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

# Business Plans and Matters Related to Growth Potential

## FY2025 mid-year updates


(TSE：4883)

**Modalis therapeutics Corporation**

August 7, 2025

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As requested by TSE, This document is updated once a year, and disclosure is scheduled to be made around March of each year. In the event of significant changes in the business plan, changes may be made irregularly,

# Major updates since the last report (February 2025 version)

| | |
|---|---|
| p7 | Updated corporate info |
| p17 | Updated IP position |
| P57 | Newly added details of the technical partnership with Broad regarding muscle tropic capsid technology. |
| p65 | Newly added DMD disease model mice study data |
| P45, 71, 93, 94 | Updated along with the business progress |
| P99-101 | Added info of most recently announced finance |





MODALIS

# Outline of the strategy

- Adopt a business strategy centered on the development of MDL-101
- Prioritize research and development of neuromuscular diseases for which the know-how cultivated with MDL-101 can be applied
- Advance the development of subsequent programs on the premise of funding, such as partnering
- Resume development of neurological diseases on the condition of identifying delivery tools and allocating resources. Research will continue.





MODALIS

# Table of contents

# 1. Corporate Overview

Updated

# Corporate Overview (As of June 30, 2025)

Modalis Therapeutics is a biotech company to develop CRISPR-based gene therapies

| | |
|---|---|
| Name | Modalis Therapeutics Corporation<br>(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.<br>(43 Foundry Avenue, Waltham, Massachusetts) |
| Business | Drug Development |
| Capital stock | 1,372,205 thousand yen |
| Outstanding share | 76,928,198 shares of common stock |
| Number of employee | 18 (including 6 Ph.D.) (5 in Japan, 13 in US) |

| Date | History |
|---|---|
| Jan 2016 | Founded in Tokyo as EdiGENE Corporation |
| Apr 2016 | Established 100% owned US subsidiary EdiGENE Inc. (Now Modalis Therapeutics Inc.) |
| Aug 2019 | Company name changed to Modalis Therapeutics |
| Apr 2020 | Entered into a license agreement with **Editas Medicine**, Inc to obtain access to foundational CRISPR IP. |
| Aug 2020 | Listing on Mothers, Tokyo Stock Exchange (Ticker symbol: 4883) |
| Oct 2021 | Lab moved to To Waltham MA, which is adjacent to Cambridge |
| Apr 2022 | Moved from the Mothers to the Growth market in accordance with the market reorganization classification of the Tokyo Stock Exchange. |





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**Modalis is a gene therapy company dedicated to translating evolutional science into life-changing treatments for rare disease patients.**


*Every life deserves attention*





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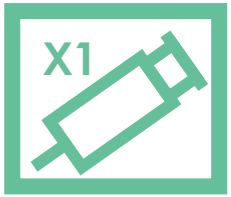
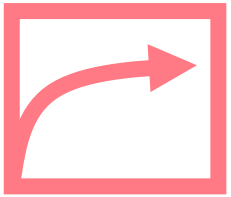
# CRISPR-GNDM® is a promising new therapeutic modality

## 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





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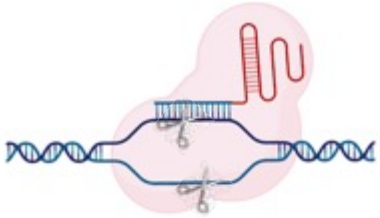
# Non-cleaving CRISPR = CRISPR-GNDM®

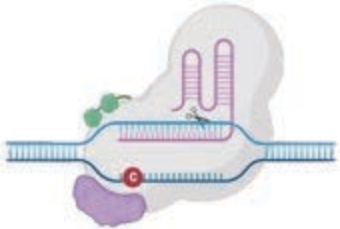
Enables treatment of genetic disorders by controlling epigenetic ON/OFF switch

**GTx Technologies**

**Gene Editing** | **Base/Prime Editing** | **siRNA / ASO**



*Permanent Removal*

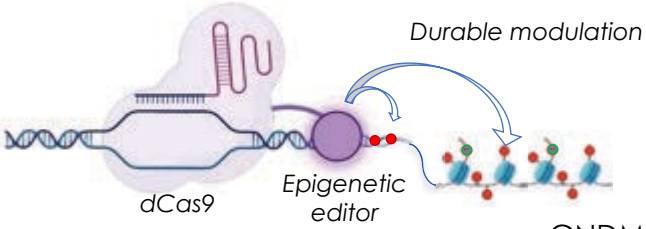


*Permanent Replacement*

*Temporal silencing*

**Epigenome Editing(CRISPR-GNDM®)**

Bind without cleaving
No DNA damage




GNDM=Guide Nucleotide Directed Modulation





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# 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 in multiple species (mouse, cyno) resulting in functional **efficacy without serious toxicities**

Pipeline of preclinical assets 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 lead programs

**Experienced team** with deep knowledge of platform

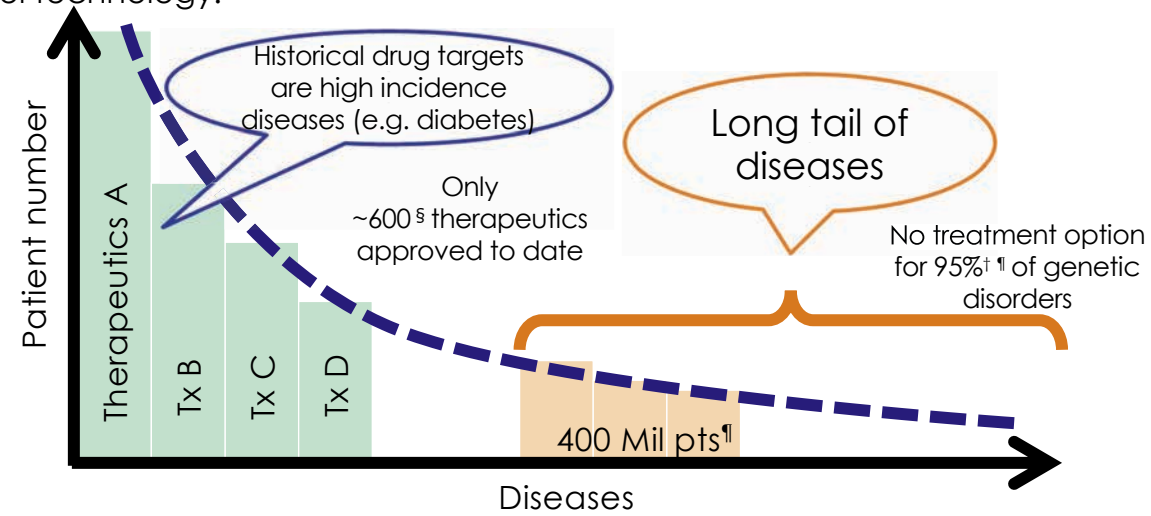
Strong **IP portfolio and strategy** that includes granted patents

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

# Providing a solution for the long tail of disease

Using technology to solve the problem of low productivity in the development of treatments for rare diseases

It is believed that of10,000* human diseases, about 7,000#are rare diseases which consist of "long tail" diseases. Of these, 80%† overlap with genetic disorders and 95% remain untreated. The company is committed to identifying cures with our powerful novel technology.




Scalable efficient approach is required to tackle the divided population

reference: *21st Century Cure Act, #NIH GARD †innovation.org ¶GlobalGenes.org
§Active therapeutics of 491 NME, 106 BLA, 17 cellular and gene therapy products @FDA as of 2019.7.22 Source from KEGG





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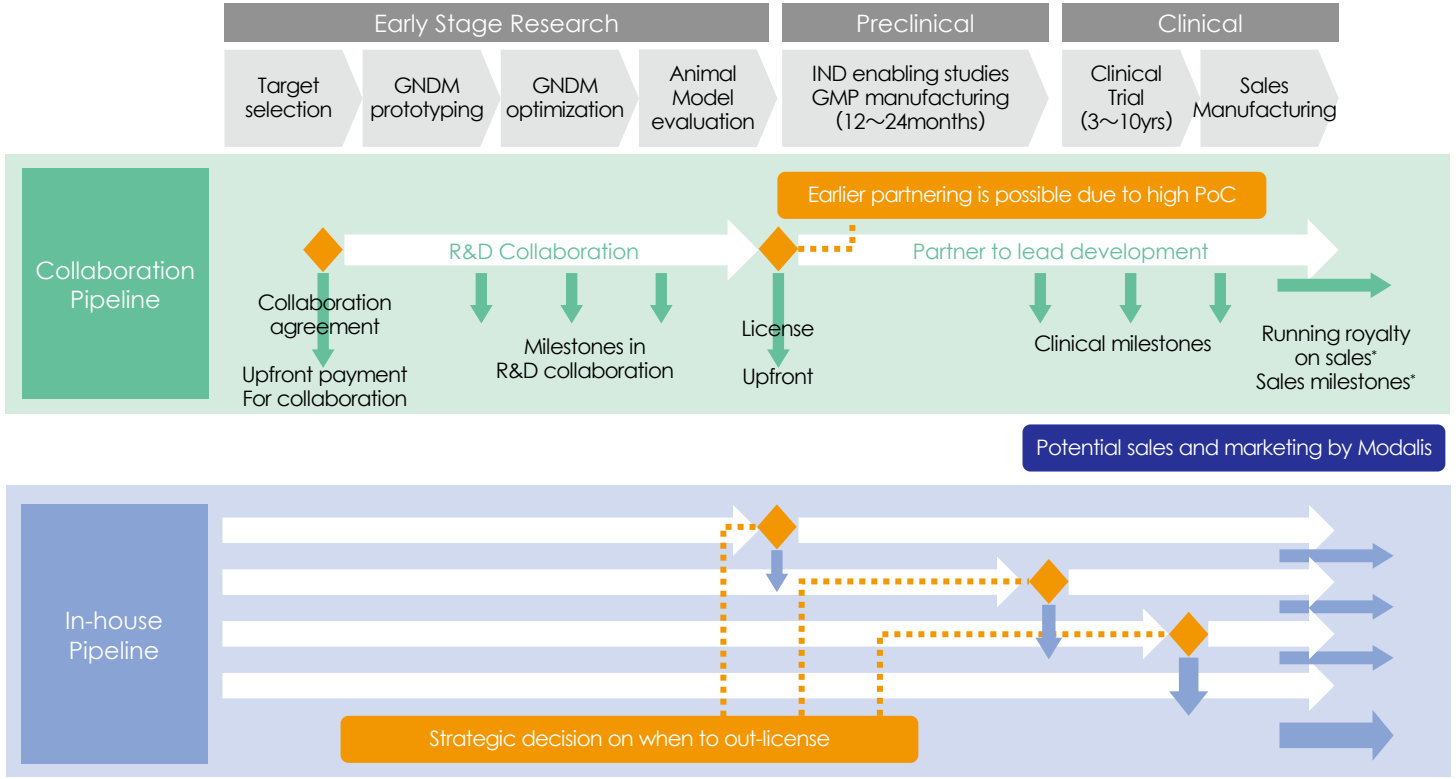
# Business Model

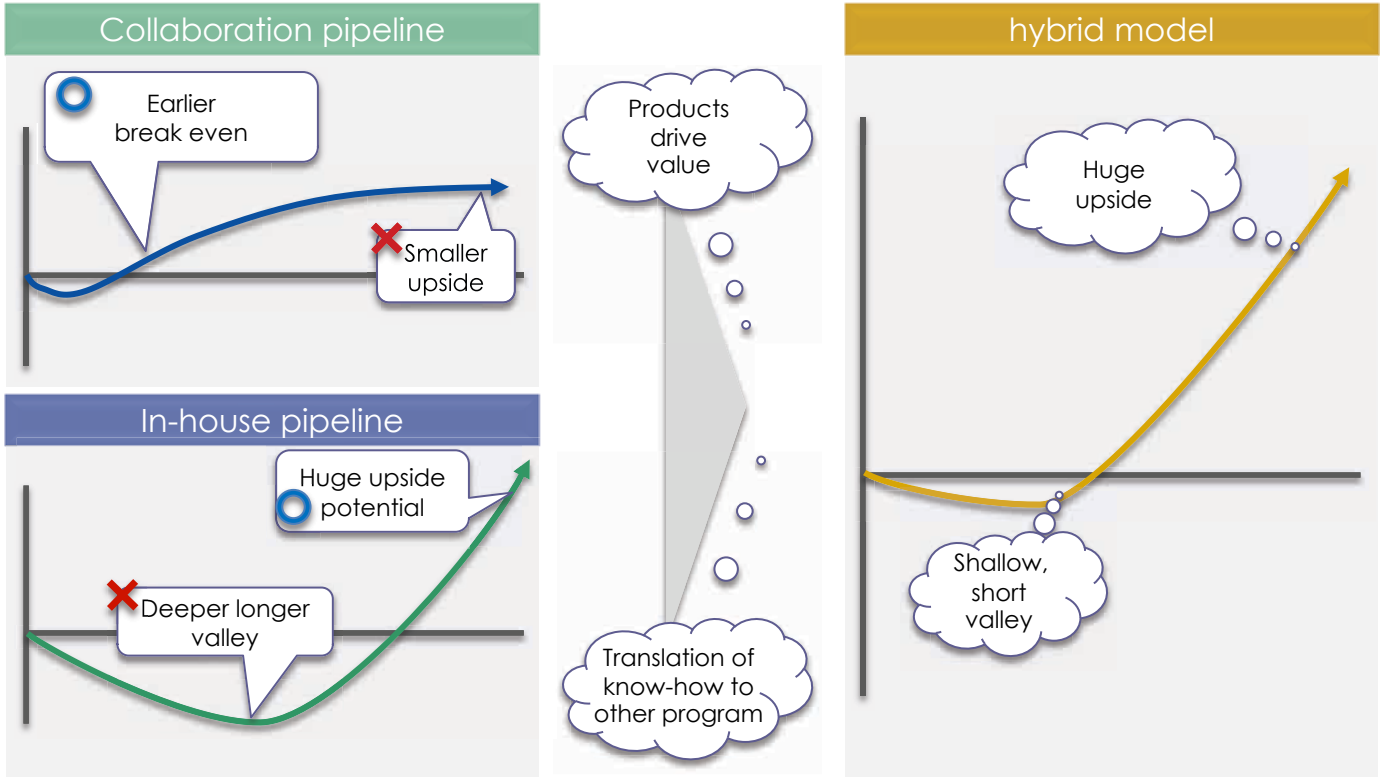
Hybrid of own pipeline and collaboration pipeline




