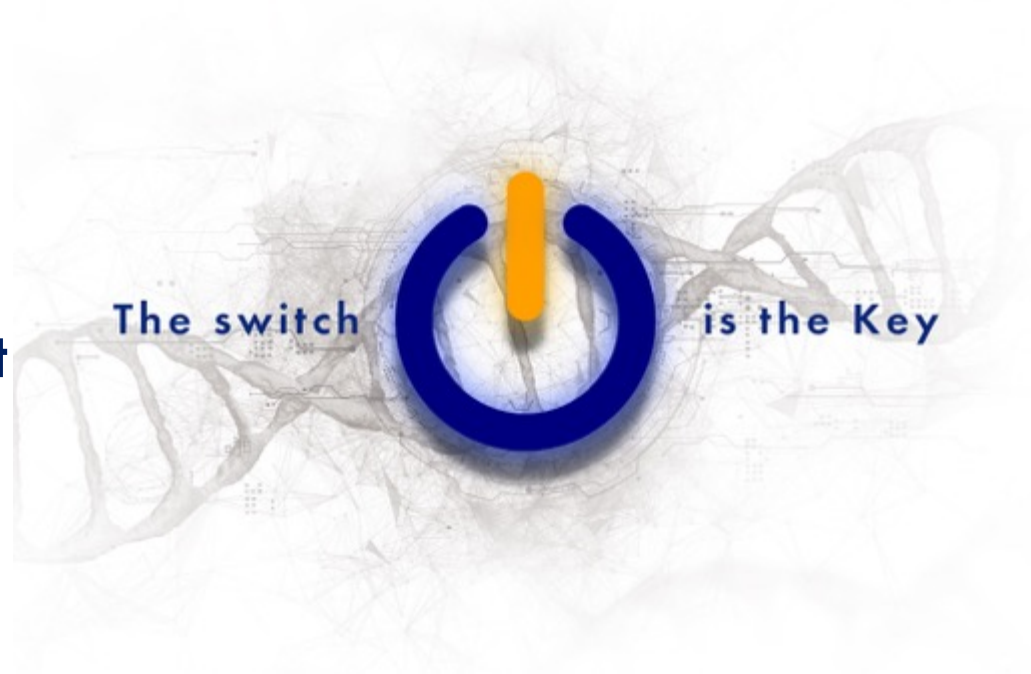




The second Quarter of 2026 Business and Financial report

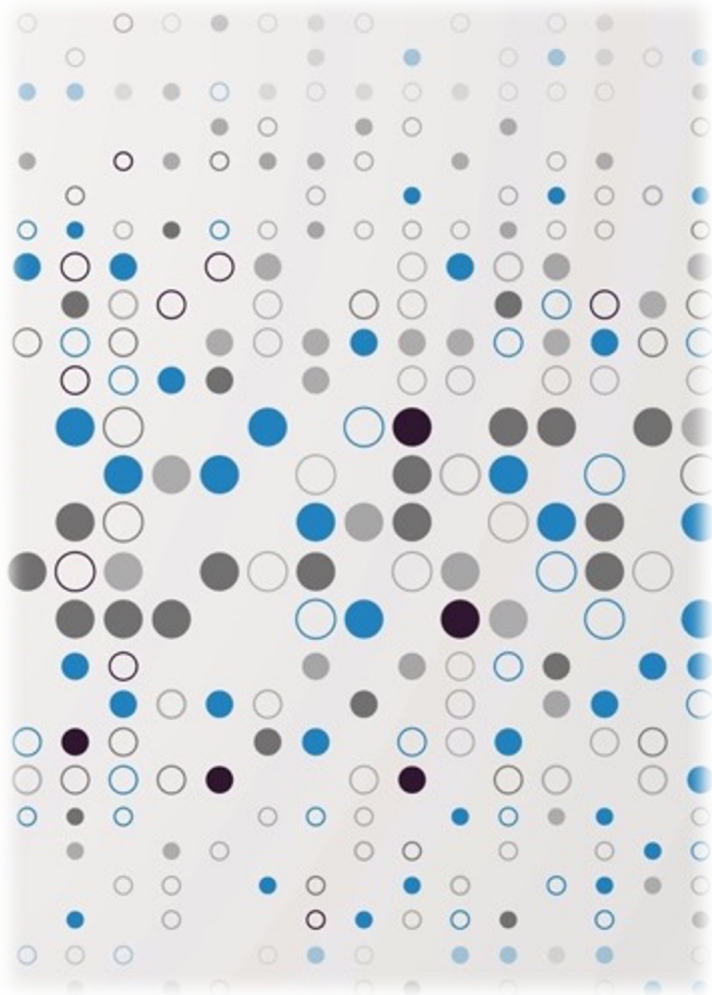
**MODALIS THERAPEUTICS
CORPORATION**
TSE 4883

Aug 10th, 2026





0. Corporate Overview



Corporate Information (As of June 30th, 2026)



Every Life Deserves Attention

Name	Modalis Therapeutics Corporation (Ticker symbol: 4883)
Foundation	Jan 2016
President CEO	Haru Morita
HQs	3-11-5 Nihonbashi-Honcho, Nihonbashi-Lifescience-Bldg.2 7F Chuo-ku, Tokyo 103-0023 Japan
US subsidiary	Modalis Therapeutics Inc. (43 Foundry Avenue, Waltham, Massachusetts)
Capital stock	885 million yen
Outstanding share	97,334,098 shares of common stock
Number of employee	21 (including 8 Ph.D.) (5 in Japan, 16 in US)

What is Modalis?

One Gene Regulation Platform
CRISPR-GNDM®
an epigenome editing technology

↓
Multiple Disease Applications



Turning beneficial genes **ON**
and harmful genes **OFF**

MODALIS Value Highlights

Building the Next Generation of Genetic Medicines

Platform: CRISPR-GNDM®

Programmable gene activation and repression without DNA cutting

1st

company advancing CRISPR-based gene activation therapeutics toward the clinic

4

Programs across neuromuscular diseases

Multiple

therapeutic targets validated in vivo

IND

MDL-101 is Making Progress Toward

Competitive Advantages

Gene Regulation Without DNA Cleavage

Demonstration of Long-Term Gene Expression Regulation

Applicable to neuromuscular to CNS disorders

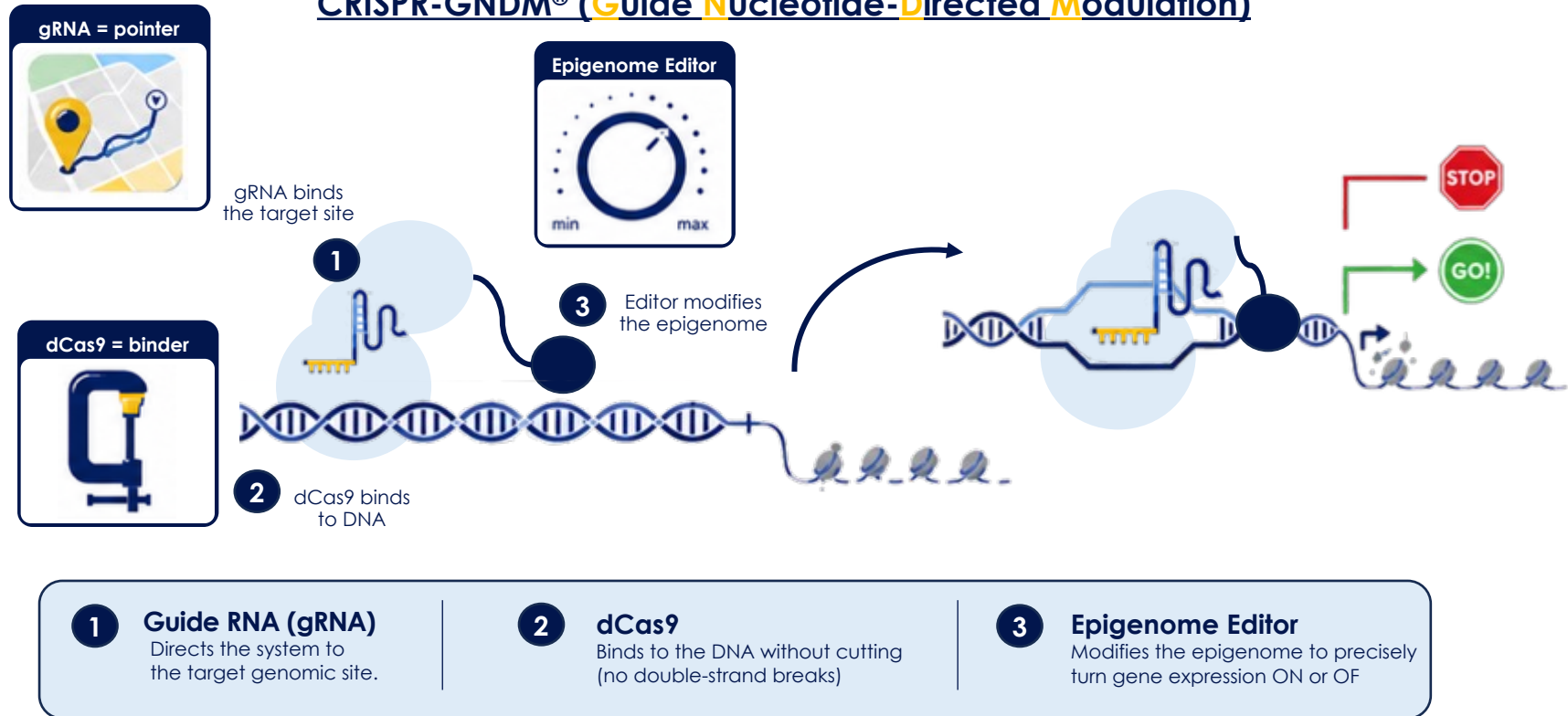
Establishing tissue-selective AAV Delivery

