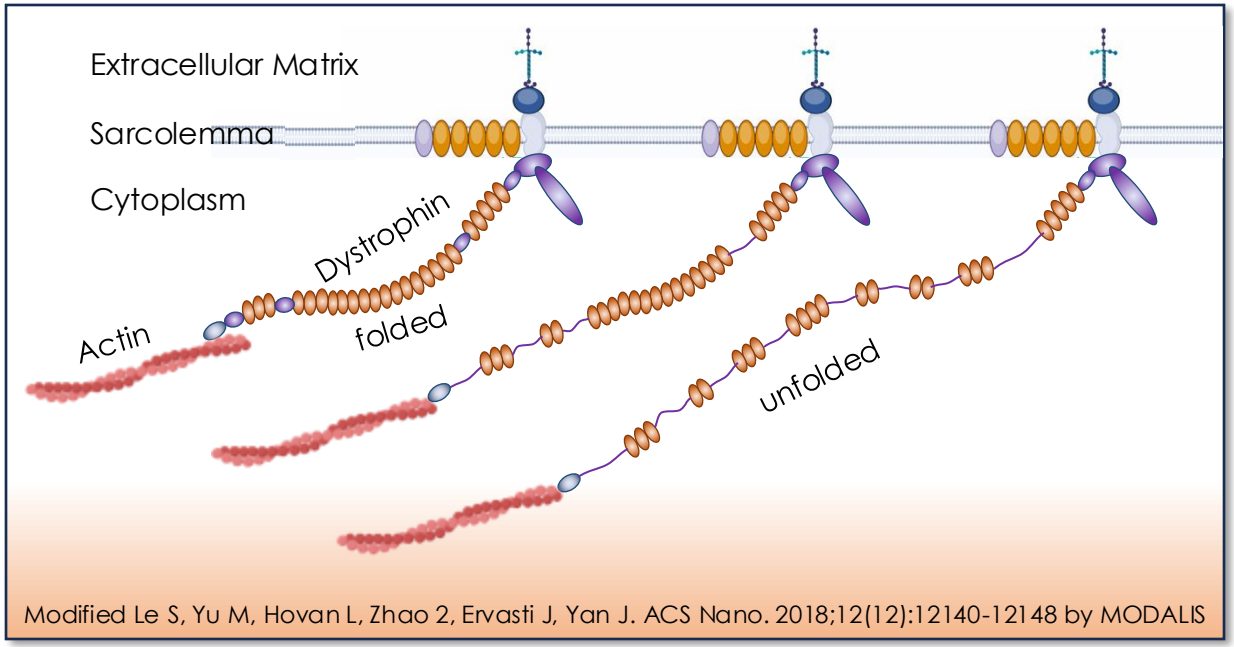
Dystrophin's function

Functions as a shock absorber and signal transmitting molecule in muscles

Dystrophin location



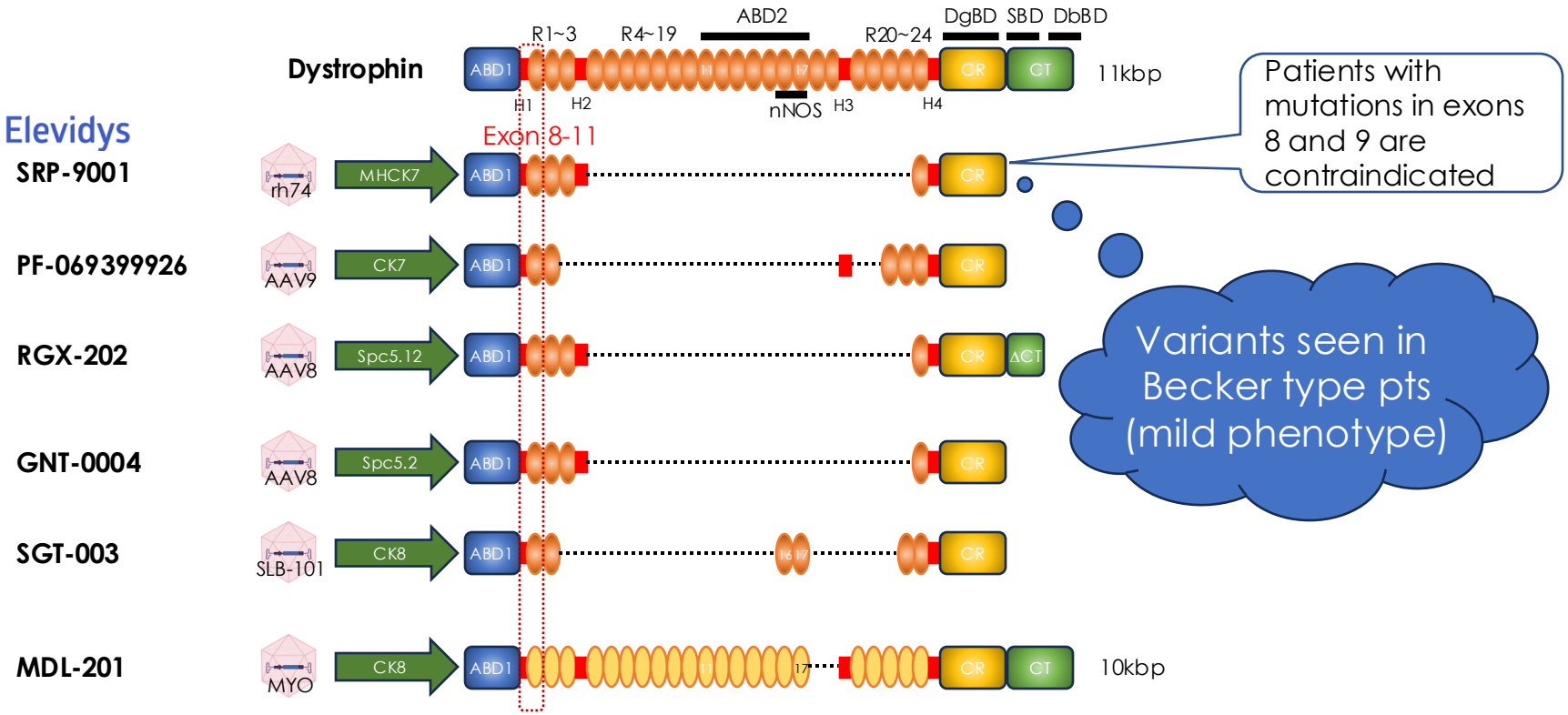
Dystrophin stretches and contracts to connect the cell membrane and actin



micro-Dystrophins payload comparison

Due to size constraints, small dystrophin derived from Becker patients is used for GTx