* future plan

# Modalis is pursuing a hybrid model

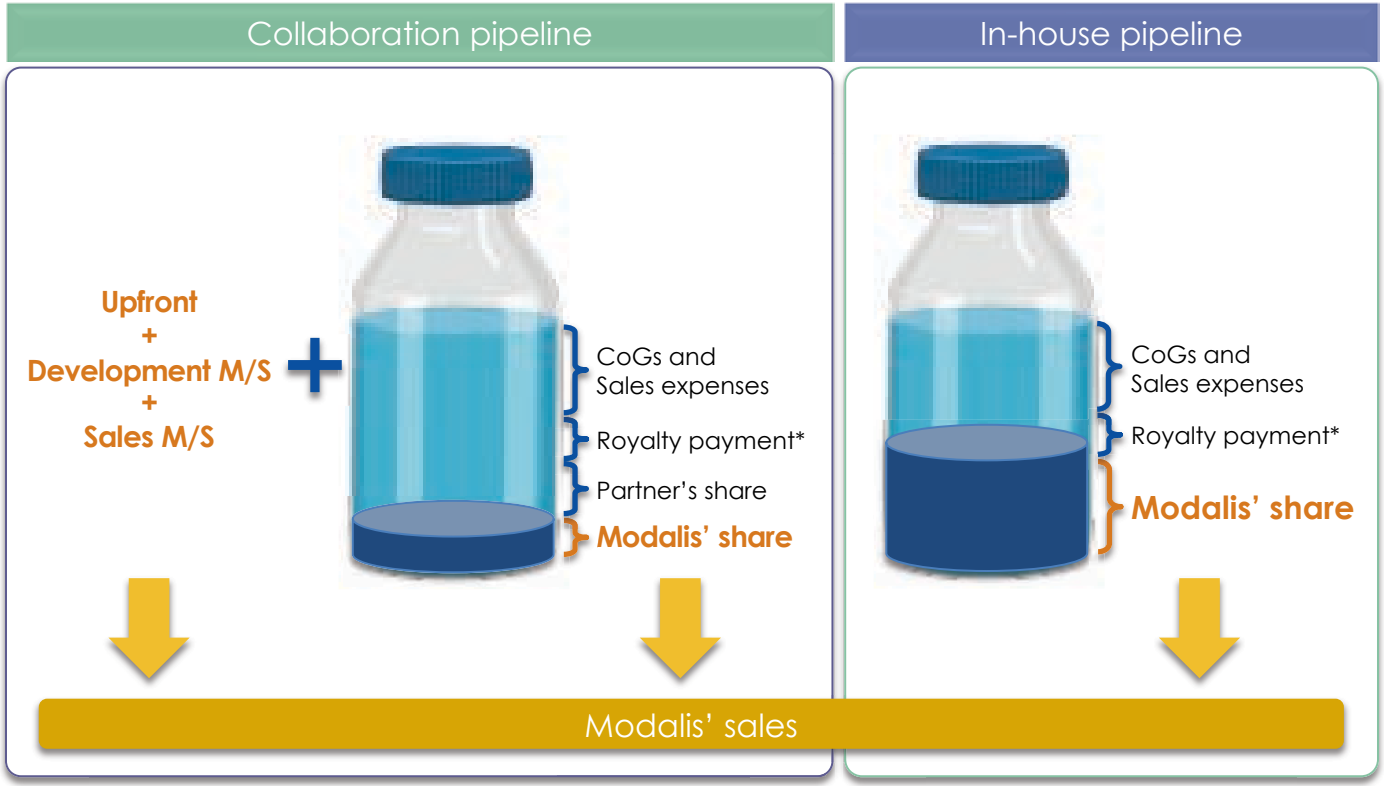
Combination of upside from in-house pipelines and earlier cash stream from collaboration pipelines




* The above is only an image and does not suggest or guarantee our future performance.

# Risk - profit share model

While collaboration model brings earlier cash, In-house pipeline has higher profit with higher risks




* : As a consideration for the licensed in intellectual property, a certain percentage of sales after market launch is paid to the intellectual property holding organization.





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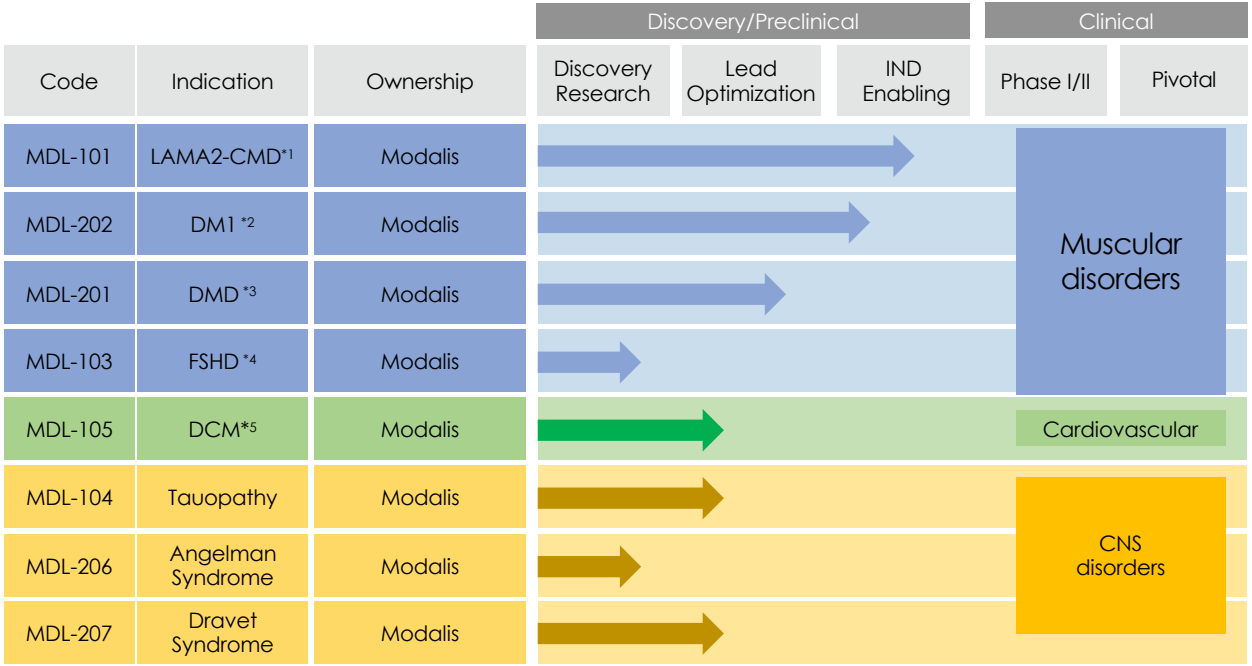
# Set the muscular disease-centered strategy

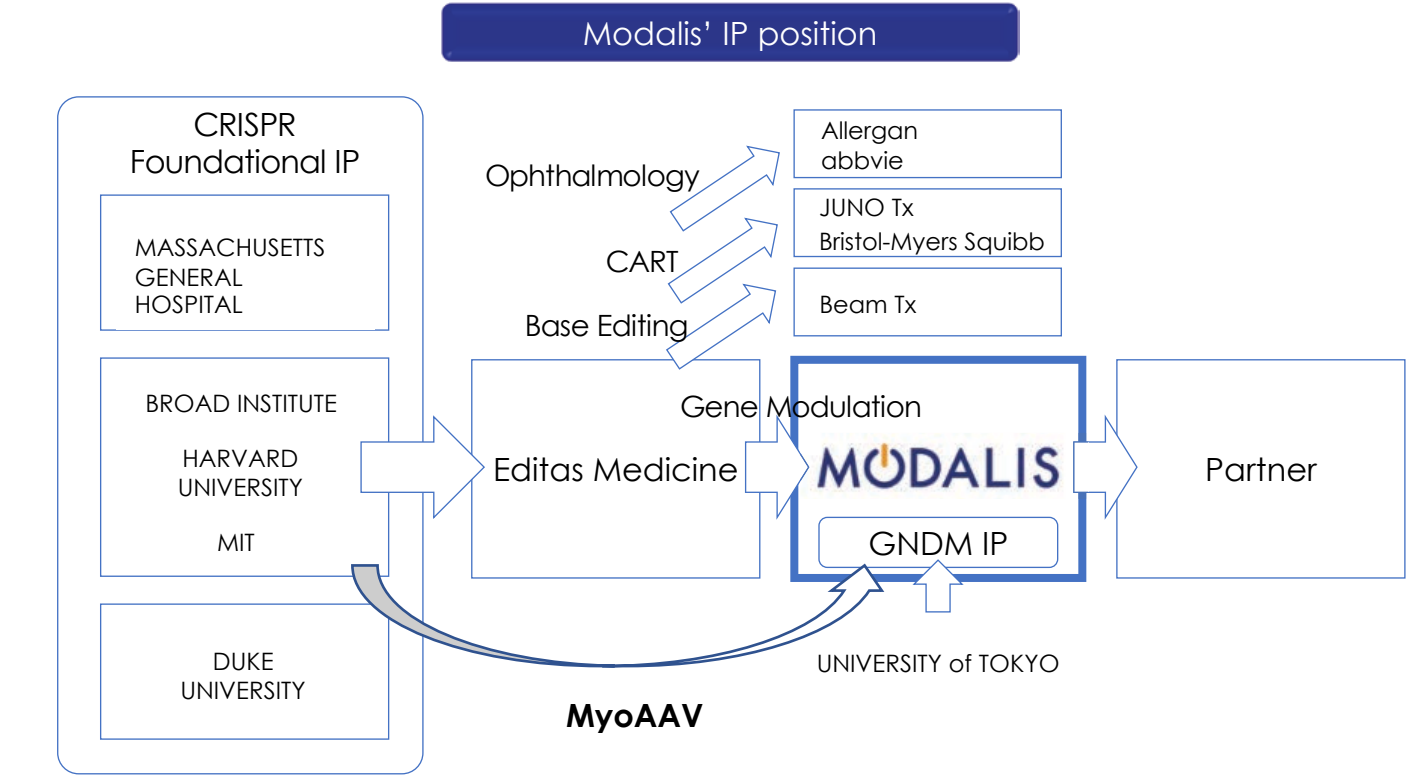



*1: LAMA2-related congenital muscular dystrophy
*2: Myotonic Dystrophy Type 1
*3: Duchene Muscular Dystrophy
*4: facioscapulohumeral muscular dystrophy
*5: Dilated Cardiomyopathy

Updated

# Intellectual Property position

Established IP with foundational CIRPSR IP from Broad and engineered Cas9 from Univ of Tokyo




Source : disclosed information by each company





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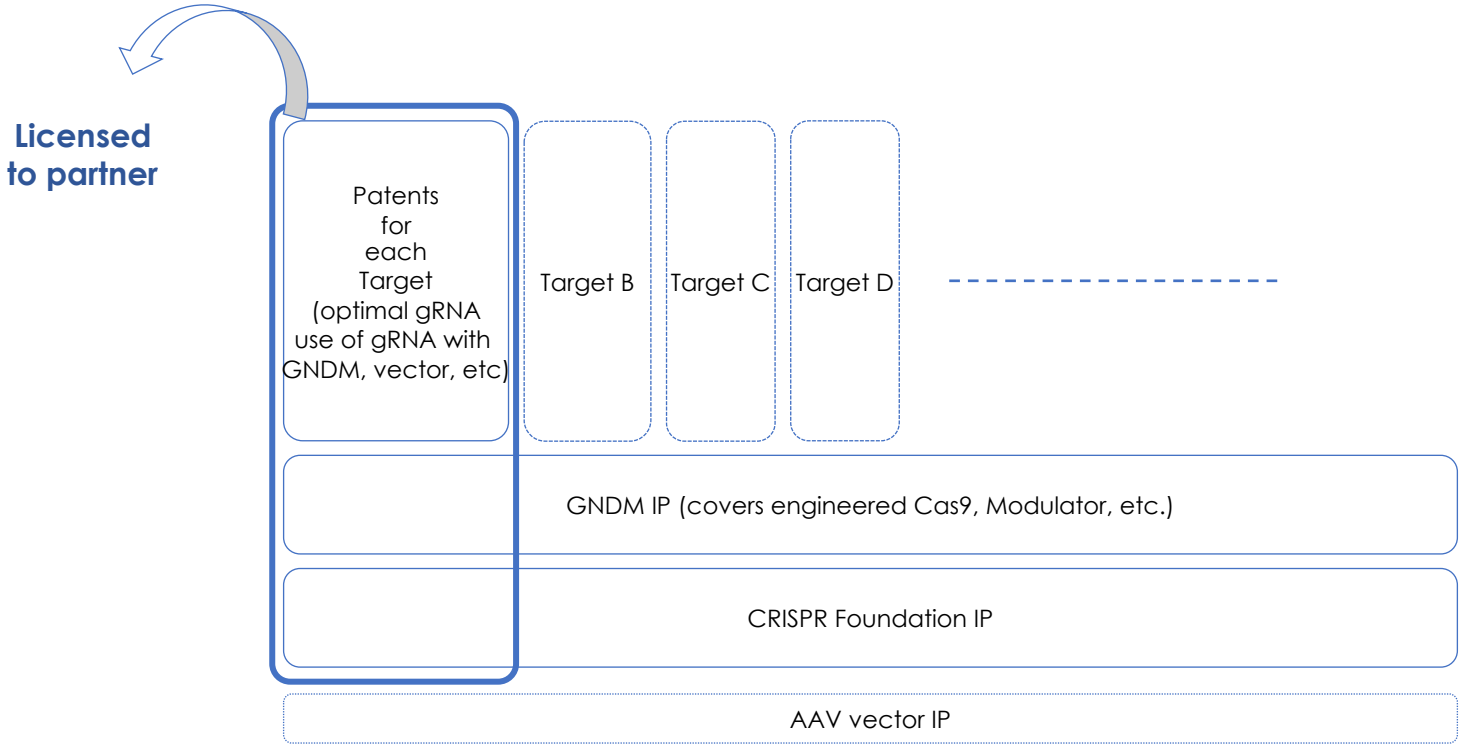
# Intellectual Property Structure