A robust intellectual property portfolio

CRISPR-GNDM[®]'s mechanism of action

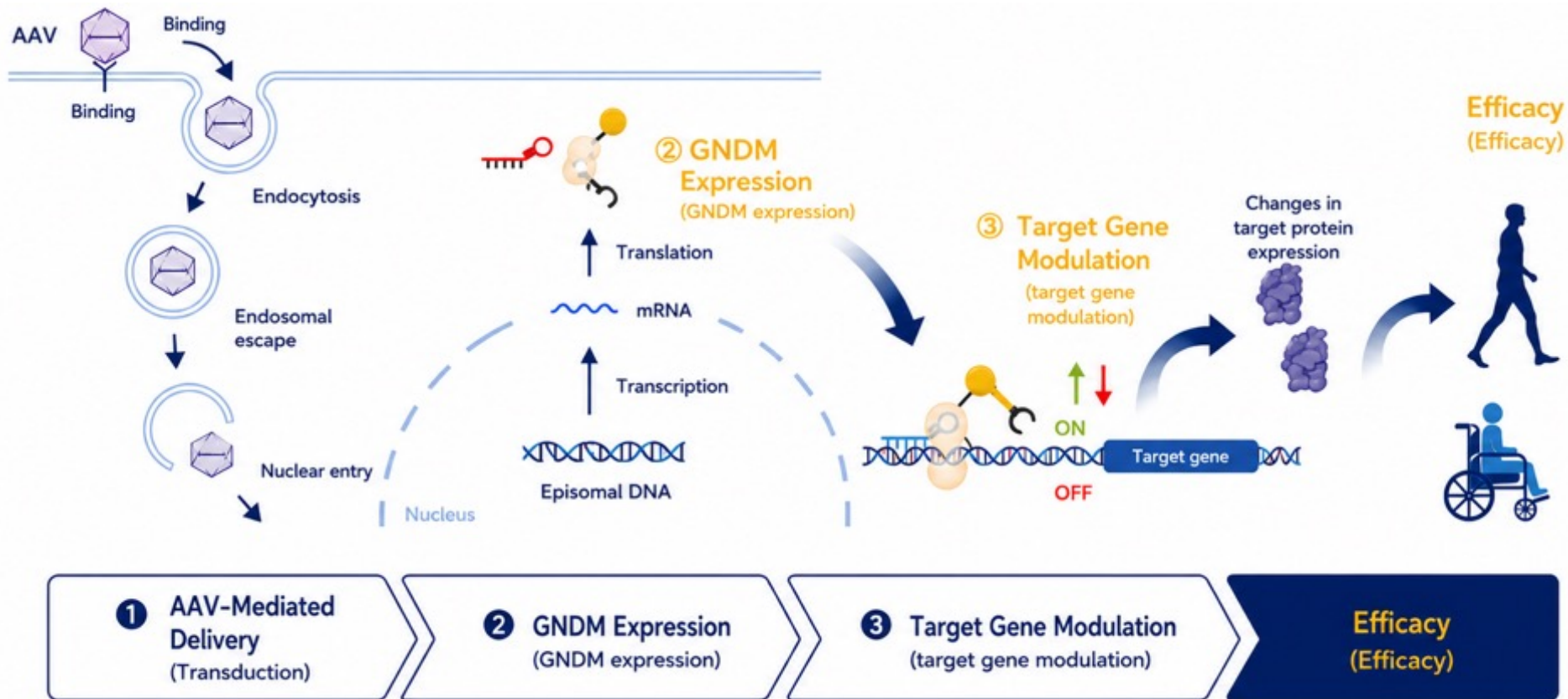
GNDM restores the controls target protein expression through epigenetic regulation

CRISPR-GNDM[®] (Guide Nucleotide-Directed Modulation)



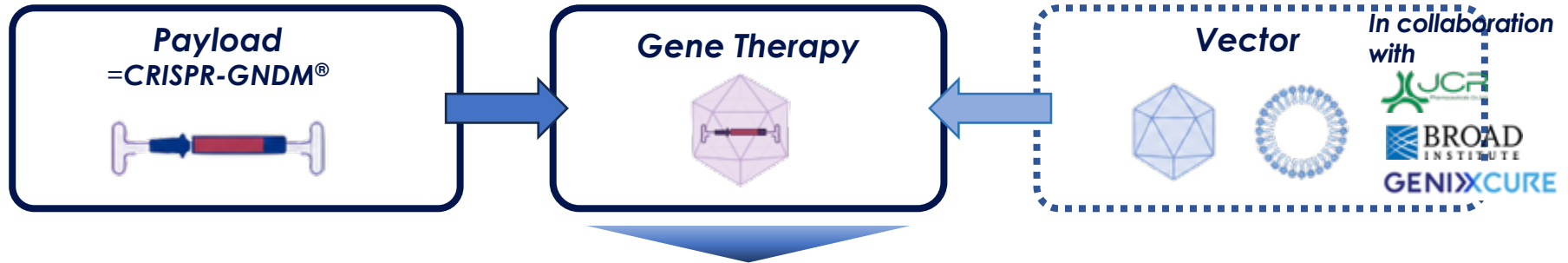
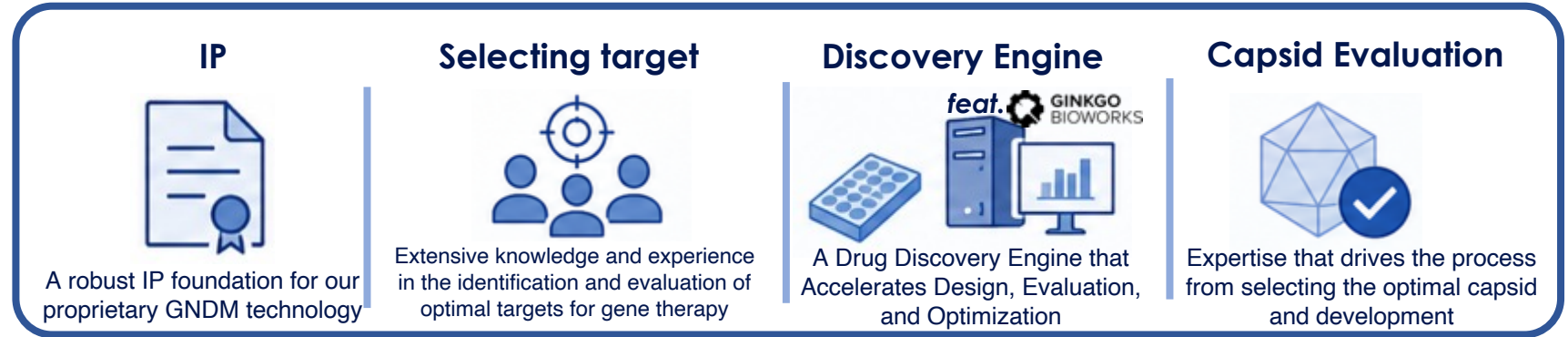
Three Steps from Dosing to Therapeutic Efficacy

AAV delivers GNDM to target cells, GNDM is expressed as a protein, and then modulates the target gene to generate therapeutic benefit



Our core competency = GNDM payload

intellectual property, target selection expertise, drug discovery engine, and the selection of capsids and our subsequent development capabilities



By integrating these strengths, we will accelerate the realization of gene therapy and deliver value to patients.