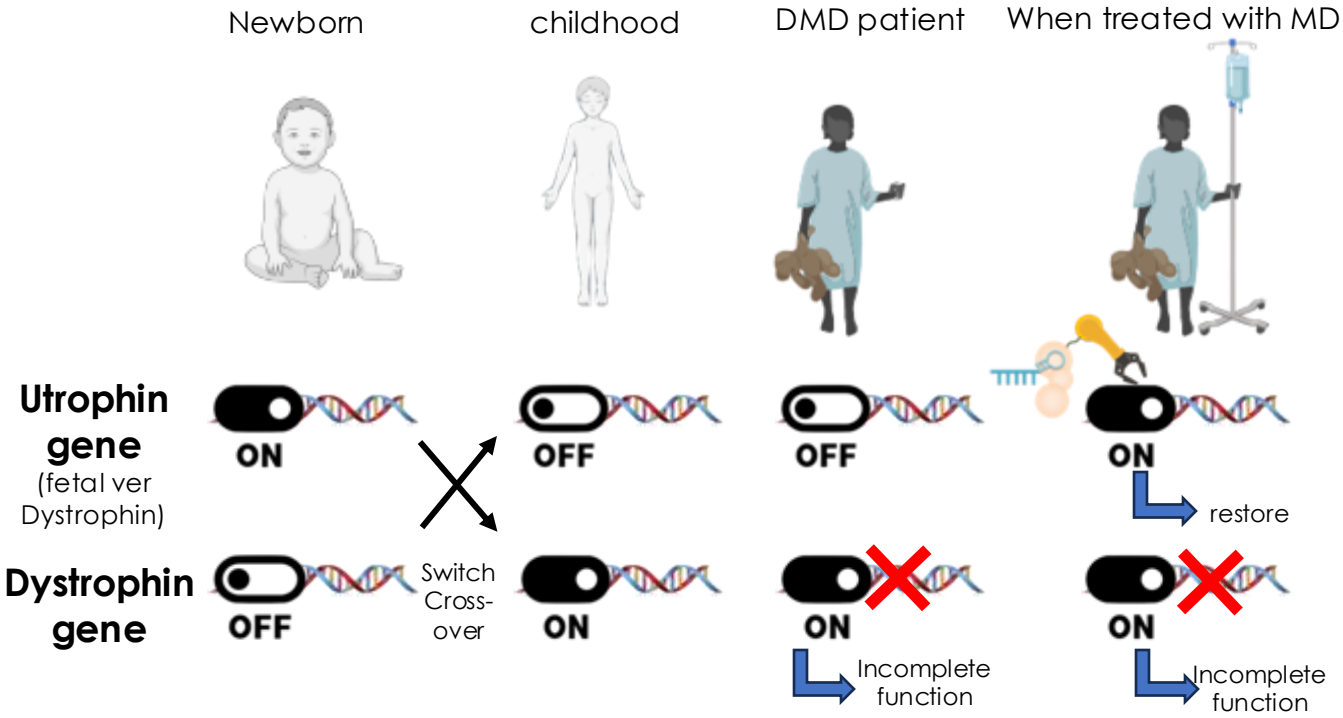
Dystrophin/Utrophin and mini-Dystrophin structure

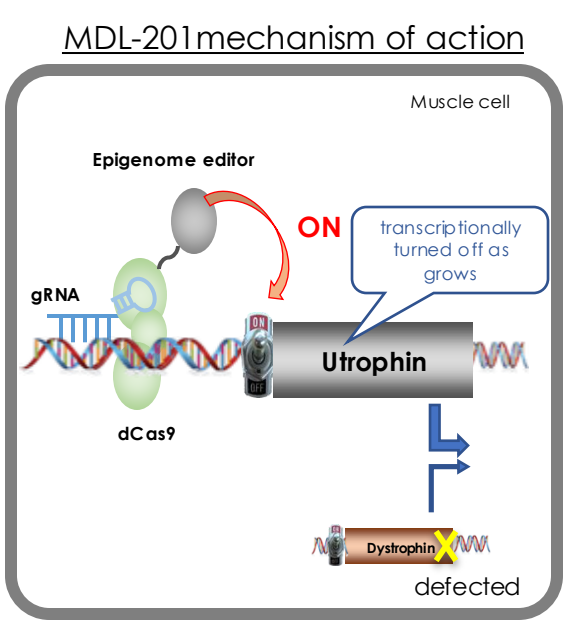


Modified from Crudele &Chamberlain, 2019

MDL-201 therapeutic concept

Reboot Utrophin genes , which is intact in patient, to compensate Dystrophin function