Each product will be protected by multiple layers of IP



# Management Team and Board of Directors

Seasoned team

## Executive Officers

Haru Morita Co-founder, President, CEO, and Chair of the board
- REGiMMUNE, Founder, President and CEO
- Y's Therapeutics, Booz Allen and Company, Kyowa-KIRIN

Tetsuya Yamagata MD PhD: Chief Technology Officer
- Glaxo Smith Kline, Tempero Pharmaceuticals, Joslin Diabetes Center, Harvard Medical School

Yosuke Nakashima MBA: VP Operations and Business Development
- Sumitomo Chemical

## Board of Directors

Haru Morita Co-founder, President, CEO, and Chair of the board

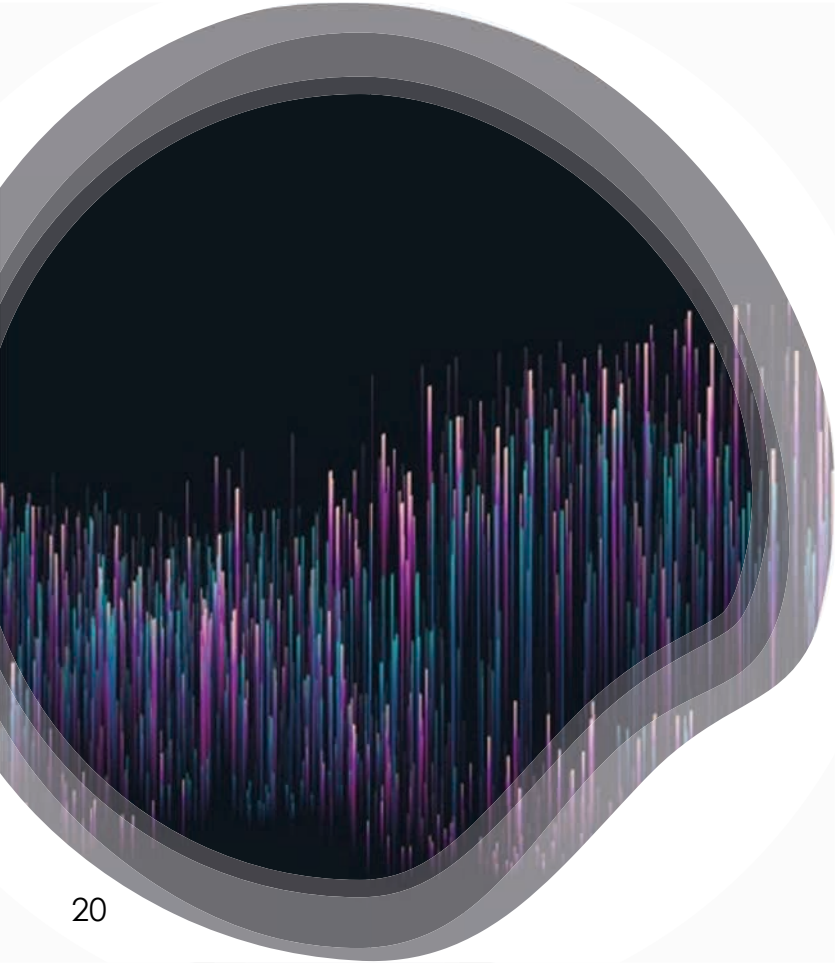
Hideki Takeda Board member
- President, Medical Patent Research
- Healios KK former president, Fujisawa (merged into Astellas)

Joseph S. McCracken DVM Board member
- Roche Head of Global license, Genentech, Sanofi

Miyuki Shimane Board member, Audit committee
- Chugai Pharma

Teruhisa Tajima Board member, Audit committee, CPA
- President Tajima CPA office
- Corporate Auditor (Quantum Biosystems, OncoTherapy, Prism Bioscience)

Toshio Furuta Board member, Audit committee, Attorney at Law
- Representing attorney, Clair Law Firm
- Corporate Auditor (NetYear Group, Canbas, Zenrin DataCom)



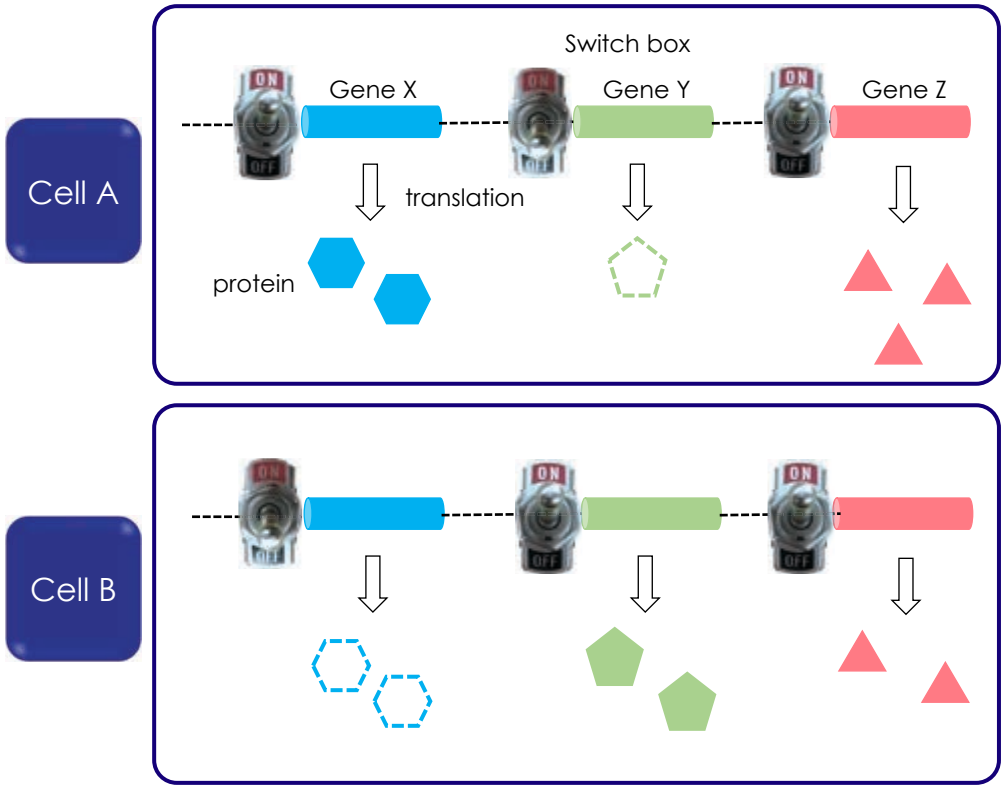
# 2． Gene Therapy and Gene Editing



20

# How multiple cell types are created from the same DNA code

Each of 20,000 genes have ON/OFF switches that control cell type specific expression




- There are **37.2 Trillion cells** in our body
- **200 cell types** in our body have the same DNA code despite differences in appearance and function
- Differences in cell types and their states are controlled by ON / OFF switches of the expression of **20,000 genes** coded by **3 billion bases of DNA**





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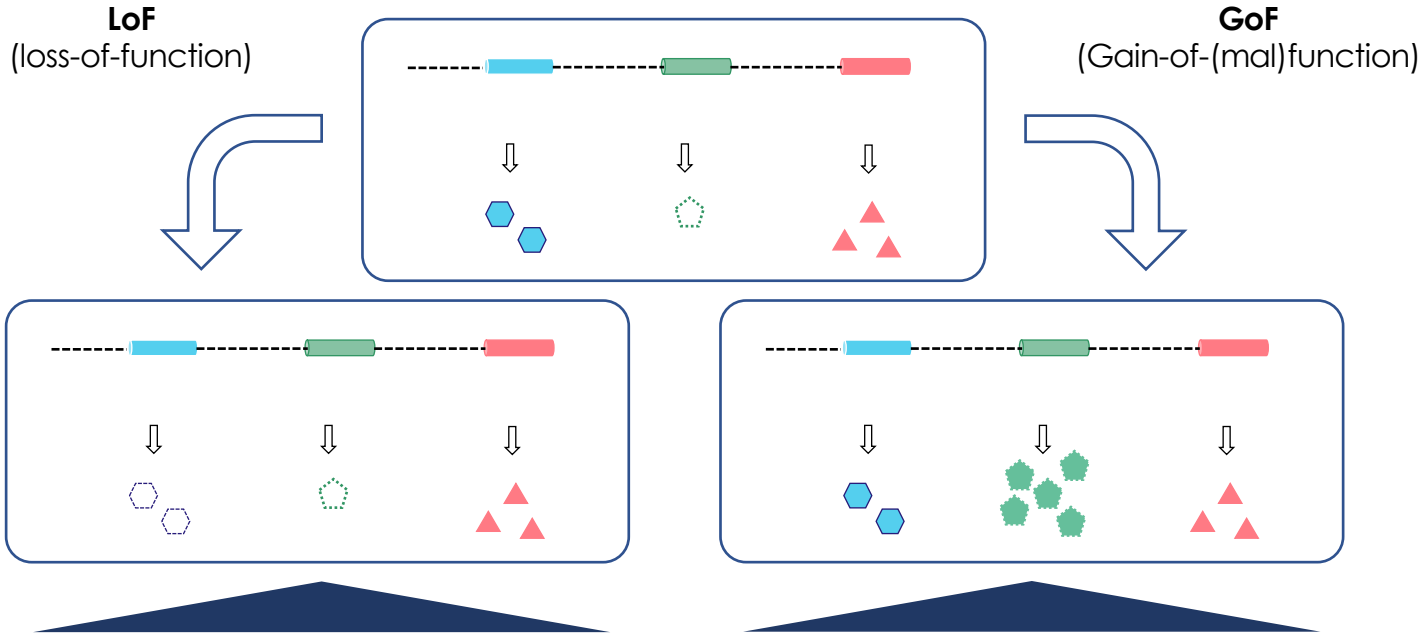
# Genetic Disorders are caused by loss-of-function or gain-of-function

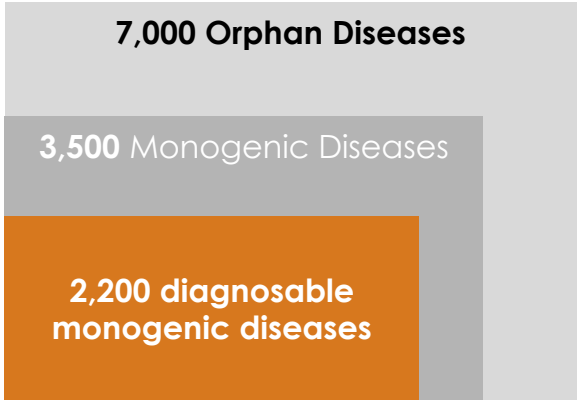
To address the issues, GTx supplement missing functions or silence the malfunction



# Untapped opportunities in monogenic disorders

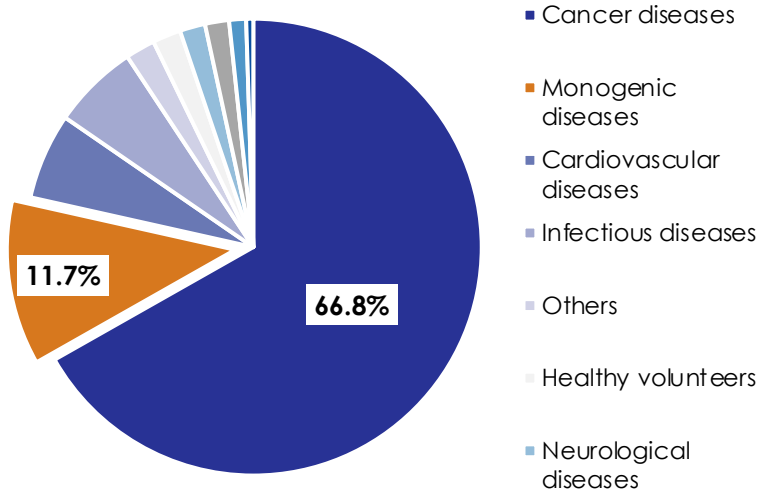
Only limited number of drugs are approved or in clinical development for monogenic disorders