Our vision: *Every Life Deserves Attention*

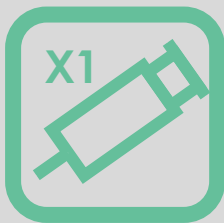
Leveraging CRISPR Epigenome Editing technology to provide fundamental solutions to rare diseases

Key Benefits of Our CRISPR-GNDM® Technology



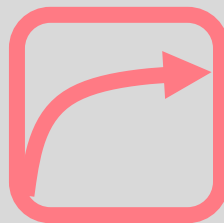
No DNA Cutting

Regulates gene expression without altering DNA



Single dose

Doesn't require Repeated dosing



Long-lasting

Sustained effect for years or decades



Disease Modifying

Aims to provide transformative benefit

Approval Status of GTx

Otarmeni, a Treatment for Hereditary Hearing Loss, Receives Approval

In vivo gene therapies approved by US FDA

Trade Name	Year of Approval	Price	Indication	Manufacturer	Patient Population	WW market size* (mil USD)
Lxturna	2017	\$850k	RPE65	Roche(Spark)	2 per 100,000	\$65M
Zolgensma	2018	\$2.1M	SMA	Novartis(Avexis)	1 in 15,000 live births (Approx. 100s ~1000 patients in US)	\$1.3B ^{#3}
HEMGENIX	2022	\$3.5M	Hemophilia B	uniQure CSL Behring	1 in 30,000 male	\$88M ^{#3}
Vyjuvek	2023	\$631k per patient year	DEB ^{*2}	Krystal	3.5–20.4 in 1 million	~\$200M ^{#2}
Roctavian		\$2.9M	Hemophilia A	BioMarin	1 in 5,000 male	\$262M ^{#4}
beqvez	2024	\$3.5M	Hemophilia B	pfizer	1 in 30,000 male	\$88M ^{#3}
ELEVIDYS		\$3.2M	DMD	Sarepta	1 in 3,500 male birth	\$4.1B ^{#4}
Itivisma	2025	\$2.6M	SMA	Novartis	Over 2yrs SMA patients Approx. 1000s ~10k patients in US	~\$10B ^{#2}
Otarmeni	2026	TBD	hearing loss	Regeneron	50 newborn in a year/US	\$130 million

Source: National Organization for Rare Disorder, #2 Fierce Biotech #3 Corporate website # Mordor Intelligence, 2026 #5 Fortune Business Insight

*1: Spinal muscular atrophy *2: dystrophic epidermolysis bullosa *3: Duchenne muscular dystrophy *4: severe leukocyte adhesion deficiency type 1

Epigenome editing competitive landscape

The field is gaining more traction and 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 for LAMA2-CMD Gene activation	IND enabling
Tune	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	P1/2
Epicrispr	2022	Series B (\$68M, 2025)	Cas12f-fused with demethylation enzyme x AAVrh74	EPI-321/FSHD Gene suppression	P1/2
Epigenic	2022	Series B (\$60M, 2025)	dCas+editor x LNP	EPI-001 PCSK9 for hypercholesteremia Gene suppression	Chinese IIT
Scribe	2018	SerC? (\$75M, 2025)	dCas+repressor x LNP	STX1150 PCSK9 for hypercholesteremia Gene suppression	IND enabling
Mammoth	2017	Corp.Minority (\$2024, \$95M)	miniCas x editor x LNP	MB-111 APOC3 for Triglycemia Gene suppression	IND enabling

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1. **Status of Business**
2. **Financial updates**
3. **Growth Strategy**
4. **Summary**
5. **Q&A**





1. Status of Business

1. Business Highlights of the 2Q/2026

Highlights



01

**MDL-101 Progress and
Timeline**



02

**Progress in the other
programs**

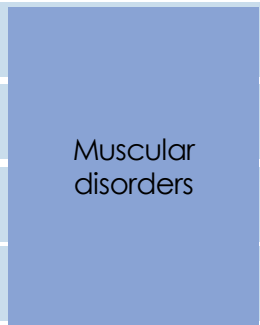
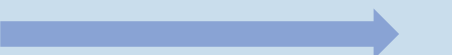
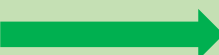
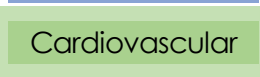


03

**Finance and the other
progress in the business**

The current pipeline of MODALIS

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

				Discovery/Preclinical			Clinical	
Code	Indication	Mode	Ownership	Discovery Research	Lead Optimization	IND Enabling	Phase I/II	Pivotal
MDL-101	LAMA2-CMD*1	 ON	Modalis					
MDL-202	DM1*2	 OFF	Modalis					
MDL-201	DMD*3	 ON	Modalis					
MDL-103	FSHD*4	 OFF	Modalis					
MDL-105	DCM*5	 ON	Modalis					
MDL-104	Tauopathy	 OFF	Modalis					
MDL-206	Angelman Syndrome	 ON	Modalis					
MDL-207	Dravet Syndrome	 ON	Modalis					

*1: LAMA2-related congenital muscular dystrophy

*2: Myotonic Dystrophy Type 1

*3: Duchene Muscular Dystrophy

*4: facioscapulohumeral muscular dystrophy

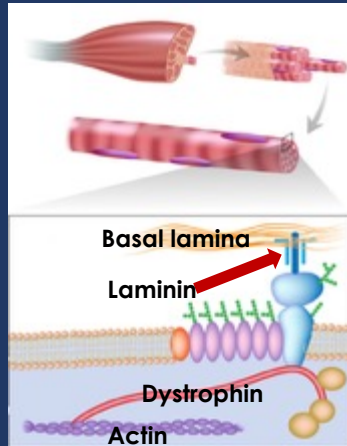
*5: Dilated Cardiomyopathy

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*
2500 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+



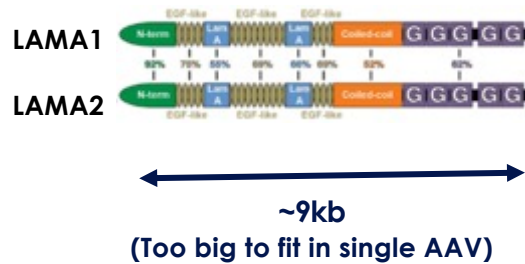
Source: *Estimating the Prevalence of LAMA2 Congenital Muscular Dystrophy using Population Genetic Databases (2023)

Mechanism of Action of CRISPR-GNDM®

Restores muscle function by activating the sister gene LAMA1 in response to LAMA2 mutations

Protein structure of LAMA1 and 2

LAMA1 and LAMA2 are sister genes with high sequence homology (approximately 9 kb) that encode similar laminin a chains.



Due to their high homology, LAMA1 can compensate for the LAMA2

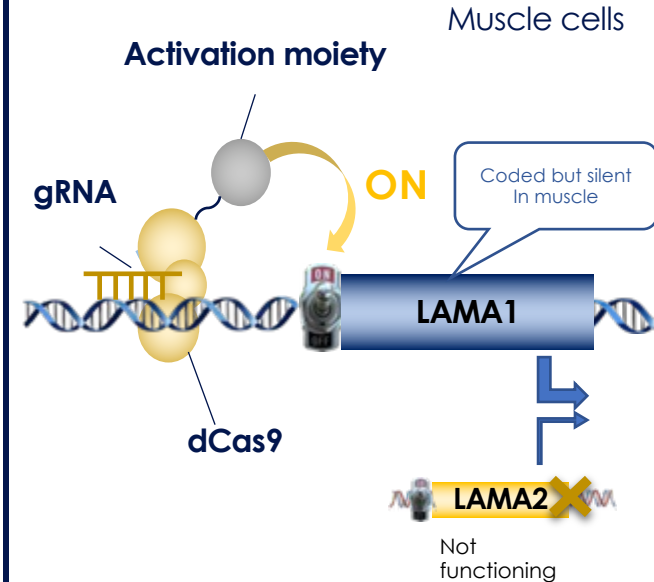
Expression pattern of LAMA1 and 2 by tissues

	LAMA1		LAMA2	
Tissues	RNA	Protein	RNA	Protein
Brain	ON	ON	ON	ON
Endocrine tissues	ON	ON	ON	ON
Blood cells	ON	ON	ON	ON
Muscle	ON	ON	ON	ON
Lung	ON	ON	ON	ON
Liver & bladder	ON	ON	ON	ON
Pancreas	ON	ON	ON	ON
GI tract	ON	ON	ON	ON
Kidney and UB	ON	ON	ON	ON
Male tissues	ON	ON	ON	ON
Female tissues	ON	ON	ON	ON
Adipose & soft t.	ON	ON	ON	ON
skin	ON	ON	ON	ON