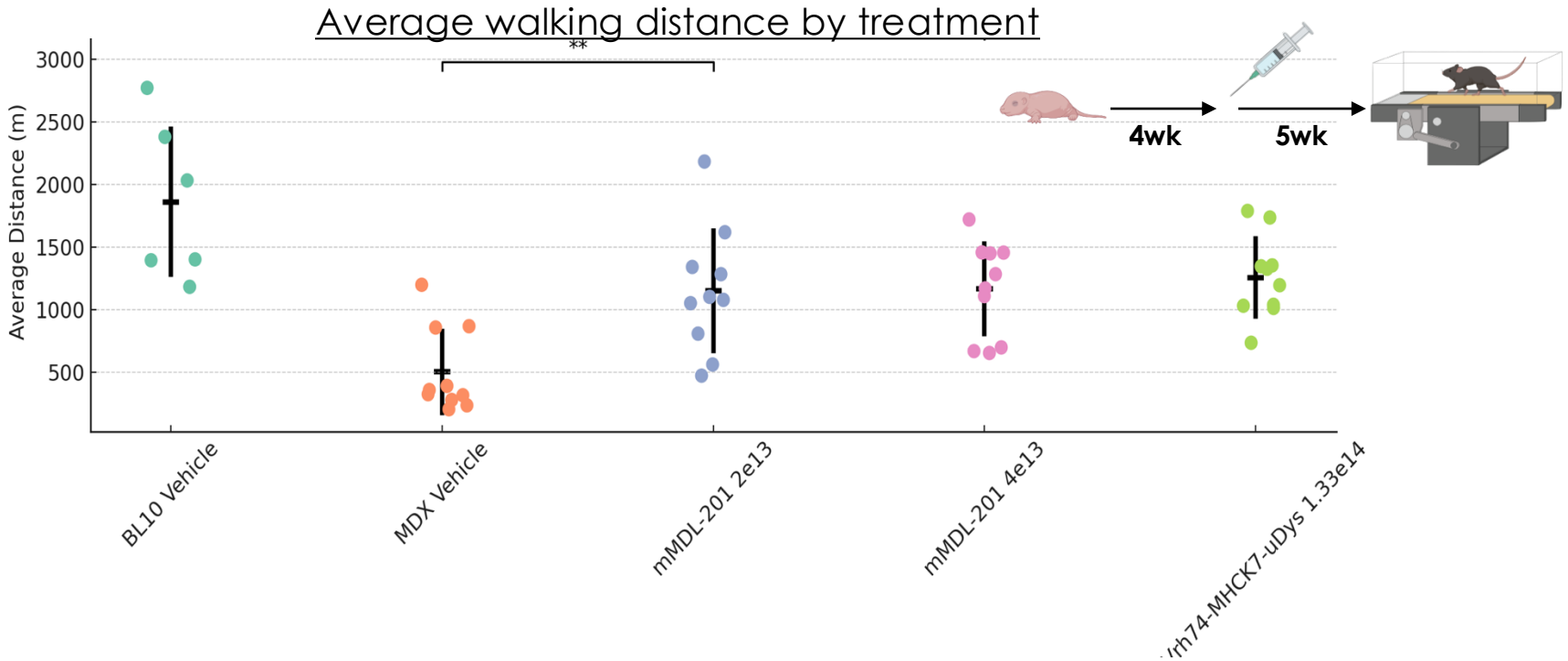
activating Utrophin using GNDM is expected to have a greater medicinal effect than mini-Dystrophin

MODALIS

Previously reported

Functional improvement of DMD by MDL-201

achieves the same level of efficacy as the benchmark drug at a dose one order of magnitude lower



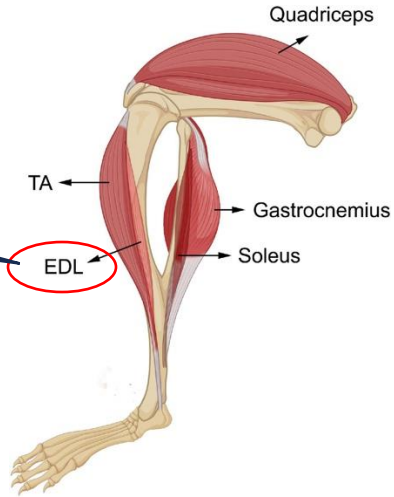
Data is presented as mean ± SEM. Normality was assessed using Shapiro-Wilk tests for all treatment groups. Post-normality test, unpaired t-tests were performed between the BL10 Vehicle and MDX Vehicle groups for both A and B (### p<0.001). Non-parametric ANOVAs (Kruskal-Wallis tests with Dunn's post-hoc test for multiple comparisons) were performed to compare all treatment groups against the MDX Vehicle (**p<0.01; ***p<0.001).

NEW

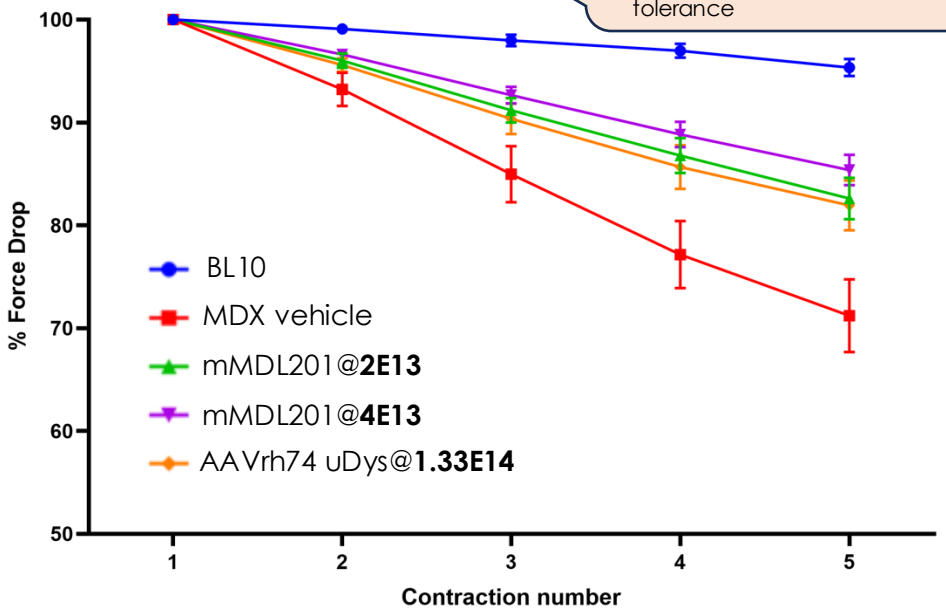
Muscle recovery effect

mMDL-201 achieves muscle recovery effects equivalent to the benchmark at a lower dose in EDL muscle testing