## Monogenic Disease




Source: Discovery Medicine

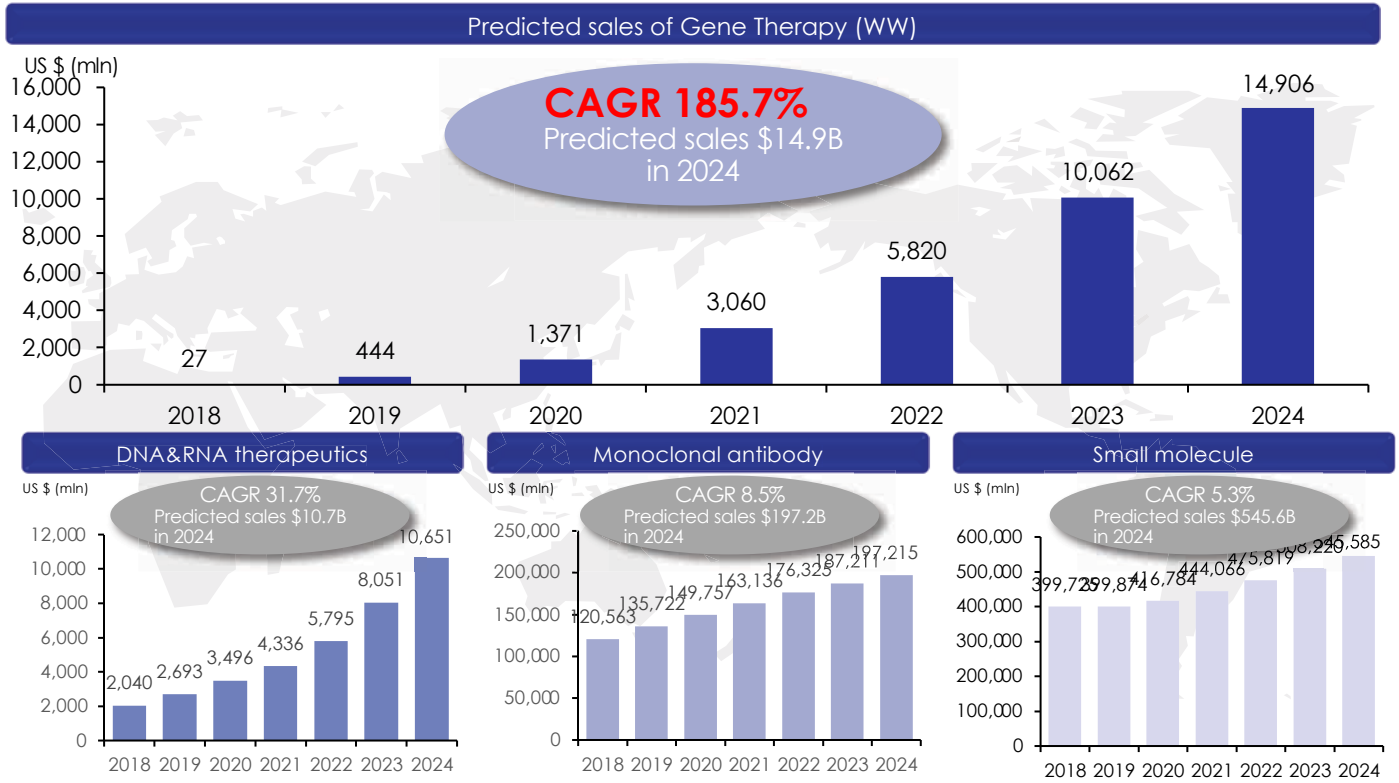
## Breakdown of GTx clinical trials (1989~ Worldwide)




Source: The Journal of Gene Medicine (2019)

# Sales growth of pharmaceutical modalities

GTx is growing faster than other modalities




Source : Evaluate Ltd (in Aug 2019 data) *CAGR=2018 to 2024. 2019 to 2024 are predicted sales





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Updated

# With the full approval of ELEVIDYS, 3 GTx have been approved in 2024

Based on recent successes, gene therapy is expanding its target from local to systemic administration

Gene therapies approved by US FDA

| Trade Name | Year of Approval | cost | Indication | Manufacturer | Patient Population | WW market size* (mil USD) |
|---|---|---|---|---|---|---|
| **Lxturna** | 2017 | $850k | RPE65 | Spark/Roche | 2 per 100,000 | $65M[#3] |
| **Zolgensma** | 2018 | $2.1M | SMA | Novartis (Avexis) | 1 in 10,000 live births (Approx. 10,000 to 25,000 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] |
| **ELEVIDYS** | | $3.2M | DMD | Sarepta | 1 in 3,500 male birth | $4.1B[#4] |
| **Roctavian** | | $2.9M | Hemophilia A | BioMarin | 1 in 5,000 male | $262M[#4] |
| **Casgevy** | | $2.2M | SCD | CRISPR Tx/Vertex | 100,000 in America | >$2B[#5] |
| **LYFGENIA** | | $3.1M | | Bluebird | | |
| **Lenmeldy** | 2024 | $4.25M | Metachromatic Leukodystrophy | Orchard/KyowaKirin | 1 in 100,000 live birth | ? |
| **beqvez** | | $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] |

Source: National Organization for Rare Disorder、#2 Fierce Biotech #3 Corporate website #4Grand view research #5 Fortune Business Insight
*1: Spinal muscular atrophy *2: dystrophic epidermolysis bullosa *3: Duchenne muscular dystrophy





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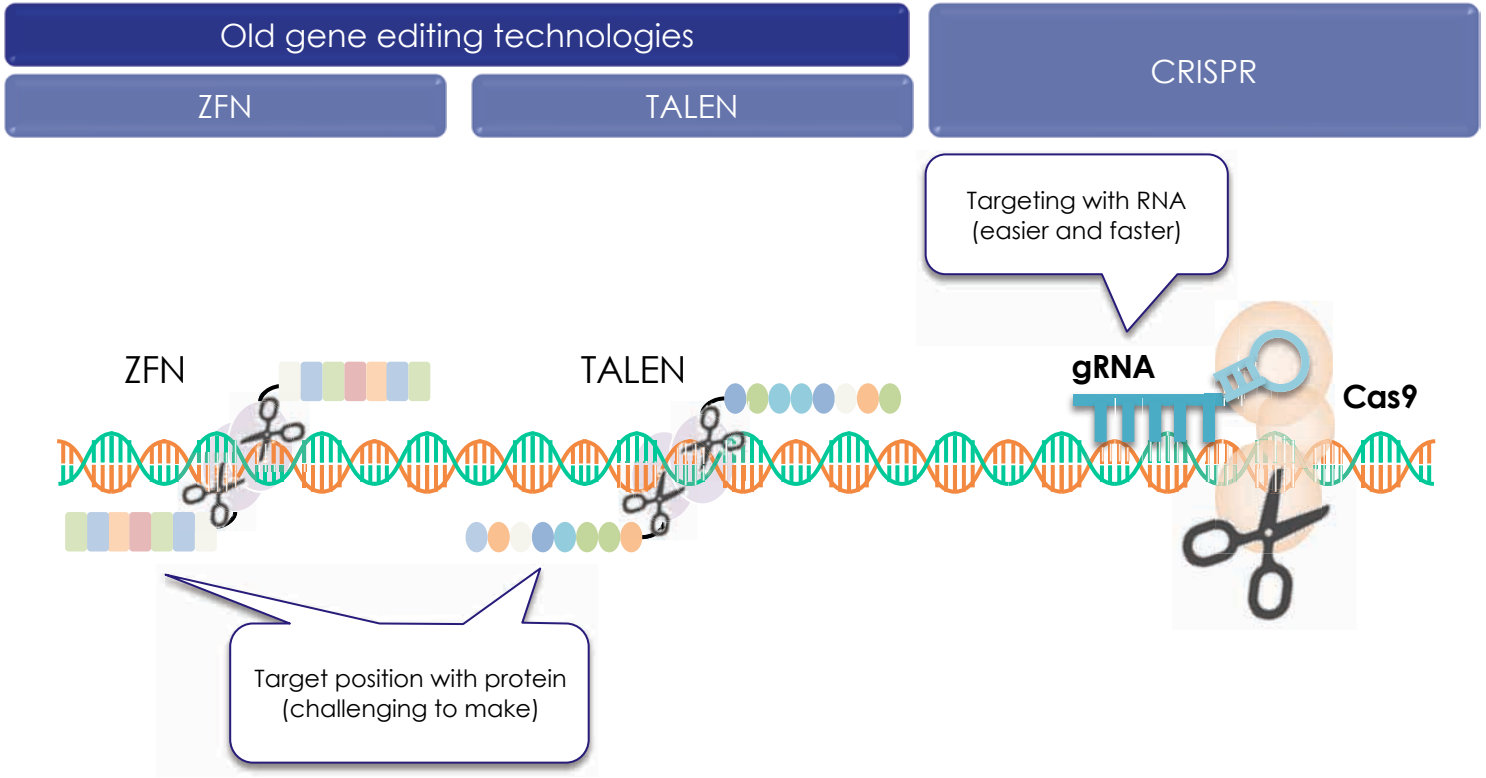
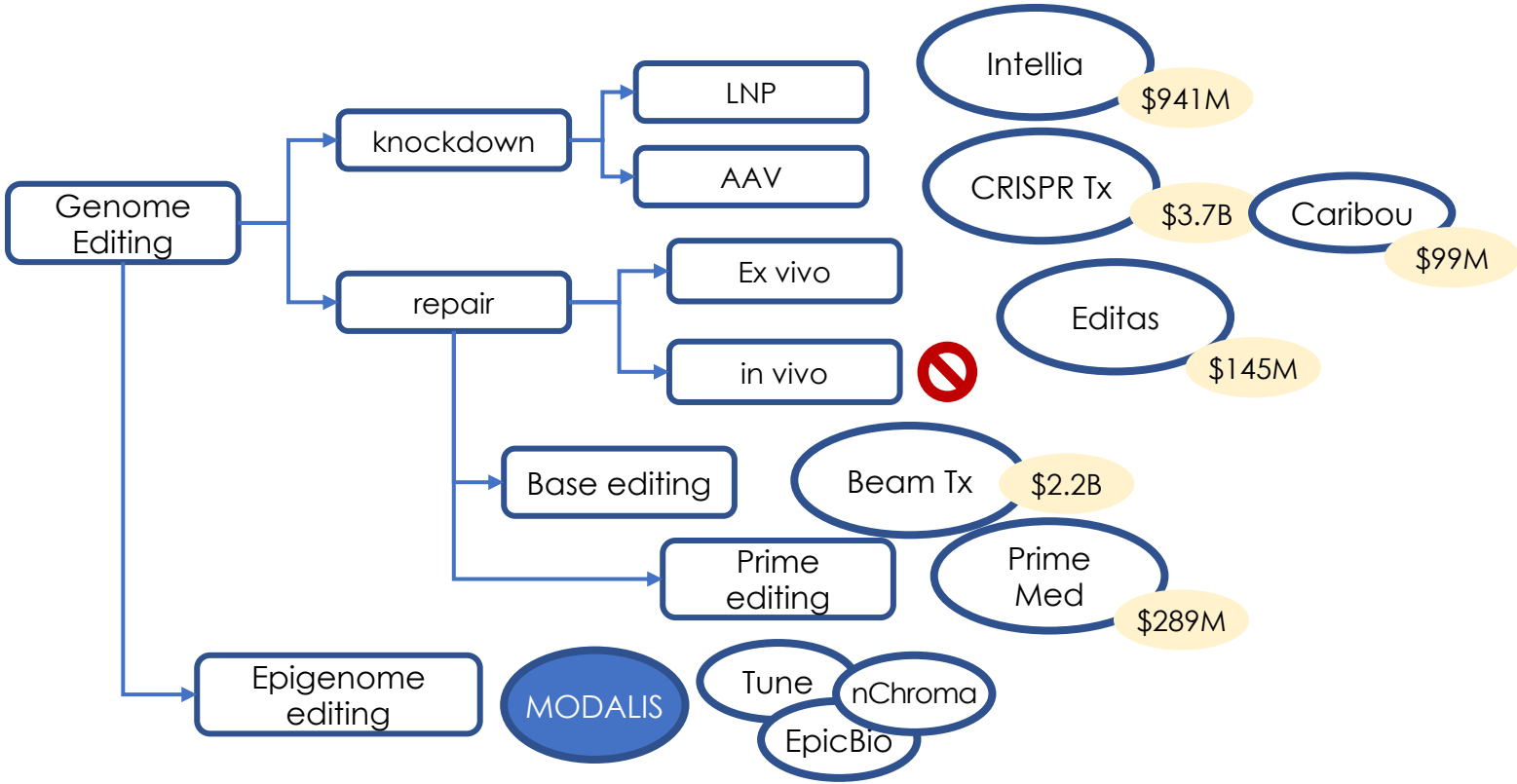
# CRISPR is a novel gene editing technology

Faster and higher throughput due to limited variable region which is easily synthesizable as gRNA



# Genealogy of CRISPR based Technology and major players

The whole CRISPR area has been expanding, but there are also areas that have become dead ends.




Note: The yellow circle shows the market capitalization as of the closing price on March 4, 2025.





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# 3. CRISPR-GNDM® and its advantages

# Gene Modulation is CRISPR 2.0

"I think one interesting possibility is that we'll see CRISPR being used not to edit genomes, or at least not to make permanent changes to genomes, but **instead to regulate them, to control levels of human proteins that are produced from different genes.** This is a newer way of using the CRISPR technology. I think it has a lot of potential to allow control of cells that doesn't require actual permanent chemical changes being made to the DNA."