LAMA1 is typically silent in muscle cells

Targeted LAMA1 activation using CRISPR-GNDM®



Enabling LAMA1 compensates for the loss of function caused by LAMA2 deficiency



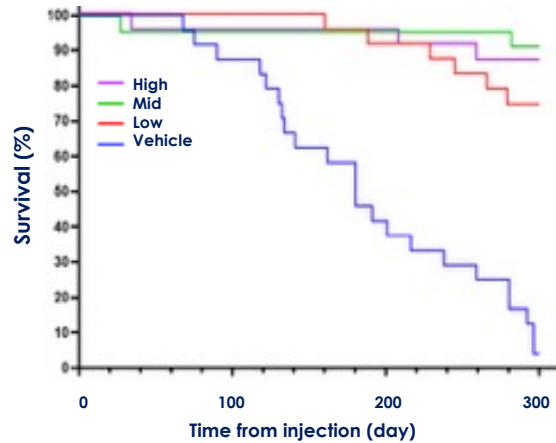
CRISPR-GNDM® aims to restore muscle function in patients with LAMA2 deficiency by targeting the sister gene LAMA1



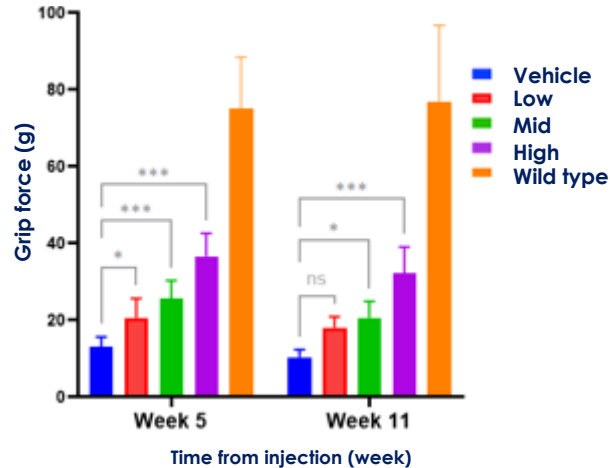
Improvements in body weight, grip strength, and survival in disease model mice

Administration of mMDL-101 significantly improved functionality and survival of the mice backed by sustained expression of GNDM and LAMA1

Improved survival by mMDL-101

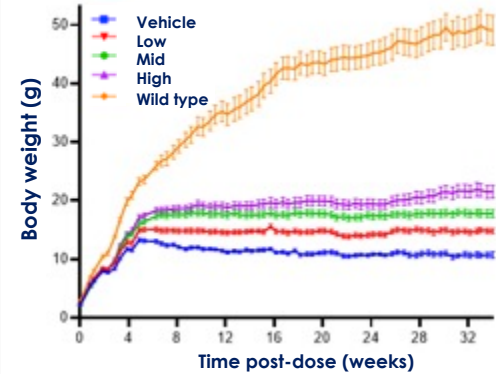


Improved Grip Strength by mMDL-101

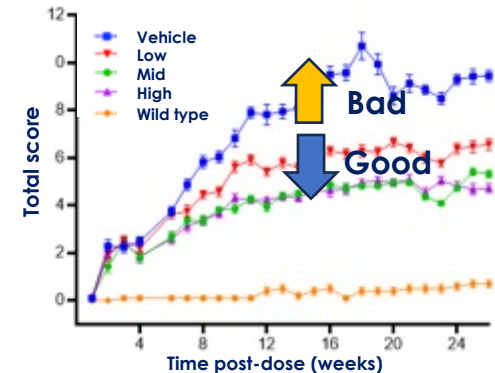


Sustained expression of GNDM and LAMA1

Body weight



Health deficit



MDL-101: Key Milestones Advancing Toward IND Submission

Key nonclinical, CMC, and clinical preparation activities toward IND submission have become more concrete, increasing the visibility of our development plan to submit IND in late 2026 to Q1 2027

1



Mouse IND-enabling studies completed

In disease model mice, we confirmed vector delivery to target tissues, transgene expression, upregulation of LAMA1, and pharmacological efficacy.

2



NHP validation supports clinical translation

In multiple CRO studies, we confirmed vector delivery to muscle and LAMA1 upregulation. Optimization of the pre-treatment protocol has clarified mitigation strategies for factors that may impact efficacy evaluation.

3



Execution plan toward IND, including GMP manufacturing, is becoming concrete

- Additional GLP toxicology study is progressing (dosing start in early Sep 2026; 3-month data readout and evaluation)
- GMP manufacturing (plasmid GMP in progress; AAV GMP to start in 3Q)
- Clinical trial implementation readiness and IND submission preparation are advancing



MDL-101 is on track to submit IND in late 2026 to Q1 2027, with the goal of advancing toward first-in-human clinical trials.

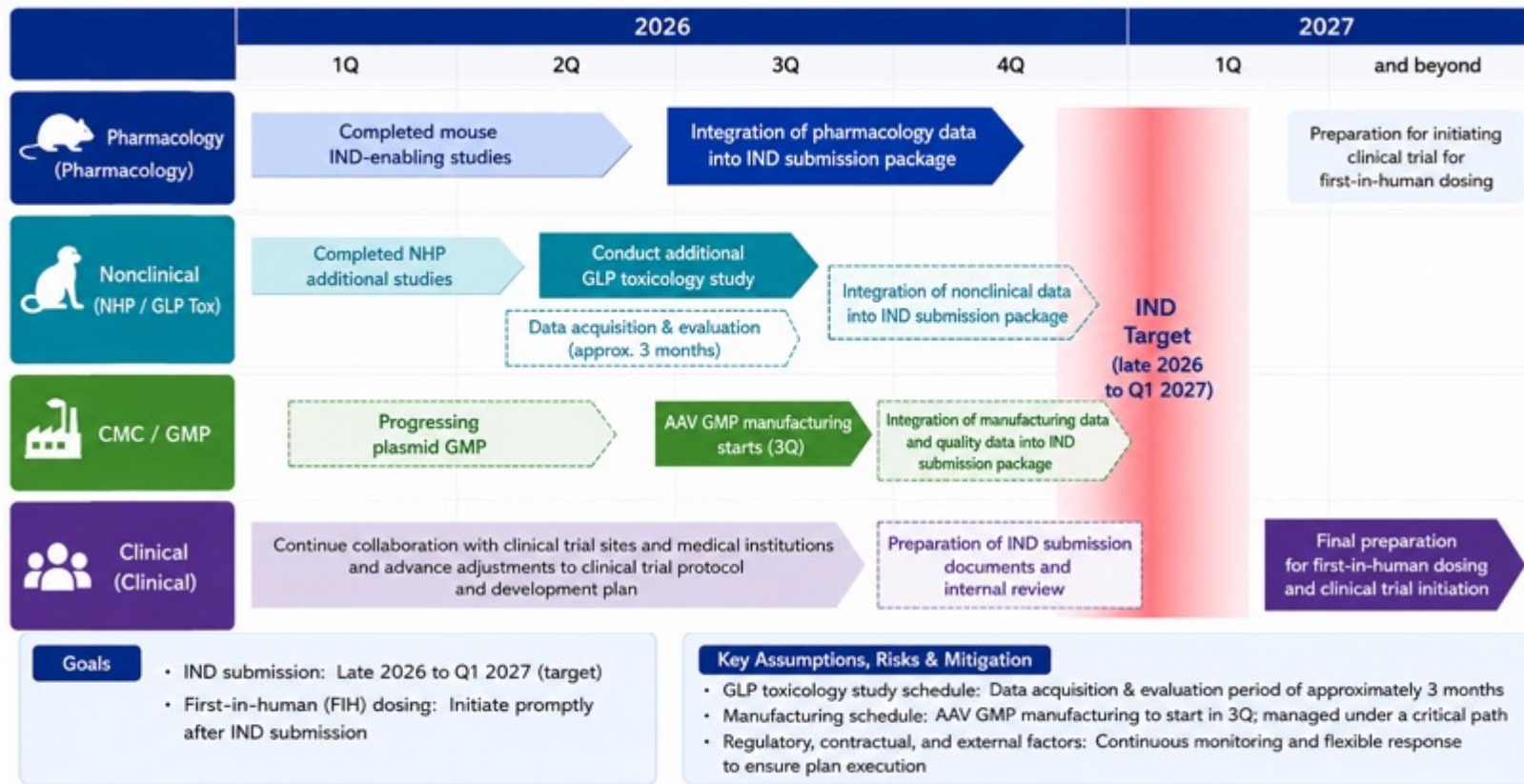
MDL-101: Development Status

All key workstreams related to nonclinical, CMC, and clinical preparation are progressing as planned toward our target IND submission in late 2026 to Q1 2027