- Fast-twitch muscle dominant
- Preparation for extraction
- Standard model for membrane injury disease



- Reduction in contraction force from a state where muscles contract while being stretched by external force
- Quantitative indicator of fascia damage tolerance



EDL: Extensor Digitorum Longus

N=5 in BL10 Vehicle, N=9 in the MDL201 4.0E13 treatment group, and N=10 in all other groups, **study week 11 (15 weeks of age)**

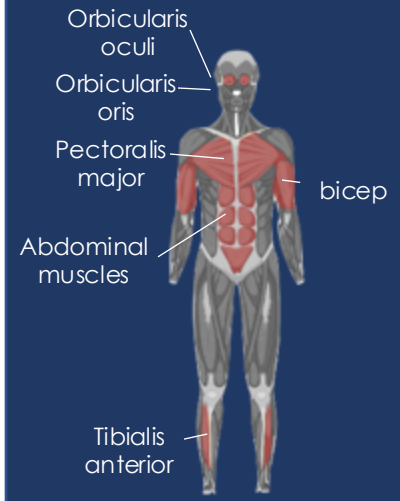
%force drop = ((ECC1-ECC5)/ECC1)*100

Facioscapulohumeral Muscular Dystrophy (FSHD)

A type of muscular dystrophy caused by impaired Dux4 gene expression

MDL-103

Potentially first-in-class treatment by silencing expression of toxic Dux4 gene product



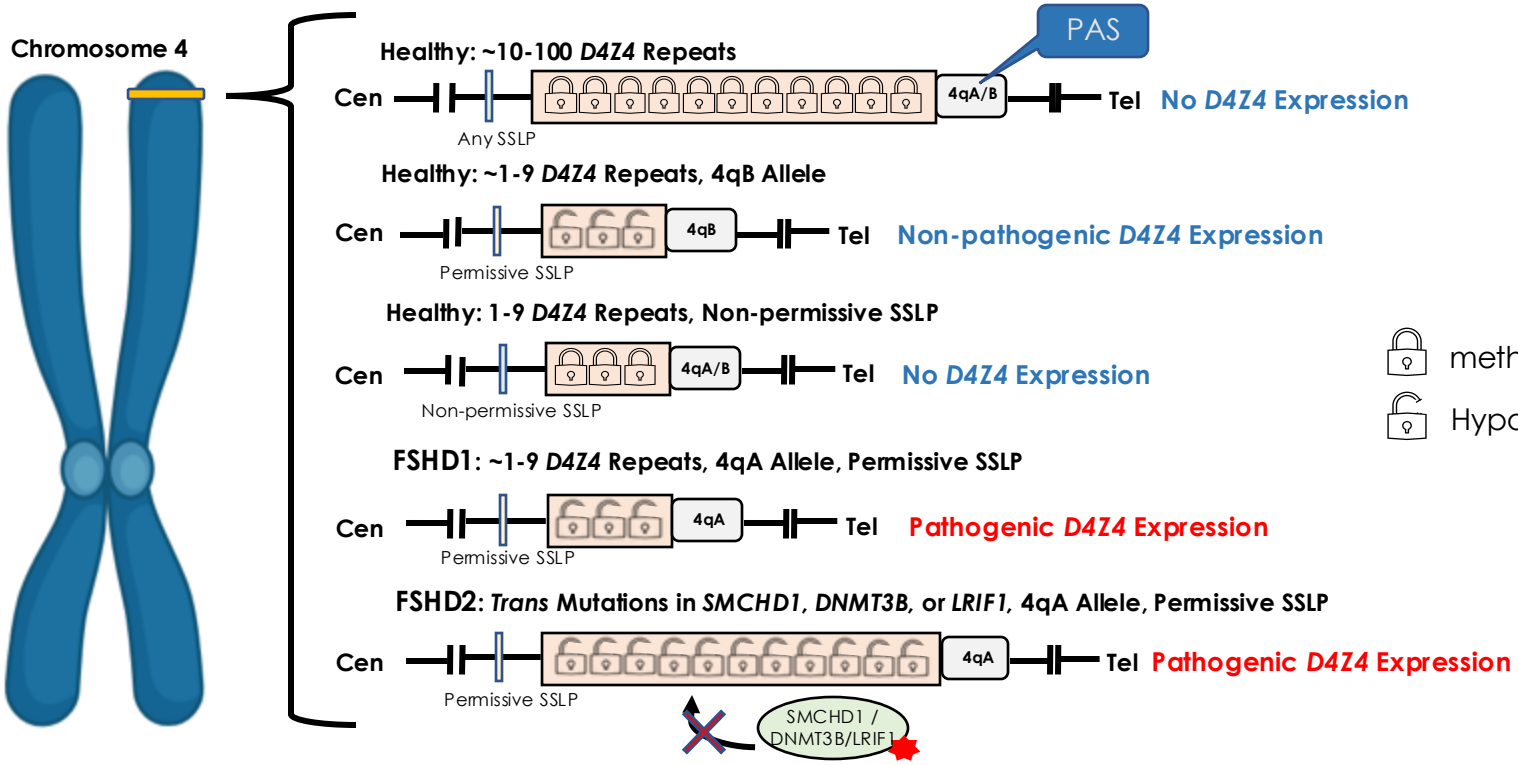
Prevalence	**1 in 10,000-20,000**	Muscular dystrophy most frequent in adults
Disease Onset	Often not recognized until the 20s and tends to worsen during adolescence	Progression of disease to face, shoulders, and arms is generally slow
Disease Burden	weakness of the facial muscles, the stabilizers of the scapula, or the dorsiflexors of the foot	Symptoms of asymmetrical (unbalanced) muscle weakness Visual impairment, vascular abnormalities, hearing impairment, etc.
Disease Causing Gene	Over expression of Dux4 gene	DUX4 is originally expressed in germline cells but need to be suppressed in somatic cells
Commercial opportunity	**$500M+**	