*-Jennifer Doudna, Nobel Prize Winner on CRISPR*
*Source:* "Fresh Off Her Nobel Prize Win, Jennifer Doudna Predicts What's Next for CRISPR"

CRISPR-GNDM®

*Source: Interview on Future Human "Fresh Off Her Nobel Prize Win, Jennifer Doudna Predicts What's Next for CRISPR"





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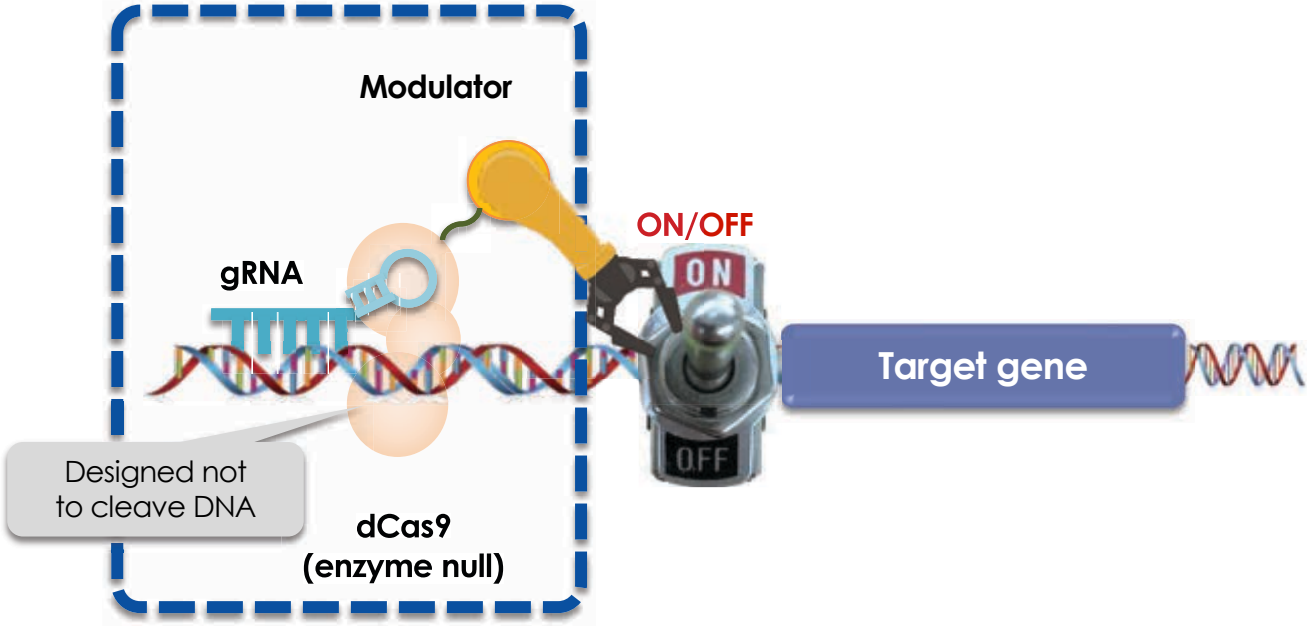
# Non-cleaving CRISPR = CRISPR-GNDM®

Enables treatment of genetic disorders by controlling ON/OFF switch

CRISPR-GNDM® (Guide Nucleotide-Directed Modulation) platform





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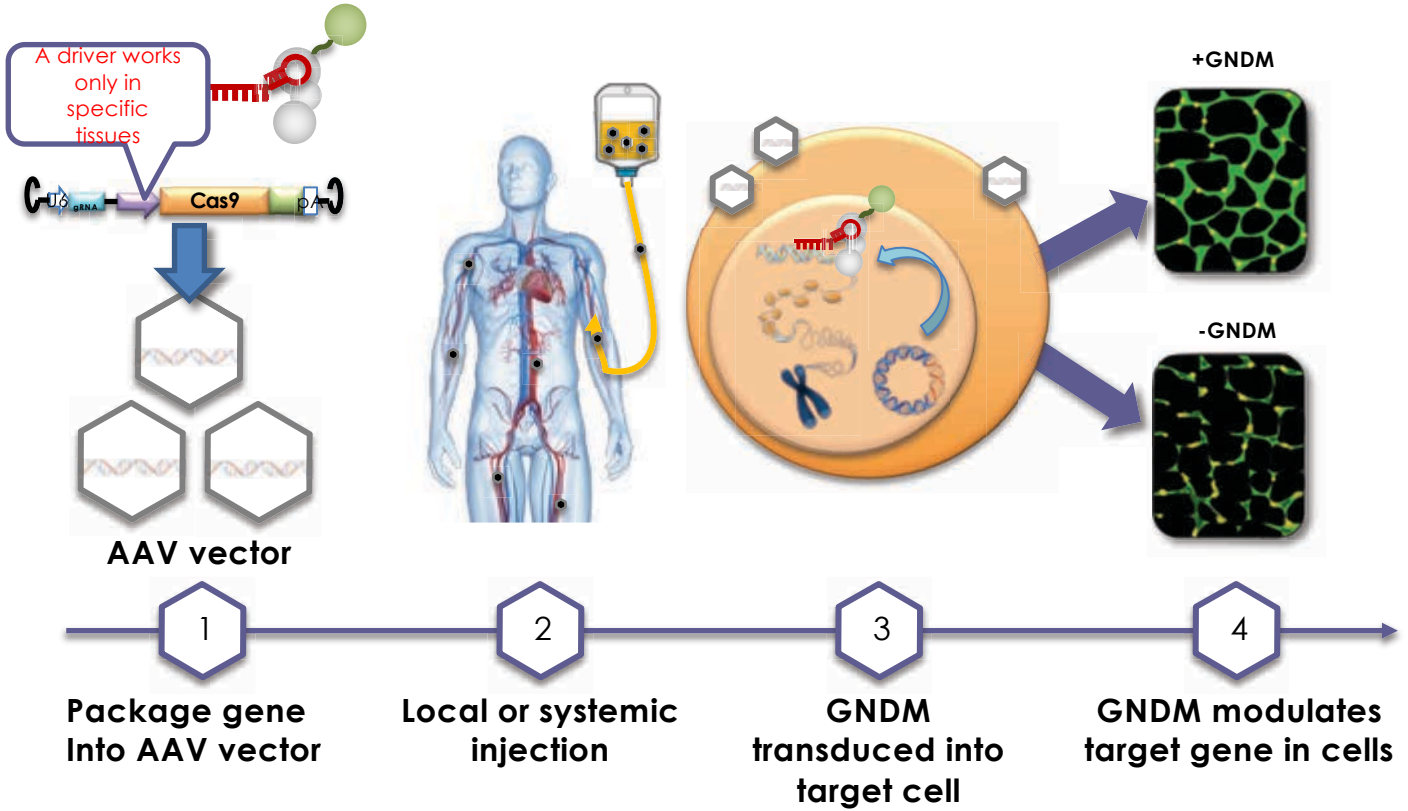
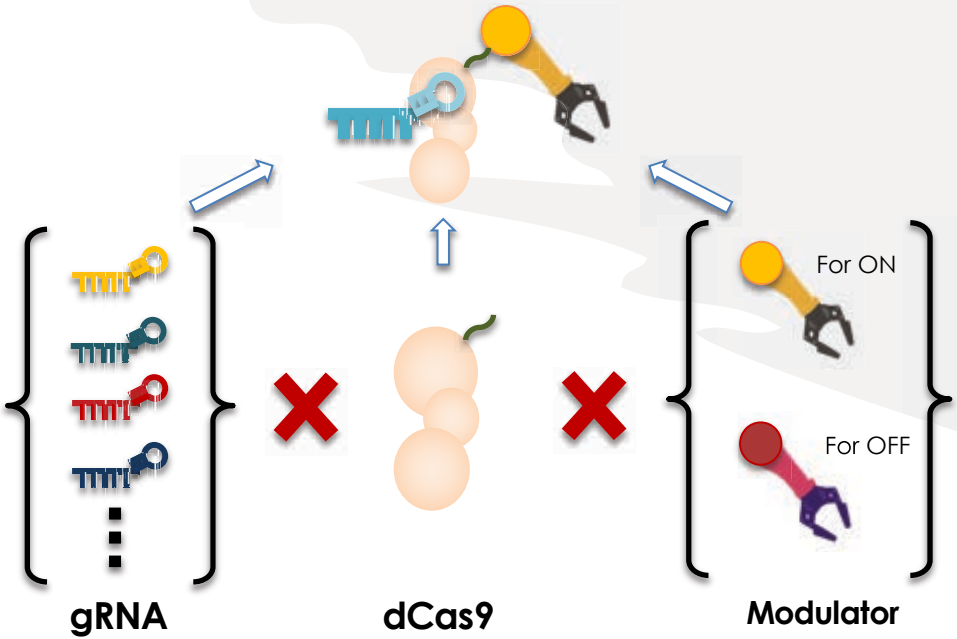
# Delivery of CRISPR-GNDM® to target

Use AAV vector to deliver GNDM to target cell



## GNDM is scalable

gRNA is the only variable which is unique for each target. Other components are off-the-shelf to assemble.



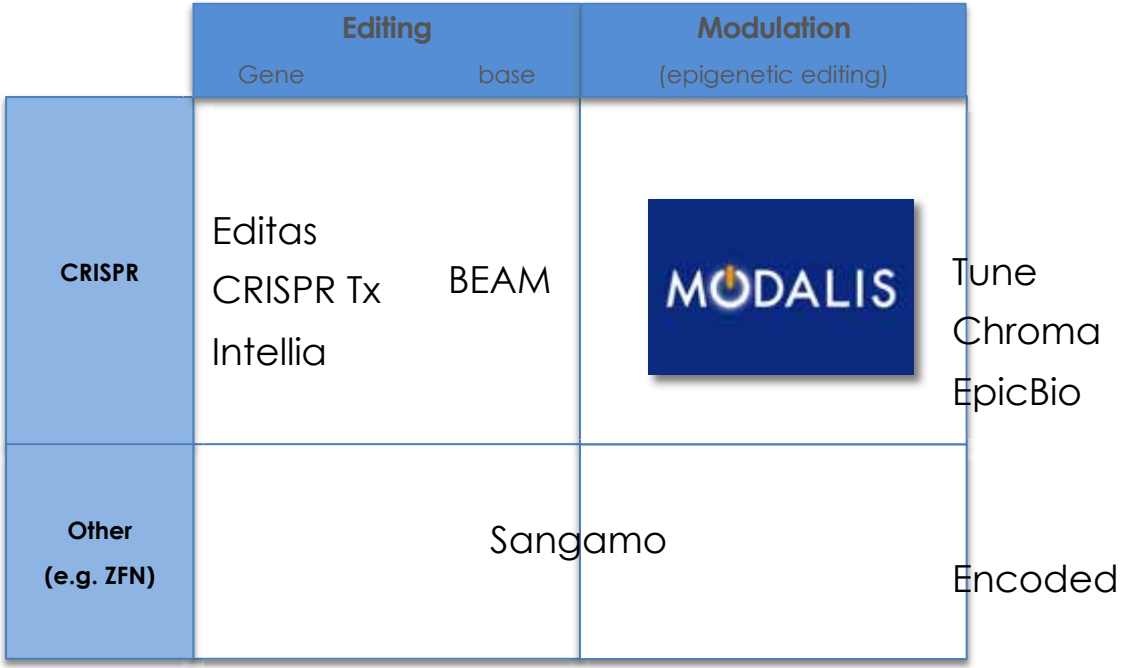
## Precision technologies are not *one-thing-fits-all*

there are many disorders that GNDM has the advantage over the other technologies

| | Conventional Gene therapy | Gene Editing | ASO siRNA | CRISPR-GNDM |
|---|---|---|---|---|
| **Precise targeting** | Yes | Yes | Delivered to off-target tissues | Yes |
| **Durability** | Years | Permanent | Require repeated injection | Years |
| **Applications** | LoF ONLY | Mostly GoF | GoF only | **LoF and GoF** |
| **Target gene limitation** | Limited to small size genes | Limited to a specific point of mutation | Causative tissue is limited (e.g. liver) | **Size agnostic** |
| **effect on DNA** | none | Causing double-strand break | none | none |

LOF=Loss of function, GOF=gain of function

# Modalis is uniquely positioned within the CRISPR field



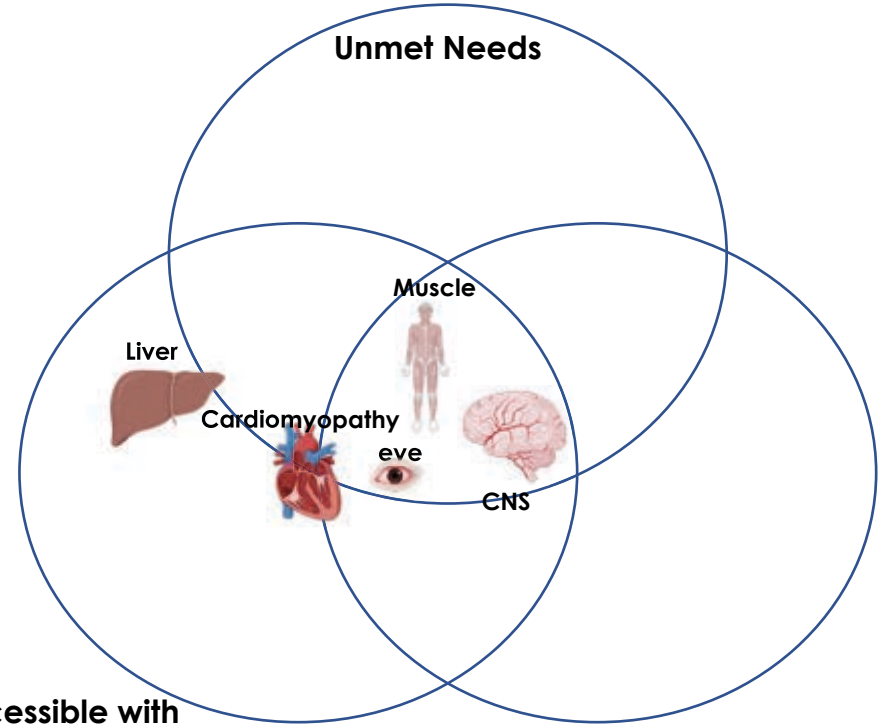
# Epigenome editing competitive landscape