Workstream	Current Progress (as of July 2026)	Next Key Steps
1  Pharmacology (Pharmacology)	- Completed IND-enabling studies in disease model mice - Confirmed vector delivery, transgene (Cas9), and LAMA1 upregulation at mRNA and protein levels - Improved survival, muscle function recovery, and durability supported by biological data - Confirmed pharmacological efficacy toward IND submission	 Consolidate data as part of the IND submission package
2  Nonclinical (NHP / GLP Tox)	- Confirmed vector delivery to muscle in multiple CRO studies - Confirmed LAMA1 upregulation and GNDM component expression - Optimization of pre-treatment protocol clarified mitigation strategies for factors that may impact efficacy evaluation - Additional GLP toxicology study is progressing (CRO selected and under contract)	 - Initiate additional GLP toxicology study in early September 2026 - Obtain and evaluate 3-month data
3  CMC / GMP	- Transitioned to modified vector and moved to plasmid GMP - AAV GMP plan consolidated with CRO (production start in 3Q, completion targeted in 4Q) - GMP manufacturing for APIs and drug product and release plans are being finalized	 - Execute GMP manufacturing - Conduct quality and stability studies
4  Clinical (Clinical)	- Continue collaboration with clinical service providers - Ongoing optimization of clinical protocol and development plan - Preparation for IND including CMC and nonclinical package is progressing	 - Prepare and internally review IND submission documents - Complete final preparations for IND submission

MDL-101: Key Coming Milestones Toward IND Submission and Future Outlook

Greater clarity has been achieved in the execution plan toward IND submission in late 2026 to Q1 2027 through the further advancement of nonclinical, CMC, and clinical preparation activities, with the goal of realizing FIH dosing.

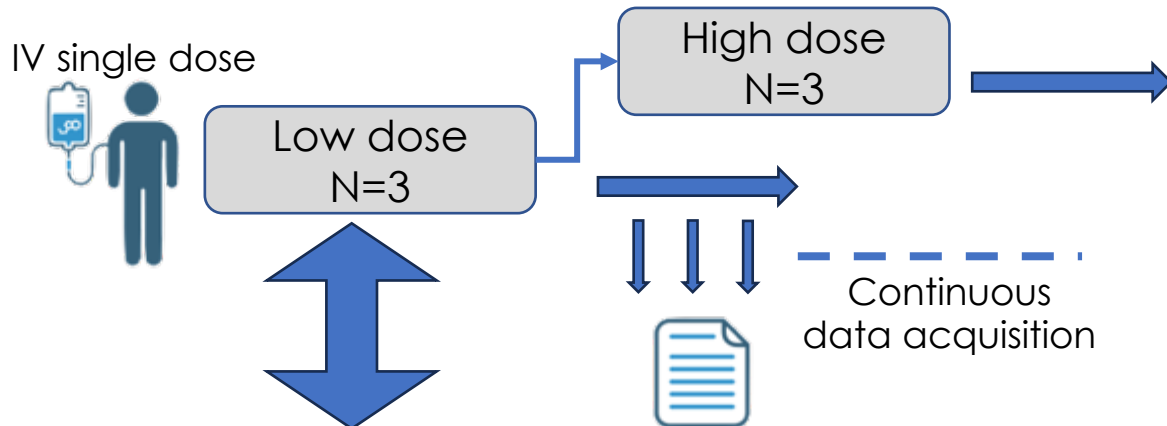


MDL-101 is advancing based on a robust database and a concrete execution plan, with the goal of IND submission in late 2026 to Q1 2027 and realizing first-in-human dosing.

MDL-101-001 Trial design

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

Phase1/2 Open-label dose escalating trial

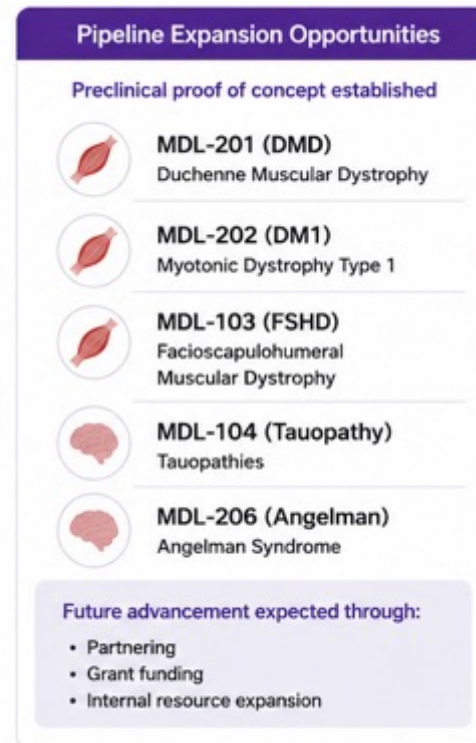
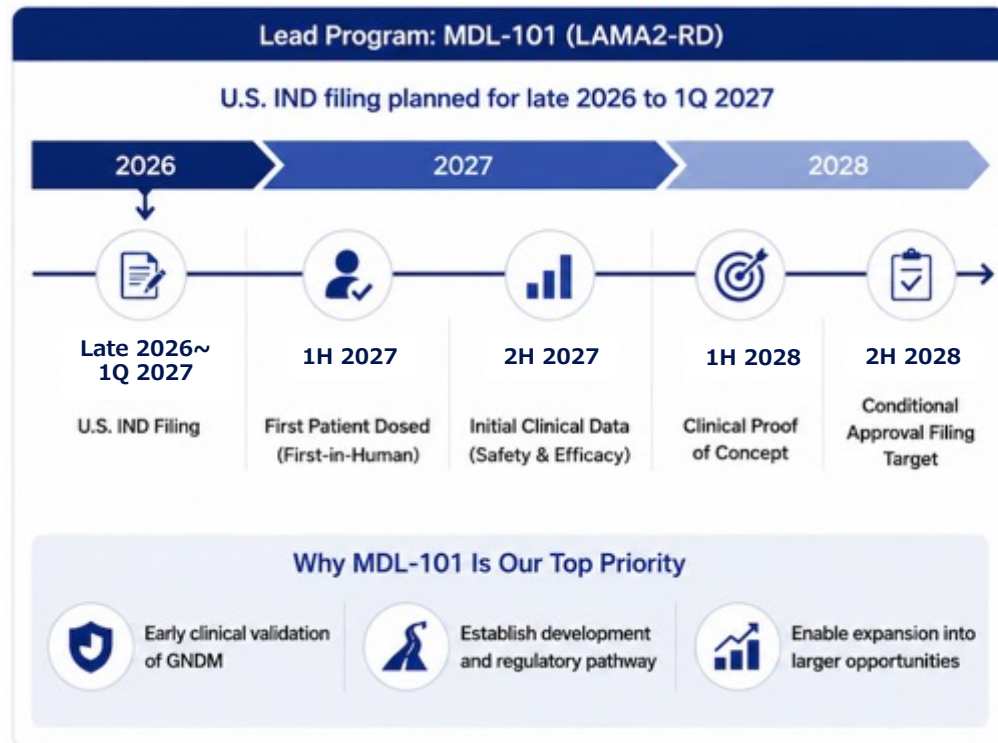


- Patients ≤ 5 years.
- Genetically confirmed, biallelic pathogenic LAMA2 mutations.
- Severe LAMA2-RD clinical phenotype. Difficulty with independent walking or sitting.
- AAV9 TAb negative.

Retrospective	Natural History
Hinkley et al., 2024 (NCT04299321) • 60 LAMA2-RD < 5 years old	NCT06132750 (LAST STRONG) • 40 (est.) LAMA2-RD or SELENON-RM patients • Est. completion Sept 2026
Zambon et al., 2020 • 42 LAMA2-RD < 18 years old • 8 'complete deficient' < 5 years old	NCT06354790 (Institut de Myologie, France) • 60 (est.) LAMA2-RD 2 to 15 years old • Est. completion Jan 2028
	NCT06503367 (READY CMD LAMA2) • 44 (est.) LAMA2-RD < 5 years old • Est. completion Sept 2028

Development Priorities and Key Milestones

Focus on advancing MDL-101 to deliver early clinical value and validate GNDM and will expand our pipeline through partnerships, funding and internal resource growth



Advancing MDL-101 is our best path to value creation. We will use partnerships and capital to accelerate the expansion of our muscle and CNS pipeline.