Source: https://doi.org/10.1212/WNL.0000000000011425
Orphanet, Raymond A. Huml MD A concise guide

MODALIS

FSHD disease mechanism

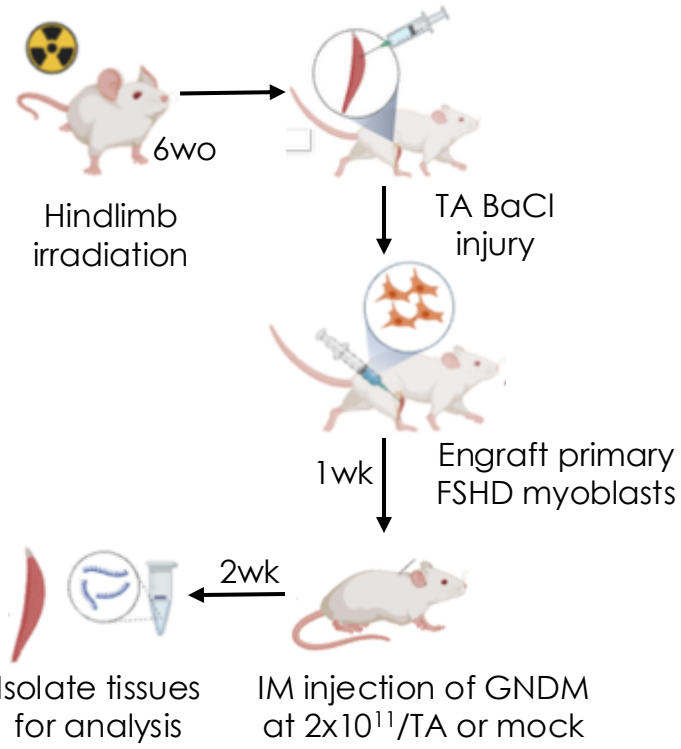
Inappropriate expression of toxic Dux4 in skeletal muscles



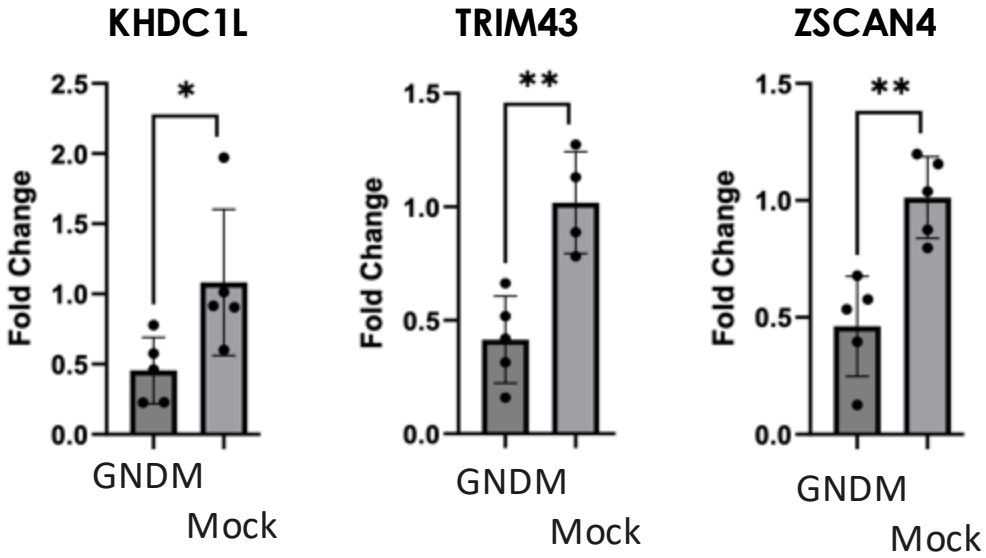
DeSimone et al. 2020, *Dis Model Mech*

SSLP: Simple Sequence Length Polymorphism PAS: polyadenylation signal

DUX4 downstream genes are suppressed by GNDM



Expression of DUX4-Target Genes In Xenografted TAs



- N=5 Normalized to hRPL13A
- Statistical significance by 1-way ANOVA with Dunnett's test

Publication and conference presentations

Preclinical data for MDL-201 was reported in 2 conferences

Recent presentation

2025 Scientific & Family Conference, Congenital Muscular Dystrophy/Nemaline Myopathy/Titinopathy (2025 SciFam) Aug 4th

"Epigenetic Editing with CRISPR-GNDM®: MDL-101 is a Muscle -Tropic AAV Vectors for the Treatment of LAMA2-CMD"

The 6th Genome Editing Therapeutics Summit October 1st

"Movement Toward the Clinic: Preclinical Development of Gene Activation programs with CRISPR-GNDM® platform"