Momentum for epigenome editing remains strong

| Company | Year Founded | Funding | Platform | Pipeline/Target indication | Stage of Development |
|---|---|---|---|---|---|
| MODALIS | 2016 | Public | CRISPR-GNDM x AAV | • MDL-101/LAMA2-CMD<br>• MDL-201/DMD<br>**Gene activation** | IND enabling |
| Tune Therapeutics | 2020 | Series B ($175M, 2025) | DNMT-KRAB fusion dCas9 x LNP | Une-401 for HBV<br>**Gene suppression** | **CTA approval from NZ on HBV** |
| Chroma Medicine | 2021 | Merged into nChroma (Dec 2024) | DNMT-KRAB fusion dCas9 x LNP | CRMA-1001 for PCSK9<br>**Gene suppression** | Unclear |
| Epic Bio | 2022 | Series B ($68M, 2025) | Cas12f-fused with demethylation enzyme x AAVrh74 | EPI-321/FSHD<br>**Gene suppression** | IND clearance of EPI-321 from FDA |

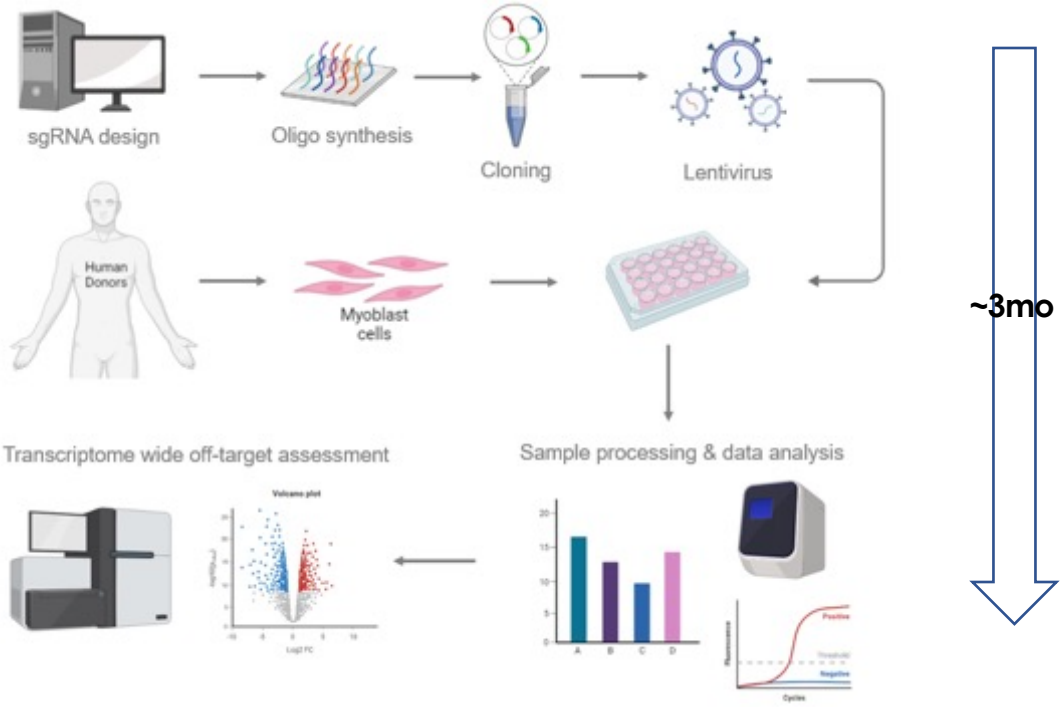
## Muscle and CNS are the areas with huge unmet medical needs

Target selection for Modalis' gene therapies



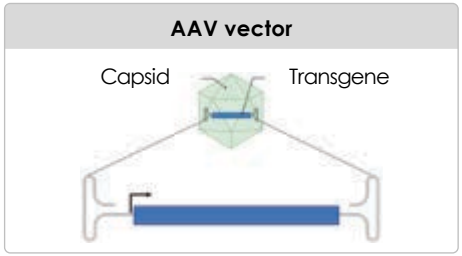

# CRISPR-GNDM® platform efficiently identifies optimal gRNA

*Lead candidate screening in human primary myoblast cells*

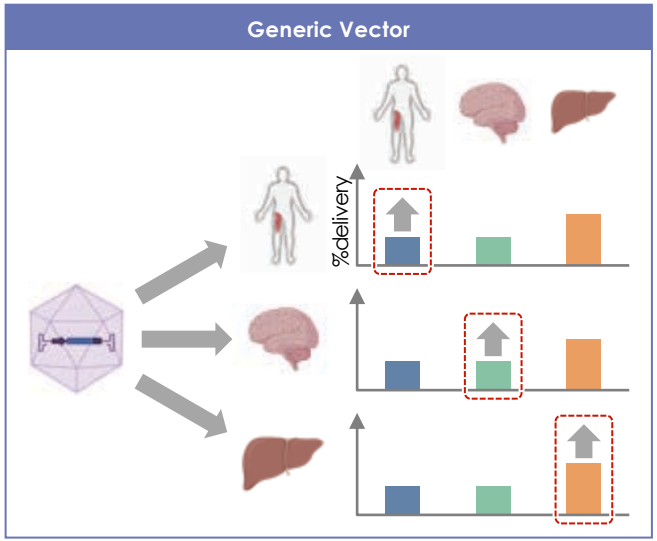


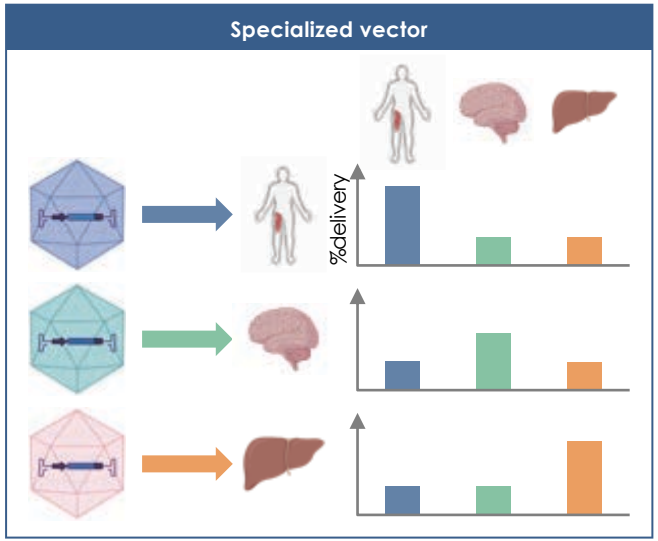
# A big innovation has been brought to GTx field

By moving from generic capsids to selective capsids, payloads can be selectively delivered to target tissues




- Previously, generic vectors such as AAV2, 6, 8, and 9 were universally used for all target diseases
- Those capsids are predominantly sequestered in the liver after systemic injection, and cause hepatotoxicity which limits dose of AAVs.
- Recently developed engineered vectors have a much higher tropism to each target organ

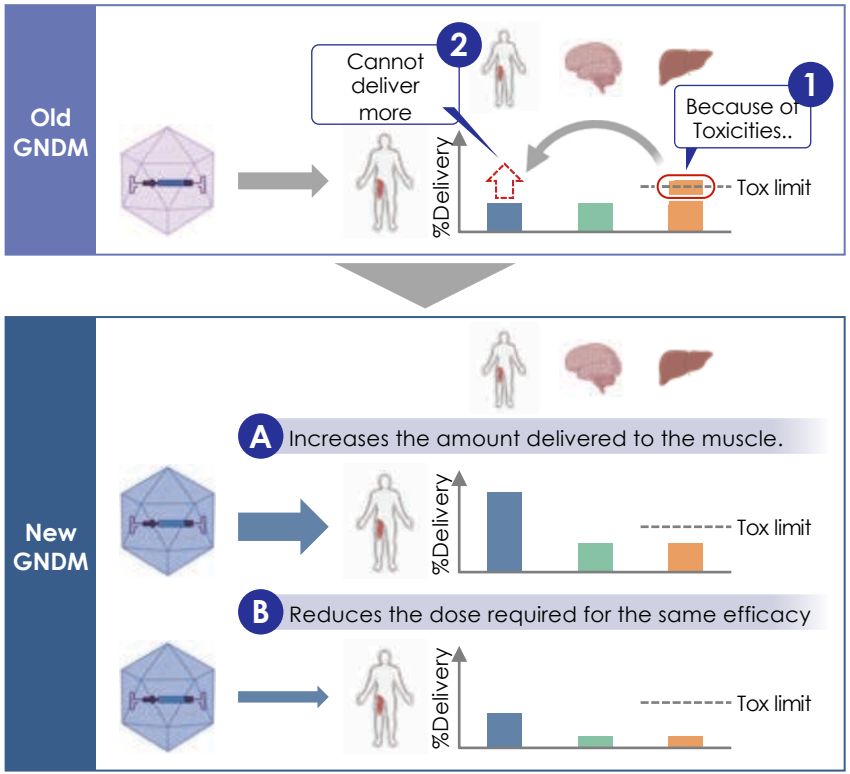


# Transition to specialized capsids is the need of the field

Selective capsids deliver more to target organs while delivering less to off-targets, lowering toxicity issues

In musclular disorders like MDL-101




- Does of generic capsids were limited by the off-target toxicity of capsid itself, such as hepatotoxicity and thrombosis

- By shifting to specialized capsids, the transduction efficiency to the target organ can be increased, which can

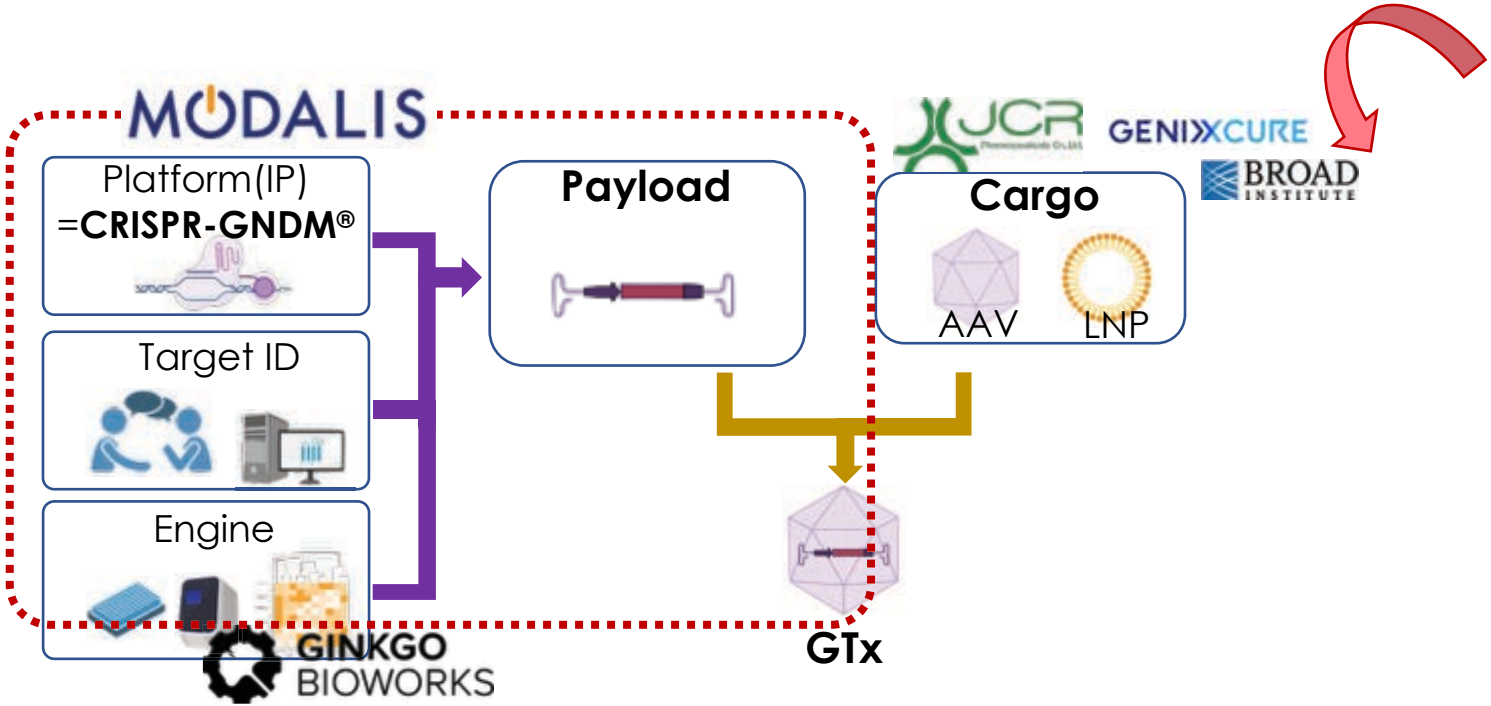
- **A** increase the amount delivered to the target organ without reaching toxic levels in other organs, or
- **B** reduce the dose required to achieve the same efficacy.

- As a result, there will be benefits in terms of costs, etc.

Updated

# MODALIS' core competence and collaboration

In the increasingly complex games, the necessary capabilities are accessed through partnership.