Pipeline Update

Prioritizing MDL-101 while steadily advancing programs and expanding and validating the GNDM platform

Program (target/mechanism)	Target Indication	R&D Stage	Recent Key Progress	Next Key Plans
MDL-101 (LAMA1 upregulation) 	Laminin $\alpha 2$ Deficiency (LAMA2-RD)	IND Preparation (Target IND filing: late 2026 to Q1 2027)	- Completed mouse IND-enabling studies - In additional NHP studies across multiple CROs, confirmed delivery to muscle tissue and increased LAMA1 expression - Optimization of the pre-treatment protocol clarified the response strategy for factors that could affect vector delivery and pharmacological evaluation	- Completed mouse IND-enabling studies - In additional NHP studies across multiple CROs, confirmed delivery to muscle tissue and increased LAMA1 expression - Optimization of the pre-treatment protocol clarified the response strategy for factors that could affect vector delivery and pharmacological evaluation
MDL-201 (Utrophin upregulation) 	Duchenne Muscular Dystrophy (DMD)	Preclinical (PoC and optimization)	- Confirmed improvements in motor function and muscle pathology in a disease model mouse - Confirmed comparable efficacy at approximately one-tenth the dose of uDys - Advancing capsid selection and payload optimization	- Conduct NHP target engagement studies - Advance global collaborations and partnering - Continue optimization toward candidate nomination
MDL-202 (DMPK suppression) 	Myotonic Dystrophy Type 1 (DM1)	Preclinical (PoC)	- Confirmed robust suppression of DMPK expression in mice (including heart and diaphragm) - Presented research findings at ASGCT 2026	- Expand nonclinical data - Further define development strategy and evaluate partnering opportunities - Continue efforts toward candidate nomination
MDL-103 (DUX4 suppression) 	Facioscapulohumeral Muscular Dystrophy (FSHD)	Preclinical (PoC)	- Confirmed suppression of DUX4 expression in mice - Presented research findings at ASGCT 2026 - Advancing a Solve FSHD-funded program and collaborative research with UMass	- Expand nonclinical data - Further define development strategy and evaluate partnering opportunities - Continue efforts toward candidate nomination
Future Programs 	Alzheimer's disease, Angelman syndrome and other CNS disorders, as well as Titin cardiomyopathy (DCM)	Exploratory (collaborative research)	- Through a strategic partnership with JCR Pharmaceuticals, advancing integration of GNDM with a BBB delivery platform - Conducting early evaluations across multiple CNS disorders including AD	- Deepen evaluation of target indications and development strategy - Advance research toward establishing nonclinical POC - Explore partnering opportunities



While prioritizing preparations for the MDL-101 IND submission, we are also maximizing the value of the platform and expanding the pipeline across multiple genetic and rare disease areas.

Data presentations at ASGCT and FSHD Society 2026 International Research Congress

ASGCT

- Title: Pairing AAV genome and capsid engineering of an epigenetic-editing modality to develop a best-in-class treatment for Myotonic Dystrophy Type 1 (DM1)
- Title: Epigenetic suppression of Dux4 using CRISPR-GNDM technology as a therapeutic for FSHD

FSHD Society 2026 International Research Congress

- title: Epigenetic suppression of DUX4 using CRISPR-GNDM technology as a therapeutic for FSHD





2. Financial updates @ the end of 2Q FY2025

BS & Financial Position at the end of 2Q/2026

Cash position improved due to the 300 million yen raised from the second issuance of ordinary corporate bonds. At the same time, liabilities increased.

(Million Yen)

	End of FY2025 (A)	2Q FY2026 (B)	(B) – (A)
Current assets	2,892	3,083	191
Cash & deposits	2,812	3,015	203
Non-current assets	71	52	△19
Total assets	2,964	3,136	172
Current liabilities	134	669	535
Non-current liabilities	36	3	△33
Total liabilities	170	673	502
Total net assets	2,793	2,462	△330
Total liabilities and net assets	2,964	3,136	172
Capital adequacy ratio	93.0%	76.9%	

Note

- While continuing investment in R&D, the exercise of stock acquisition rights progressed. As a result, cash and deposits decreased slightly.

BS & Financial Position at the end of 2Q/2026

Cash position improved due to the 300 million yen raised from the second issuance of ordinary corporate bonds. At the same time, liabilities increased.

Information
purpose only

(In thousand USD at @160yen/\$)

	End of FY2025 (A)	2Q FY2026 (B)	(B) – (A)
Current assets	18,075	19,269	1,194
Cash & deposits	17,575	18,844	1,269
Non-current assets	443	325	-119
Total assets	18,525	19,600	1,075
Current liabilities	837	4,181	3,344
Non-current liabilities	225	19	-206
Total liabilities	1,062	4,206	3,144
Total net assets	17,456	15,388	-2,069
Total liabilities and net assets	18,525	19,600	1,075
Capital adequacy ratio	93.0%	76.9%	

Note

- While continuing investment in R&D, the exercise of stock acquisition rights progressed. As a result, cash and deposits decreased slightly.

PL & Business Result at the end of 2Q/2026

1,000 million in operating expenses, mainly due to the cost of related to MDL-101 program

(Million Yen)

	2Q FY2025 (A)	2Q FY2026 (B)	(B)–(A)
Operating revenue	-	-	-
Operating expenses	1,031	1,000	△31
R&D	906	911	5
SGA	125	88	△37
Operating income	△1,031	△1,000	31
Ordinary income	△1,019	△965	53
Current Profit	△1,020	△920	△100

Operating expenses

- Continued investment in research and development as development activities centered on MDL-101 progressed.
- Meanwhile, continued promotion of financial strategies, including capital policy initiatives and the utilization of external financing.

PL & Business Result at the end of 2Q/2026

\$6.2 M in business expenses, mainly due to the cost of related to MDL-101 program

(In thousand USD at @160yen/\$)

	2Q FY2025 (A)	2Q FY2026 (B)	(B)–(A)
Operating revenue	-	-	-
Operating expenses	6,444	6,250	-194
R&D	5,663	5,694	31
SGA	781	550	-231
Operating income	-6,444	-6,250	194
Ordinary income	-6,369	-6,031	331
Current Profit	-6,375	-5,750	-625

Operating expenses

- Continued investment in research and development as development activities centered on MDL-101 progressed.
- Meanwhile, continued promotion of financial strategies, including capital policy initiatives and the utilization of external financing.

Funding Strategy for Achieving Clinical Proof of Concept and Sustained Growth

Advancing MDL-101 into clinical trials to demonstrate its value and expand the platform's potential

- 1 Continued funding is essential for development



Ongoing funding is critical to maximize the value of our clinical development and late-stage pipeline

- 2 This financing is to achieve PoC for MDL-101



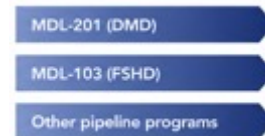
The proceeds from this financing will be used to advance MDL-101 into the clinic and generate PoC that demonstrates its safety and efficacy

- 3 Platform validation drives corporate value creation



Achieving PoC for MDL-101 will enhance the value of the asset and validate the CRISPR-GNDM® platform, leading to an increase in corporate value

- 4 Substantial growth opportunities in our pipeline



In addition to MDL-201 and MDL-103, we will strategically invest in our pipeline to capture large growth opportunities

The Value We Aim to Create Through This Financing Round



- Clinical Proof of Concept (PoC) for MDL-101
- Validation of the CRISPR-GNDM® Technology Platform

Investment in Follow-on Programs (Maximizing Growth Opportunities)



- Realizing a path to **conditional approval** in the U.S. and other countries → Potential for in-house sales
- **Increased likelihood of success** for subsequent large-scale programs



Driven by this round of funding, we aim to continuously enhance corporate value by achieving proof of concept (PoC) for MDL-101 and expanding our subsequent programs