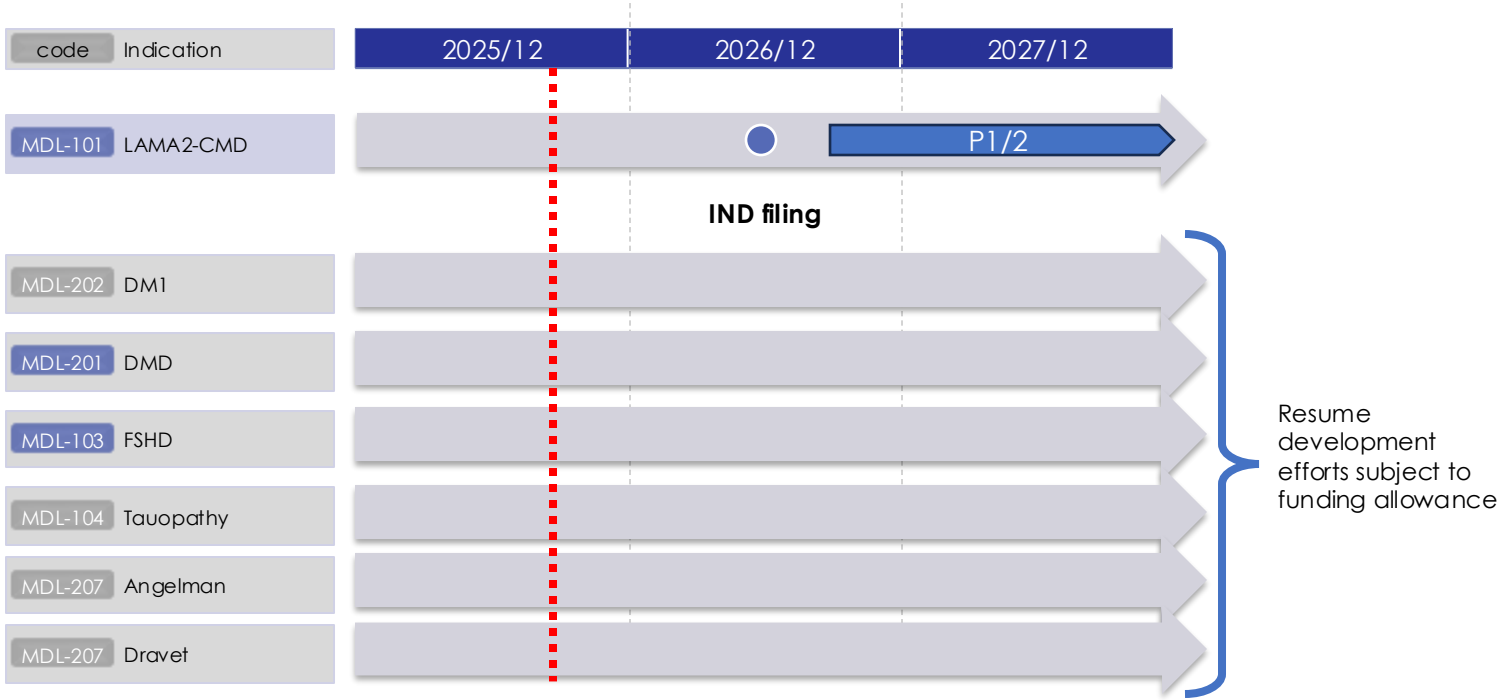
MODALIS

Updated

Pipeline status and coming milestones

Target IND submission for MDL-101 by mid-2025

Pipeline status



- Scheduled milestone events are informational in the future and subject to change

Updated

Achievements of the programs and coming milestones

	Achievement so far	Coming milestones
MDL-101 LAMA2-CMD	✓ Animal PoC ✓ Target engagement in NHP ✓ Pre-IND ✓ **GMP manufacturing (Plasmid)** ✓ ODD and RPDD designation ✓ Data presentations (**SciFam2026 (Aug), 6th Genome Editing Summit (Sep)**)	• GLP-Tox (on going) • Mice IND enabling(on going) • GMP manufacturing(AAV: ongoing) • IND (**mid 2026**) • FPFD (late 2026)

その他	• Established animal PoC
	  • MDL-201 (DMD), **additional readout**
	  • MDL-202 (DM1)
	  • MDL-104 (Tauopathy)
	  • MDL-205 (Angelman syndrome)
	  • MDL-207 (Dravet syndrome)
	• MDL-103 (FSHD): Received grant from xPrize and SolveFSHD, **confirmation of the potency in disease model mice**
	• Research collaboration with JCR in CNS
	• Collaboration with Ginkgo Bioworks, GenixCure
		• Additional readout of MDL-201
		• **Data presentation at (6th Next Generation Genome Editing Summit)**
		• Explore optimal capsid and route of administration for CNS program
		• Allocation of development funds through partnering and grants
		• Animal PoC
		• Continuing Research and Moving to Next Steps