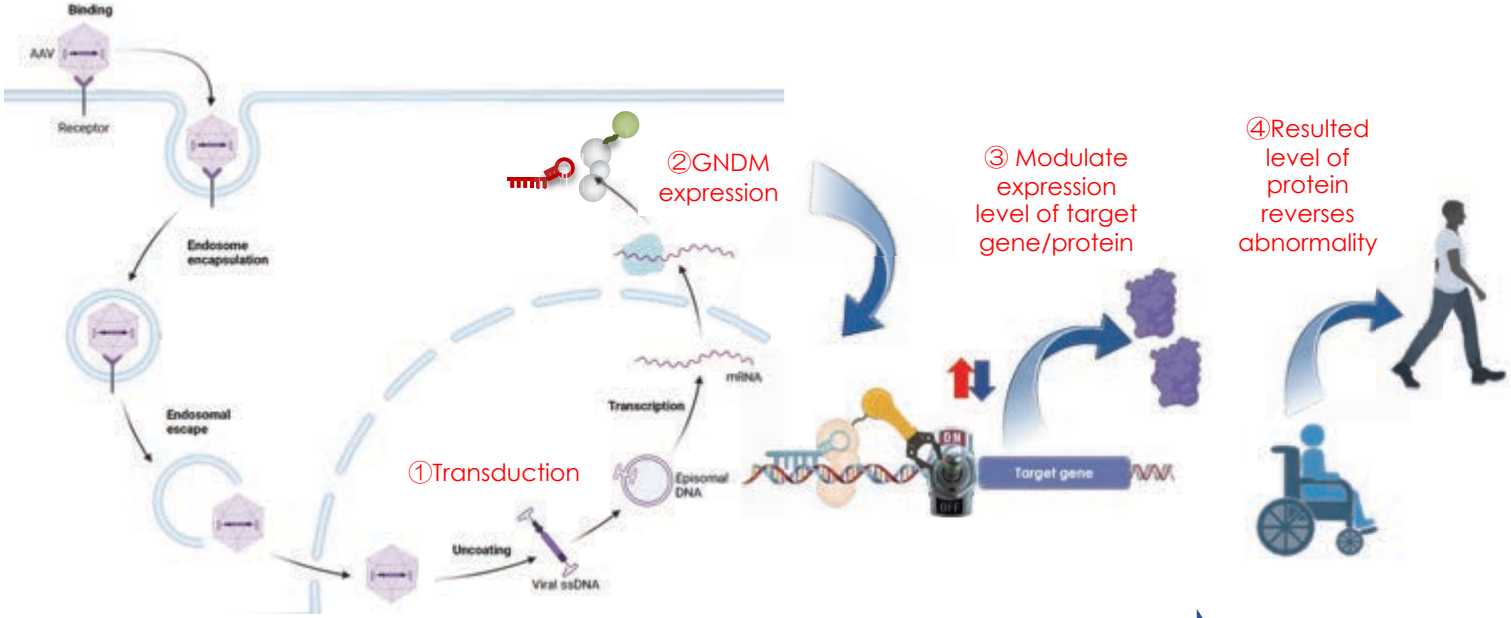
# Essentials of Technology Strategy

- Focus on mechanisms that can only be achieved through epigenome editing
  - Prioritize gene activation over silencing, which competes with other modalities
- Focus on disease groups that can make use of the characteristics of gene therapy
  - Aim to solve severe diseases that are life-threatening
- Target diseases that originate in organs for which delivery has been established or is expected to be established in the future
  - Focus on development of muscle and central nervous system diseases


4. Pipeline

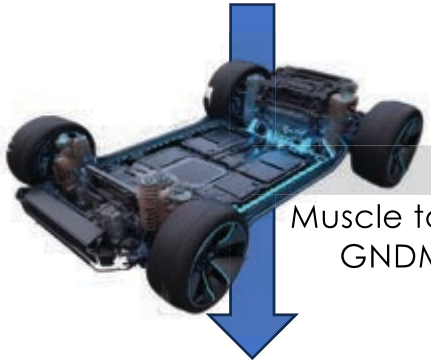
# There are 3 steps for GNDM before providing efficacy

The GNDM is transduced, expressed and engages to the target to show efficacy



# All muscle programs share the same platform as MDL-101

Other muscle programs can be achieved with relatively lower risk and effort



Muscle targeting AAV
GNDM platform

**MD-101**

**MDL-202**

**MDL-201**

**MDL-103**





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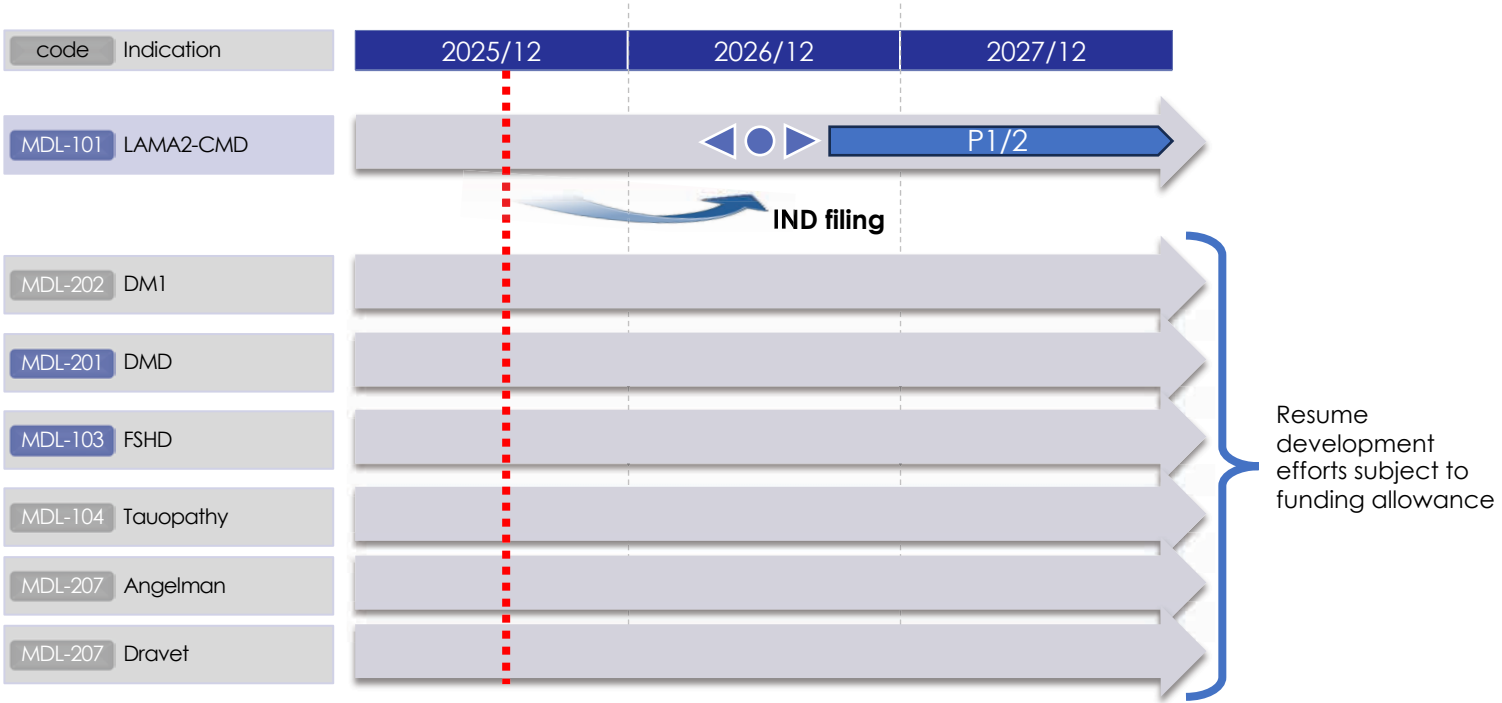
Updated

# Pipeline status and coming milestones

Reset MDL-101 IND filing target to 2026

***Pipeline status***




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

# Advantages of ODD and RPDD, which MDL-101 is granted, are…

- **Orphan Drug Designation**
  - Tax deduction for clinical trial expenses
  - Exemption from application fees, etc.
  - Exclusive status for 7 years after market launch

- **Rare Pediatric Disease Designation and Priority Review Voucher Programs**
  - Granting priority review voucher after application for approval (The voucher program will end soon)

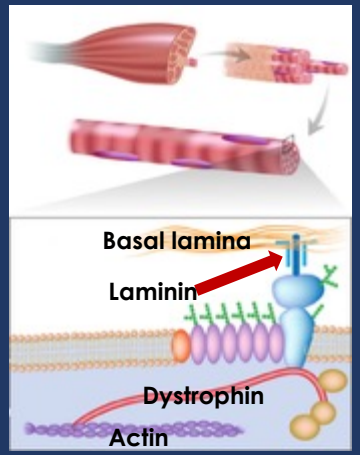
Reviewed by the rarity and medical relevance of the target disease, etc.

# 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<br>• Lack of muscle tone (hypotonia)<br>• Little spontaneous movement<br>• Joint deformities (contractures)<br>• 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)





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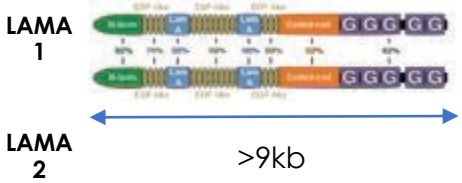
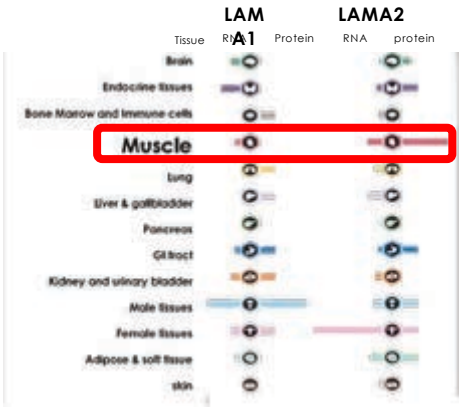
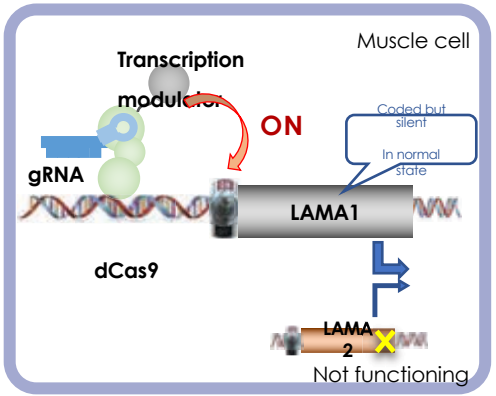
Protein structure of LAMA1 and 2




Exspression pattern of LAMA1and 2 by tissues




CRISPR-GNDM® targeting LAMA1




**MDL-101 activates LAMA-1, compensates for the missing function of LAMA2, which is too large for classical gene therapy approach**

## MDL-101 paper

Published paper on preclinical data on MDL-101 using CRISPR-GNDM®

MODALIS' first publication of CRISPR based epigenome editing

Cold Spring Harbor Laboratory

bioRxiv

THE PREPRINT SERVER FOR BIOLOGY

New Results

**Efficient and durable gene activation by Cas9-mediated epigenome editing in vivo**

Posted May 05, 2024.

Yuanbo Qin, Talha Akbulut, Rajakumar Mandraju, Keith Connolly, John Bechill, Farzaneh Assadian, Alison Shottek, Seth Levy, Jamie Benoit, Tetsuya Yamagata

**doi:** https://doi.org/10.1101/2024.05.03.592438





49

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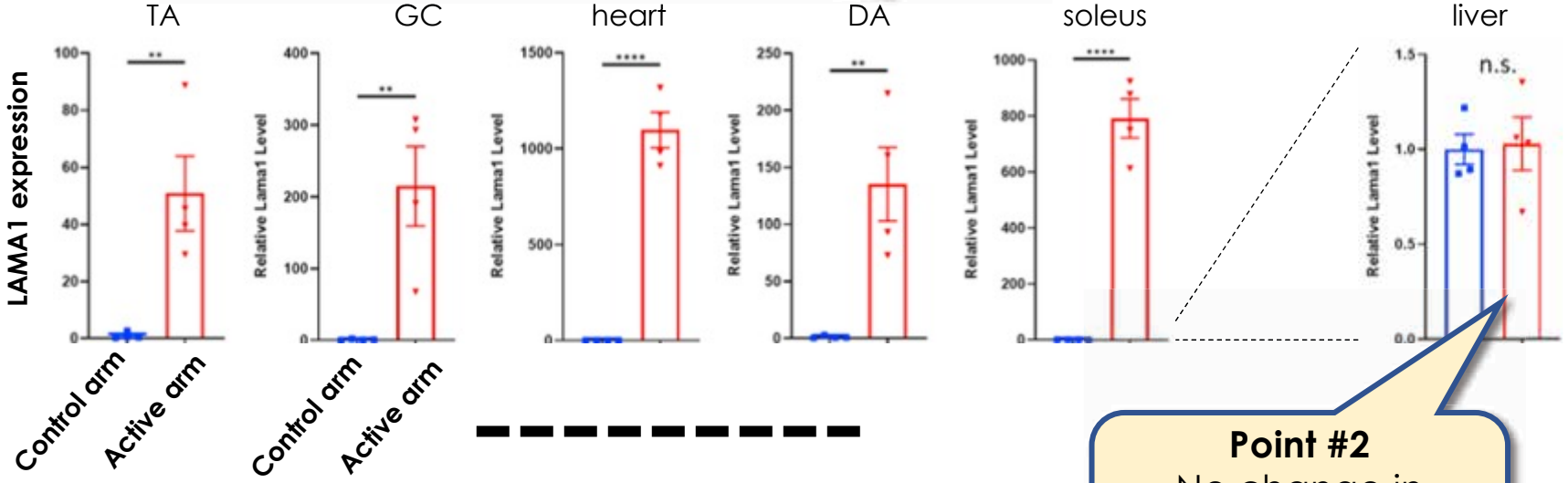
From the paper

# Significant increase in LAMA1 expression in muscles

LAMA1 increased in extensive muscle tissues following GNDM administration, with no change in liver