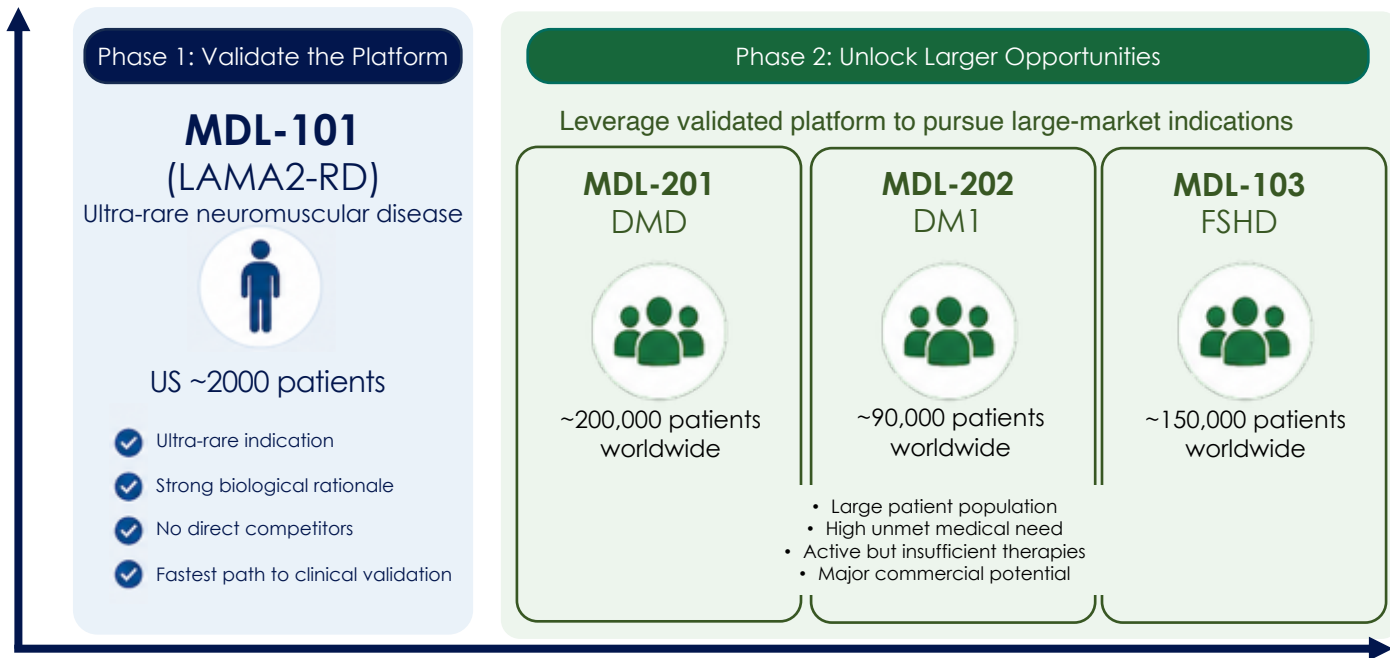
3. Where we are and the Growth Strategy



Growth Opportunity Expands Along Two Dimensions

Growth is driven by two levers: development progression of our lead program and expansion into larger indications

Pipeline Expansion
Expand into larger patient populations and new indications



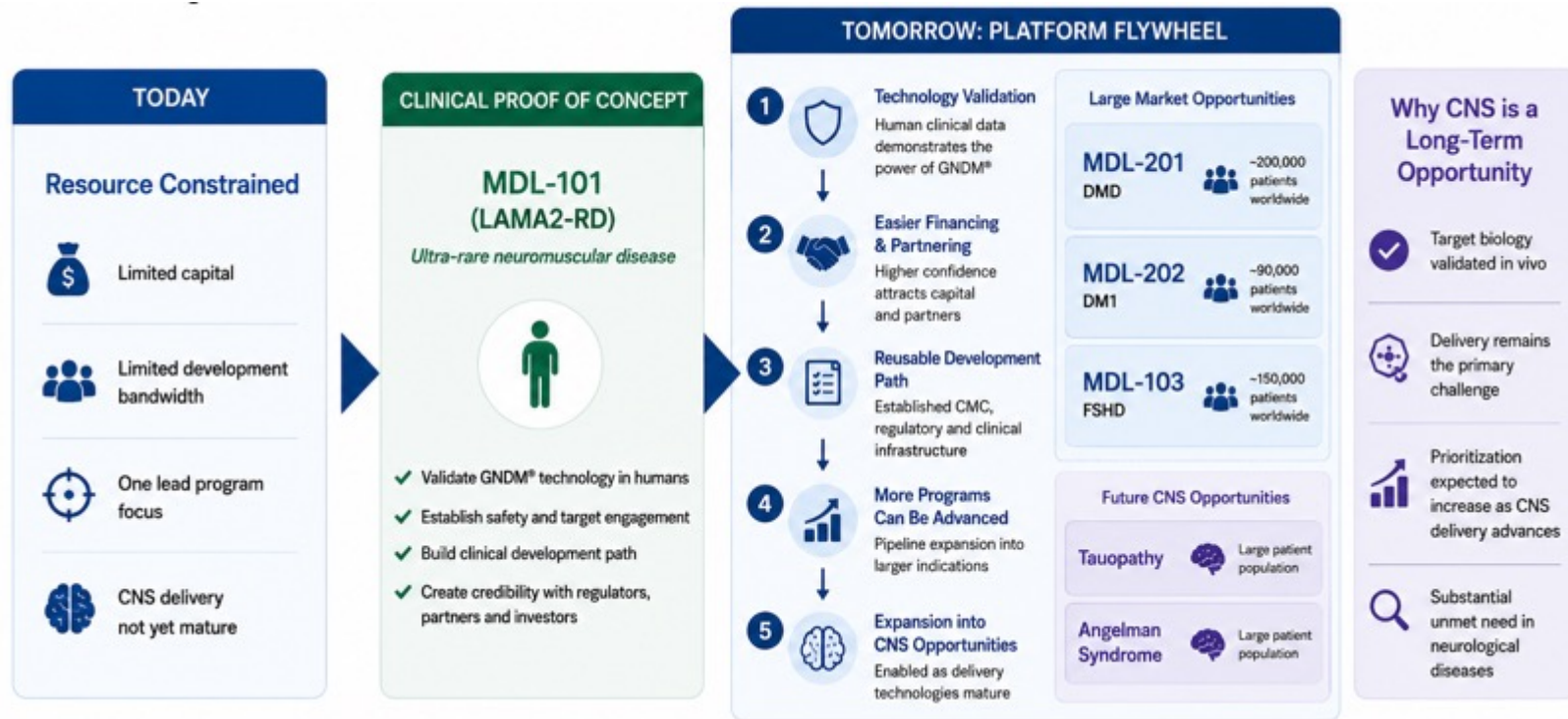
Development Progression Advance clinical development and de-risk to unlock the next wave of programs



Clinical validation of MDL-101 is expected to reduce development risk, improve funding access, and accelerate expansion into larger indications.

From MDL-101 Validation to Broad Platform Expansion

Clinical proof of concept of MDL-101 will unlock financing, partners, and bandwidth to advance a diversified pipeline and create long-term value

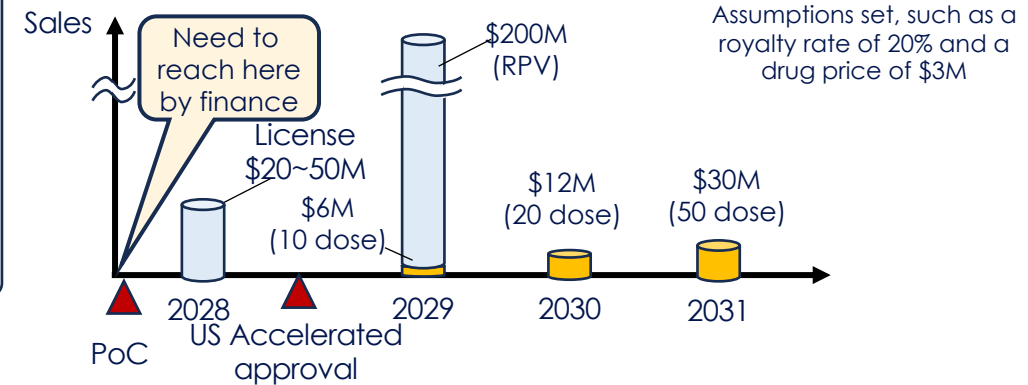
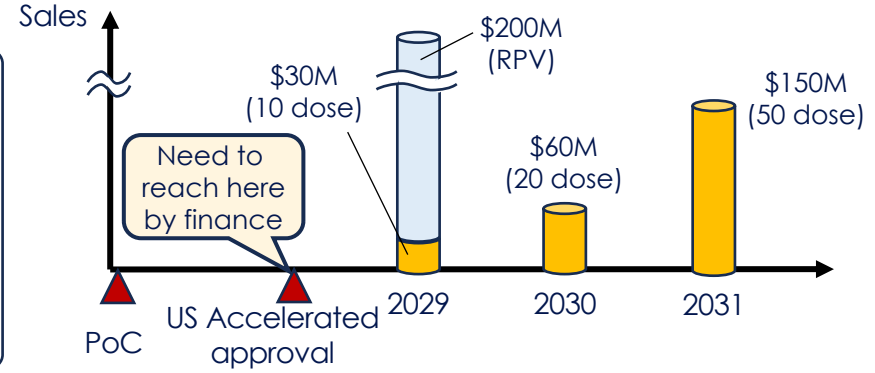
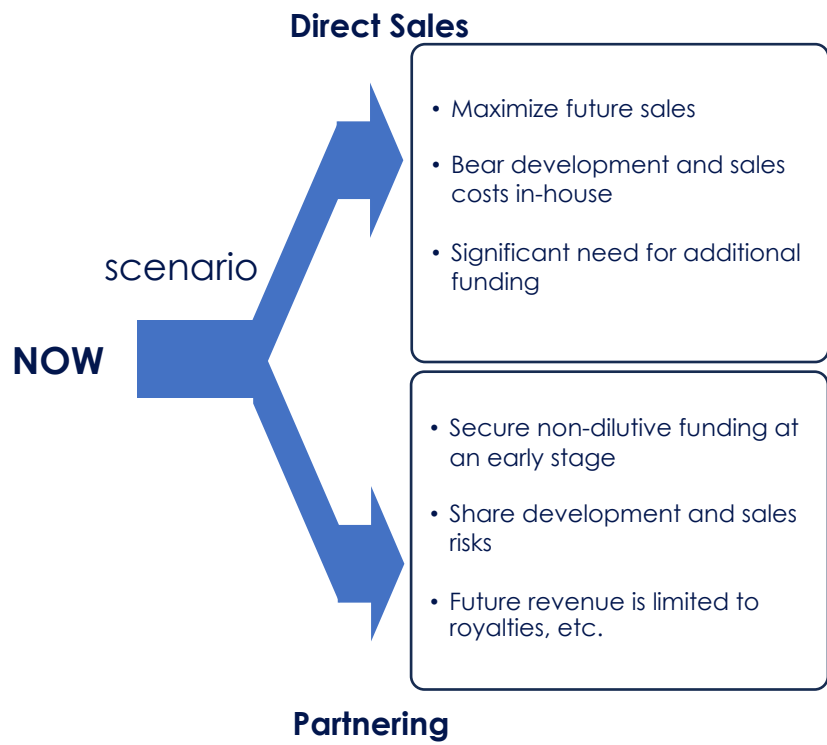