MODALIS

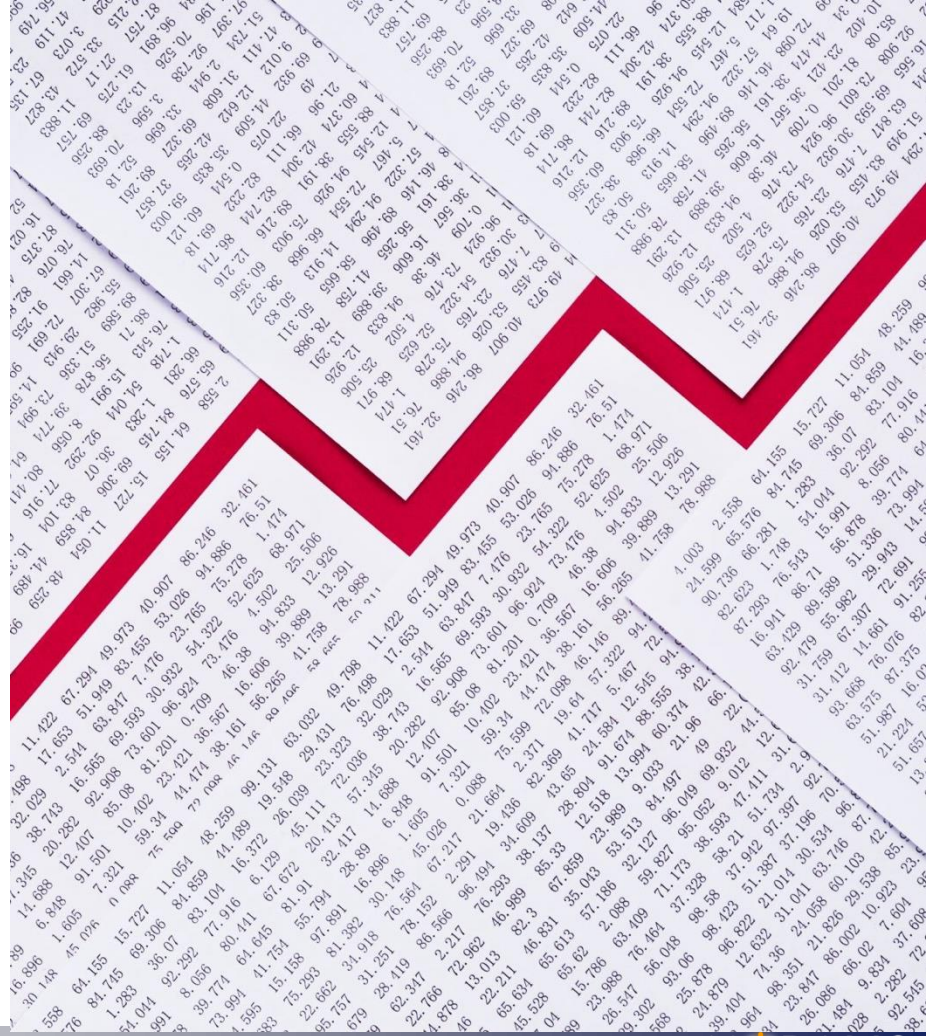
Progress on IP

MDL-103 and 104-related patent issued in Japan

- A patent has been registered in Japan (September) for a DUX4 gene-targeted therapy for facioscapulohumeral muscular dystrophy (FSHD) (JP 7736329).

- A patent for the treatment of tauopathies, including Alzheimer's disease, by targeting the tau protein (JP 7749244), also registered in Japan in September

2. Financial updates



BS & Financial Position at the end of 3Q/2025

Maintain a certain level of cash and deposits needed for operations for ~12 months

(Million Yen)

	End of FY2024 (A)	End of 3Q FY2025 (B)	(B) – (A)
Current assets	3,617	3,354	△262
Cash & deposits	3,575	3,307	△267
Non-current assets	74	68	△5
Total assets	3,691	3,423	△268
Current liabilities	117	675	558
Non-current liabilities	26	53	27
Total liabilities	143	729	585
Total net assets	3,548	2,693	△854
Total liabilities and net assets	3,691	3,423	△268
Capital adequacy ratio	95.5%	77.7%	

Note

- Despite the exercise of stock acquisition rights, cash and deposits decreased due to the increase in expenses and liabilities increased due to an increase in corporate bonds and accounts payable.

Information purpose only

BS & Financial Position at the end of 3Q/2025

Maintain a certain level of cash and deposits needed for operations for ~12 months

(In thousand USD at @150yen/$)

	End of FY2024 (A)	End of 3Q FY2025 (B)	(B) – (A)
Current assets	24,113	22,361	-1,752
Cash & deposits	23,835	22,052	-1,782
Non-current assets	496	458	-37
Total assets	24,610	22,820	-1,790
Current liabilities	782	4,505	3,723
Non-current liabilities	174	357	183
Total liabilities	956	4,862	3,906
Total net assets	23,653	17,957	-5,696
Total liabilities and net assets	24,610	22,820	-1,790
Capital adequacy ratio	95.5%	77.7%	

Note

- Despite the exercise of stock acquisition rights, cash and deposits decreased due to the increase in expenses and liabilities increased due to an increase in corporate bonds and accounts payable.

PL & Business Result at the end of 3Q/2025

1,815 million in operating expenses, mainly due to the cost of related to MDL-101 program

(Million Yen)

	3Q FY2024 (A)	3Q FY2025 (B)	(B)−(A)
Operating revenue	-	-	-
Operating expenses	1,062	1,815	752
R&D	882	1,632	750
SGA	180	182	2
Operating income	△1,062	△1,815	△752
Ordinary income	△1,059	△1,798	△739
Current Profit	△1,060	△1,801	△741

Operating expenses

- Recorded non-operating income as an upfront payment of the funding provided under a strategic partnership with SOLVE FSHD and non-operating income from the grant money won at XPRIZE
- Expenses will increase due to progress in preclinical trials and investigational drug manufacturing for clinical trials of MDL-101.

Information purpose only

PL & Business Result at the end of 3Q/2025

$12.1M in business expenses, mainly due to the cost of related to MDL-101 program

(In thousand USD at @150yen/$)

	3Q FY2024 (A)	3Q FY2025 (B)	(B)−(A)
Operating revenue	-	-	-
Operating expenses	7,082	12,100	5,017
R&D	5,881	10,883	5,002
SGA	1,201	1,216	14
Operating income	-7,082	-12,100	-5,017
Ordinary income	-7,060	-11,988	-4,927
Current Profit	-7,068	-12,011	-4,943

Operating expenses

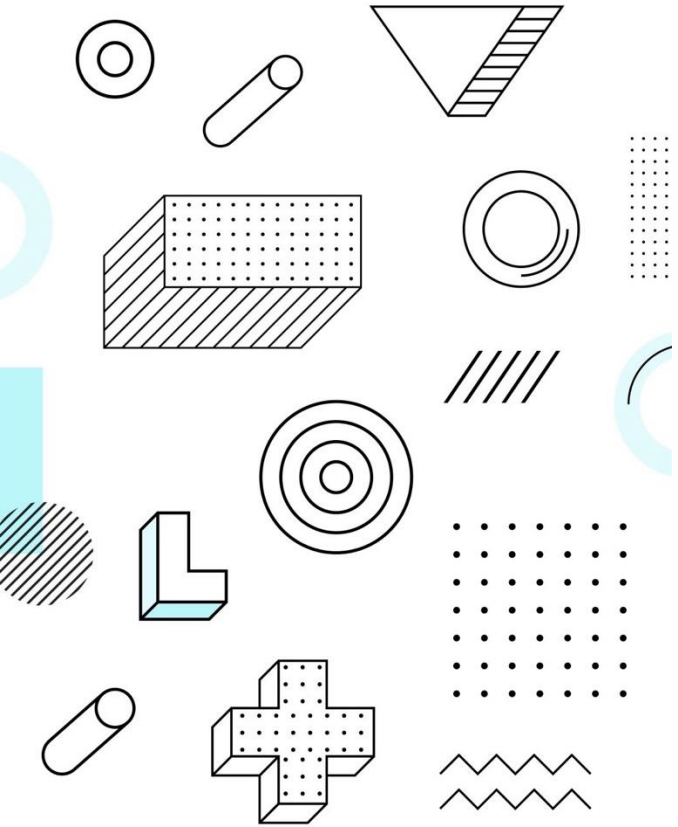
- Recorded non-operating income as an upfront payment of the funding provided under a strategic partnership with SOLVE FSHD and non-operating income from the grant money won at XPRIZE
- Expenses will increase due to progress in preclinical trials and investigational drug manufacturing for clinical trials of MDL-101.

MODALIS

3. Growth Strategy

Three-phase Growth Strategy

Diversified pipeline with their own missions



Pioneer the gene modulation
With highly suitable indications

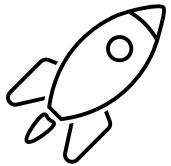
MDL-101

Expand technology opportunity with products for larger opportunity

MDL-201
MDL-202

Further approach to challenging applications

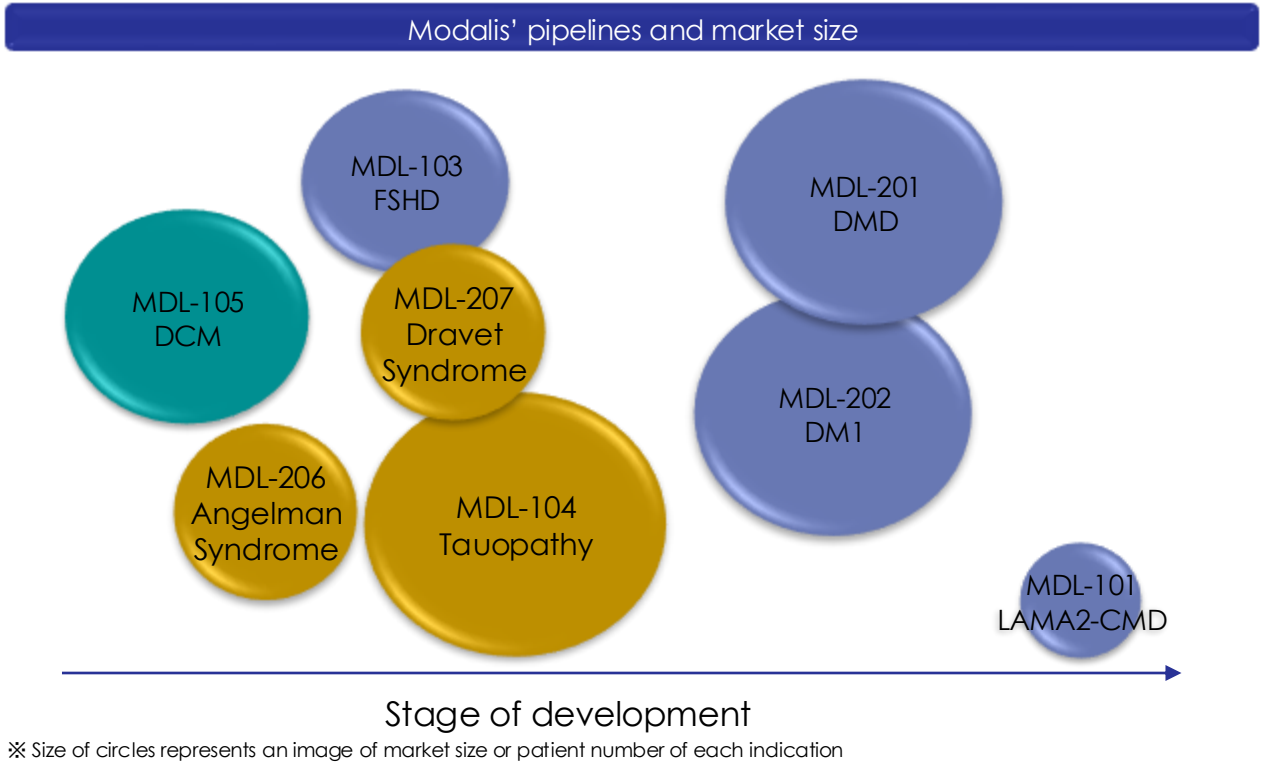
Other programs



Updated

Modalis' pipelines and market size

Large indication programs follow MDL-101 which paves the clinical path



※ Size of circles represents an image of market size or patient number of each indication

4. summary

Key Takeaway of 2025 3Q report

1. Set IND target for MDL-101 for mid-2026

2. Confirmed preclinical efficacy of MDL-201 exceeding benchmark drugs across other parameters

3. Confirmed efficacy of MDL-103 in animal model

4. Patents related to MDL-103 and 104 are issued in Japan

5. Strengthened clinical development capabilities. Recruited additional talent externally alongside promotions.

Modalis Therapeutics

MODALIS

- Based in Greater Boston area
- Pioneering the first CRISPR-based gene modulation technology since 2016
- Leading company in CRISPR epigenetic modulation
- Develops novel precision medicines for genetic disorders that have no cure

5. Q&A

Q: When in 2026 is MDL-101 expected to enter clinical trials?

- Following a thorough review of the schedule, we have set the goal of submitting the IND by mid-2026 and initiating clinical trials within the same year.

Q: How much impact will the US policy and top management change have**?**

- Since the beginning of the year, various policy and management changes have been reported one after another. While we are doing our best to keep up with them, the changes are being reported too frequently and in ways that deviate from expectations, and some are even being withdrawn. As a result, we cannot say that we have fully captured all the changes.
- Even though, some policies that may have an impact include 1) exchange rates, 2) tariffs, and 3) pharmaceutical-related policies. For example, the positive impact of yen appreciation may offset the negative impact of tariffs, and some effects may cancel each other out internally, making it difficult to evaluate at this stage.
- On the other hand, regarding pharmaceuticals, if there are significant staff reductions at regulatory authorities leading to delays in reviews, or if the previously favorable stance toward advanced medical technologies is reversed, there is a possibility that this could have some impact on our business.