MDL-101 is the key to unlock our next phase of growth-from platform validation to leadership across multiple large-market and CNS indications

Opportunities for Value Creation in Line with the Development Progress of MDL-101

The impact of reselling RPVs after the commercialization approval in US will be significant

*The following is an example scenario based on certain assumptions and does not constitute a financial forecast.



The funds raised will be used to advance the clinical development of MDL-101 toward demonstrating proof of concept (PoC) and to maximize shareholder value over the medium to long term by enhancing the value of the CRISPR-GNDM® platform as a whole.



4. Summary





Key Takeaway of 2Q/2026 report

1. Completed the disease model study for MDL-101 IND enabling. Confirmed efficacy, including extended survival and improved muscle function, and collected the underlying biological data.
2. Conducted additional validation studies in NHPs. This supports the rationale for clinical trials and improves the visibility of the IND target. Set the target for the **end of 2026 to the first quarter of 2027**.
3. The 19th series of stock options is granted and exercise underway to support the development of MDL-101 and the advancement of follow-on programs. In progress.

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



Q1. What is the basis for asserting that the outlook regarding the timing of the IND has now become clear?

For MDL-101, we have completed IND-enabling studies using disease model mice and obtained data on **pharmacological efficacy** and the underlying **biological mechanisms**. Furthermore, in additional NHP validation studies, we confirmed delivery to muscle tissue and **an increase in LAMA1 expression**, obtaining **data that support the transition to clinical trials**. Furthermore, as the **implementation plan for the IND application**—including additional GLP toxicity studies and GMP manufacturing—has been finalized, we believe the development plan, which targets an IND application between the end of 2026 and the first quarter of 2027, has become more clearly defined.

Q2. What does the completion of the mouse IND-enabling study mean to development?

In disease model mice, we confirmed the expression of VCN and the introduced gene Cas9, as well as increased LAMA1 levels, at both the nucleic acid and protein levels. Furthermore, we have obtained biological data supporting improved survival rates, recovery of muscle function, and the sustainability of that recovery. As a result, we have obtained comprehensive preclinical data supporting the **mechanism of action and pharmacological efficacy of MDL-101**, and we believe that the key components of the IND application package are now in place.

*VCN(Vector Copy Number): Number of the gene copy transduced into a cell.
Metrics for gene transduction efficiency

Q3. What was confirmed in the additional NHP verification, and why is it important?

In the additional NHP validation studies conducted at multiple CROs **under clinically relevant dosing protocols**, we confirmed vector delivery to muscle tissue, expression of the CRISPR-GNDM[®] components, and increased expression of the target gene, LAMA1. Since the central mechanism of action of MDL-101 involves using AAV to deliver GNDM to muscle tissue and induce LAMA1 expression, we believe that the confirmation of these steps in NHPs provides important data supporting the transition to clinical trials.

Q4. What does “optimization of the pretreatment protocol” mean? Does that mean there were problems in previous trials?

Through our previous analyses, we identified **factors that could affect transduction efficiencies and efficacies**; therefore, with the aim of enhancing the interpretability and reproducibility of the data in preparation for clinical translation, we proceeded to optimize the pretreatment protocol to better align with clinical practice. In this additional NHP validation study, we confirmed vector delivery into muscle tissue and an increase in LAMA1 expression under the optimized conditions, and we believe this has clarified the action plan for proceeding to additional GLP toxicity studies.

Q5. When will the additional studies begin, and what data will be required for the IND application?

Regarding the additional GLP toxicity studies, we have already selected a CRO and signed a contract to conduct the studies. We plan to **begin dosing within the third quarter of 2026**. In preparation for the IND application, we primarily anticipate collecting and evaluating **three months of data**, and we plan to incorporate those results into the nonclinical data package. Please note that the final timing of the IND application may vary depending on the study results, report preparation, quality-related data, and progress in interactions with regulatory authorities.

Q6. What is the remaining critical challenges in preparing the IND application?

The remaining key tasks are: 1) **Additional GLP tox studies**, 2) **GMP manufacturing**, 3) **Associated quality and stability testing**, 4) **Consolidation of the IND application documentation**, and 5) **Finalization of the clinical trial implementation framework**.

While all of these represent critical milestones on the path to the IND application, the implementation plans for each workstream have now been finalized. We are proceeding with development while closely monitoring progress, aiming to submit the IND application **between the end of 2026 and the first quarter of 2027**.

Q7 Will GMP manufacturing be a bottleneck during the IND filing process?

Plasmid GMP manufacturing is currently underway, and we plan to begin AAV GMP manufacturing in the third quarter of 2026. GMP manufacturing, quality testing, and release testing are critical components of the IND application process, and we are proceeding with these activities while coordinating our manufacturing plans with the CDMO. At this time, we are advancing our plans **in line with our IND application targets.**

Q8. When and where do you expect the first human dosing to take place?

MODALIS plans to file its application in **the United States** first. This process begins with the submission of an IND application and review by the regulatory authority (the FDA). Following the IND submission, we will respond appropriately to any inquiries from the regulatory authority and aim to obtain clearance (typically within 30 days). At the same time, as soon as preparations—including the selection of clinical trial sites, the supply of investigational drugs, the protocol, and the patient recruitment system—are complete, we aim to initiate the first-in-human dosing **as soon as possible**.

Q9. How do you plan to verify efficacy in clinical trials?

In the initial clinical trial, we plan to prioritize **safety** as the primary endpoint while exploratively evaluating **target engagement (such as LAMA1 expression), muscle function, developmental indicators, respiratory function, and motor function.**

Furthermore, since LAMA2-RD is a rare disease and it is difficult to establish a control group, we believe that comparison with natural history data will also be an important evaluation factor.

Q10. At what point do you think the value of MDL-101 will increase significantly?

Key value inflection points include the **IND application**, its **clearance**, the first-in-human **dosing**, confirmation of **safety and target engagement**, and the achievement of **clinical proof of concept** (PoC). In particular, we believe that if MDL-101 demonstrates safety in humans and the induction of LAMA1 expression, this will serve as a significant milestone demonstrating not only the development value for LAMA2-RD but also the clinical value of the entire CRISPR-GNDM[®] platform.

Q12. While focusing on MDL-101, how will you proceed with the other programs?

For the time being, we will give the **highest priority to the IND application and clinical transition for MDL-101**. At the same time, for MDL-201, MDL-202, and MDL-103, we will continue our efforts to expand nonclinical data and establish these as candidate compounds, while leveraging external funding, collaborative research, and partnering opportunities. We believe that as clinical validation of MDL-101 progresses, it will lead to an increase in the value of our follow-on programs and the CRISPR-GNDM® platform as a whole.





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