**Point #1**
LAMA1 is widely expresses in muscle tissues




**Point #2**
No change in expression level in liver

TA: tibialis anterior GC: Gastrocnemius DA: Diaphragm





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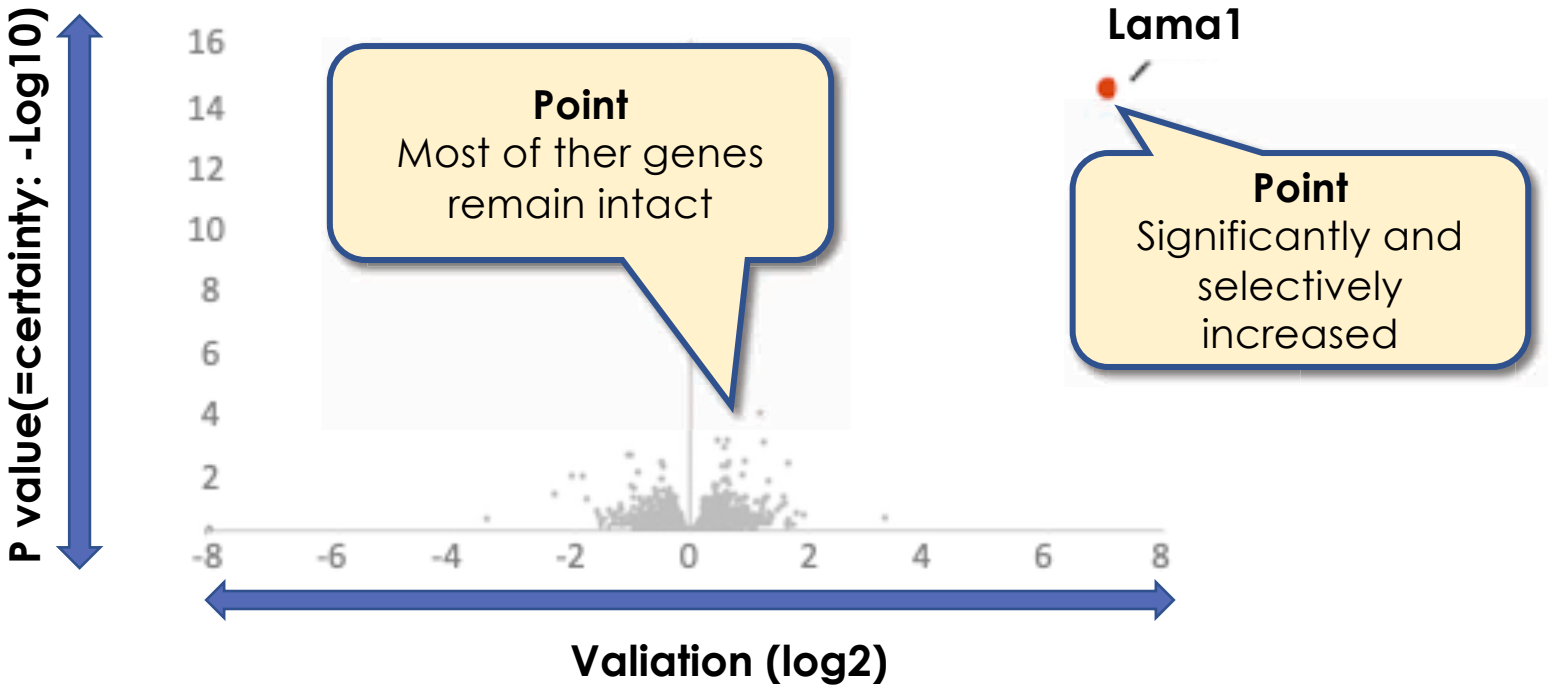
From the paper

## GNDM selectivity

LAMA1 was selectively upregulated as the other genes remain no change

*gene perturbation by GNDM-LAMA1 in RNAseq*





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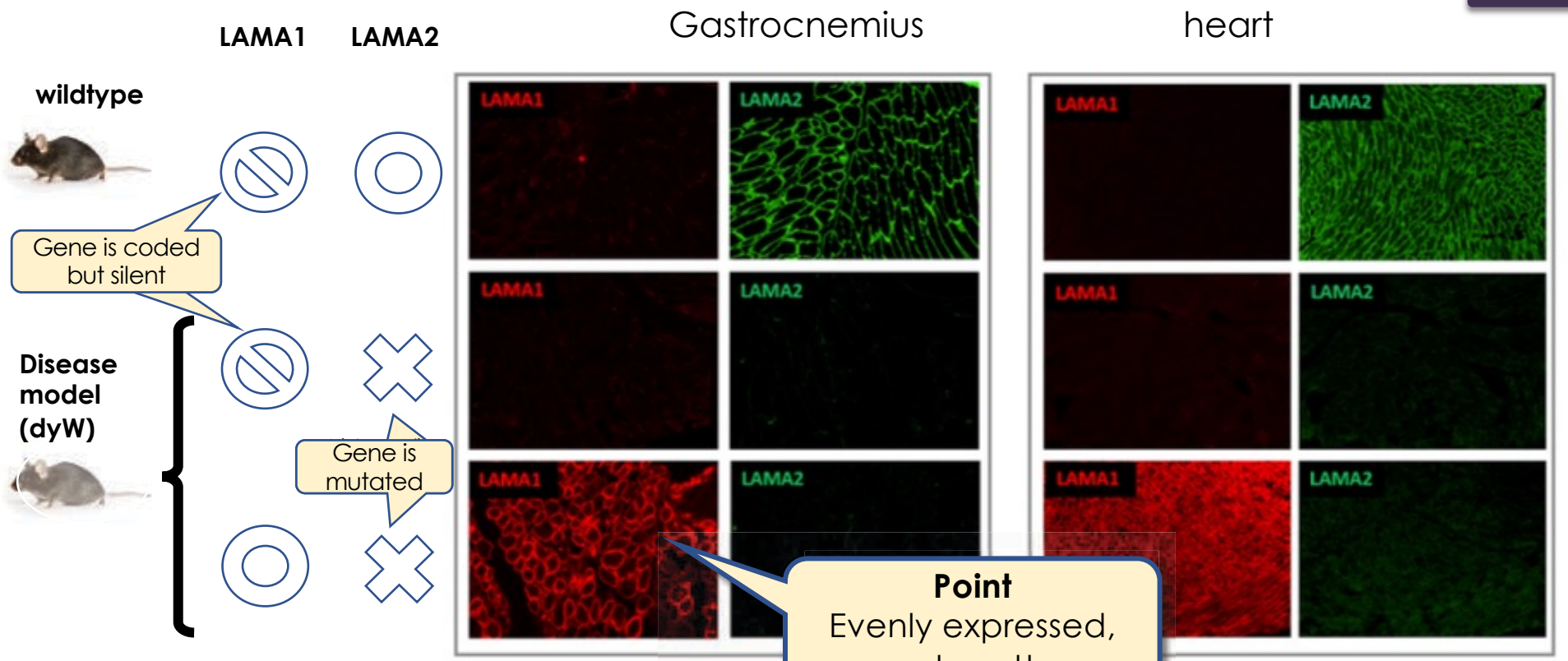
From the paper

# LAMA1 distribution by MDL-101

LAMA1 is uniformly expressed in a wide range of muscle cells





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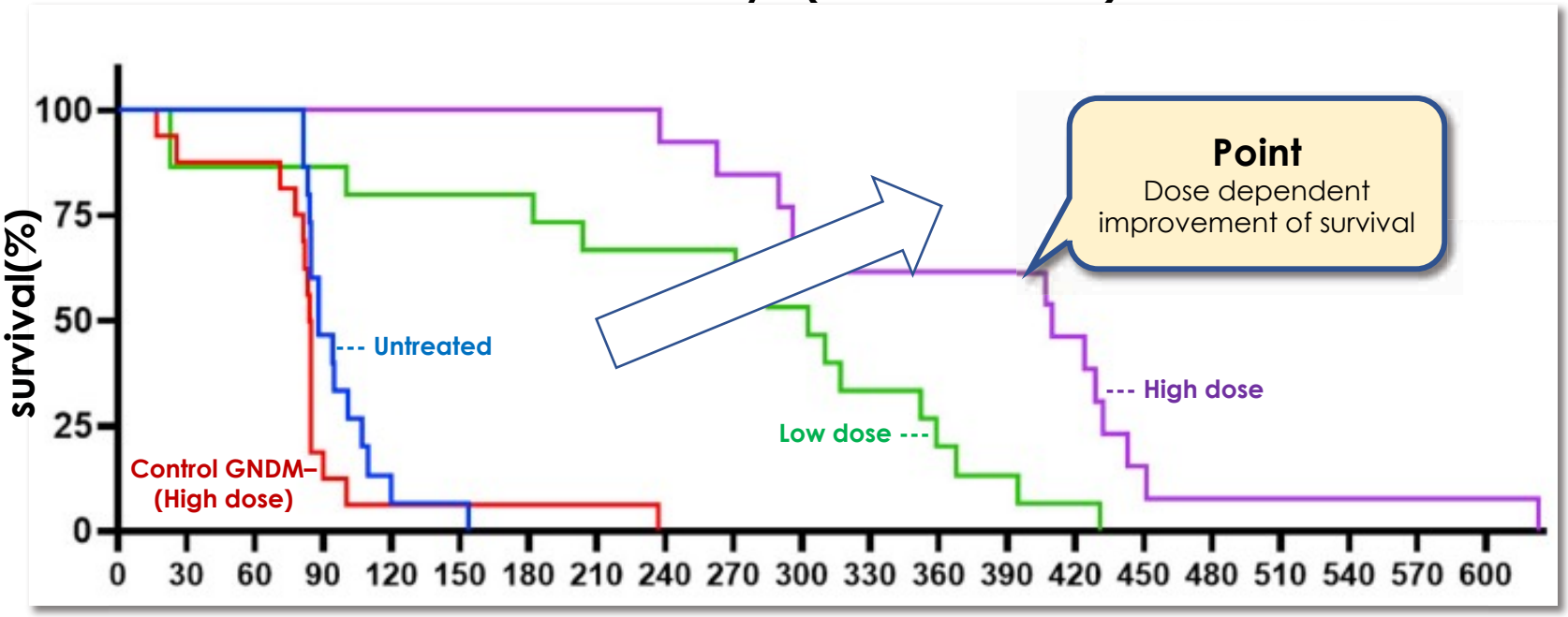
From the paper

# Survival prolongation effect of MDL-101

Survival rate was significantly improved by administration of MDL-101

## Survival curve of dyW(disease model)mice




Days post injection (d)





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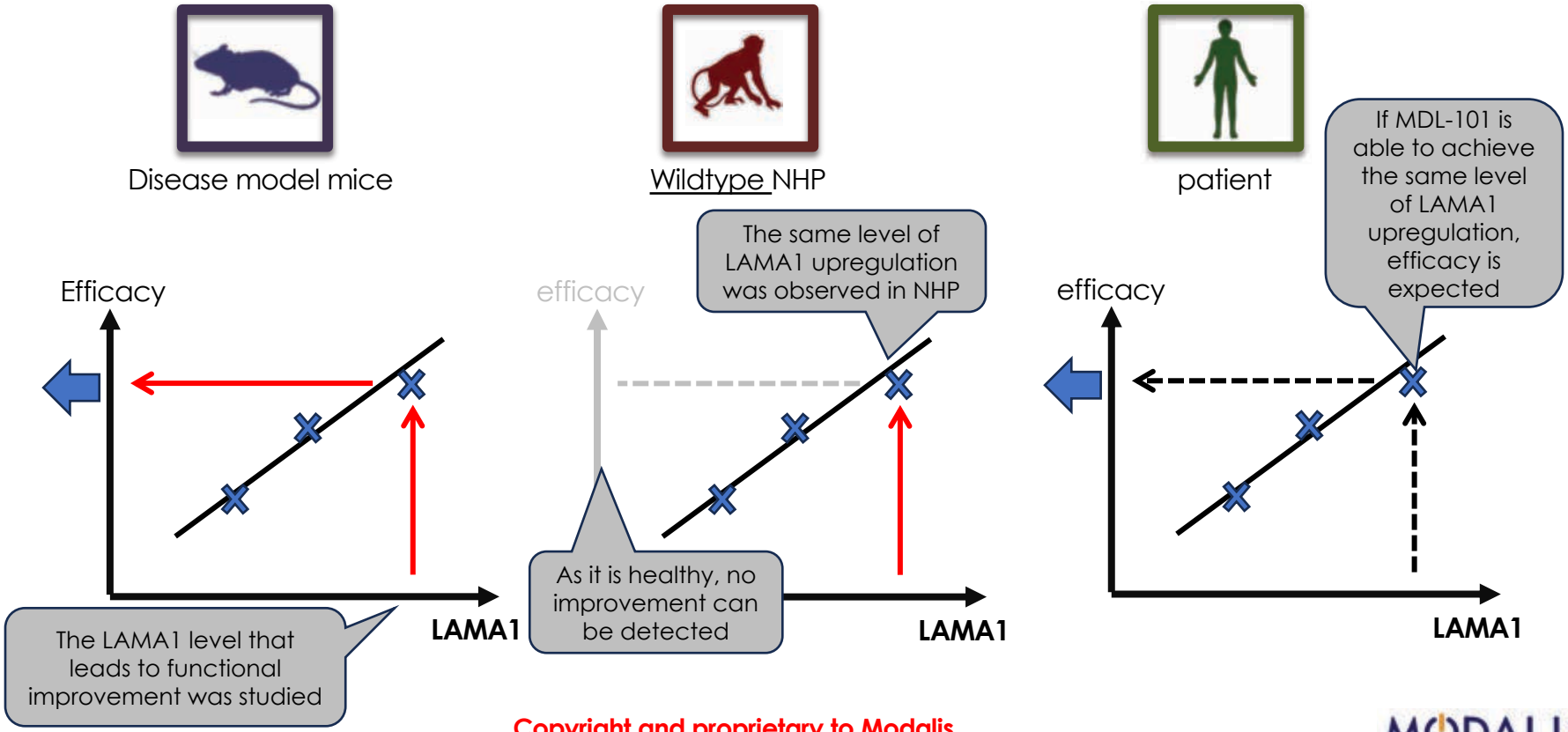
From the paper

# Estimation of drug efficacy in clinical settings

Observed LAMA1 elevation to a level at which functional improvement was observed in the disease model





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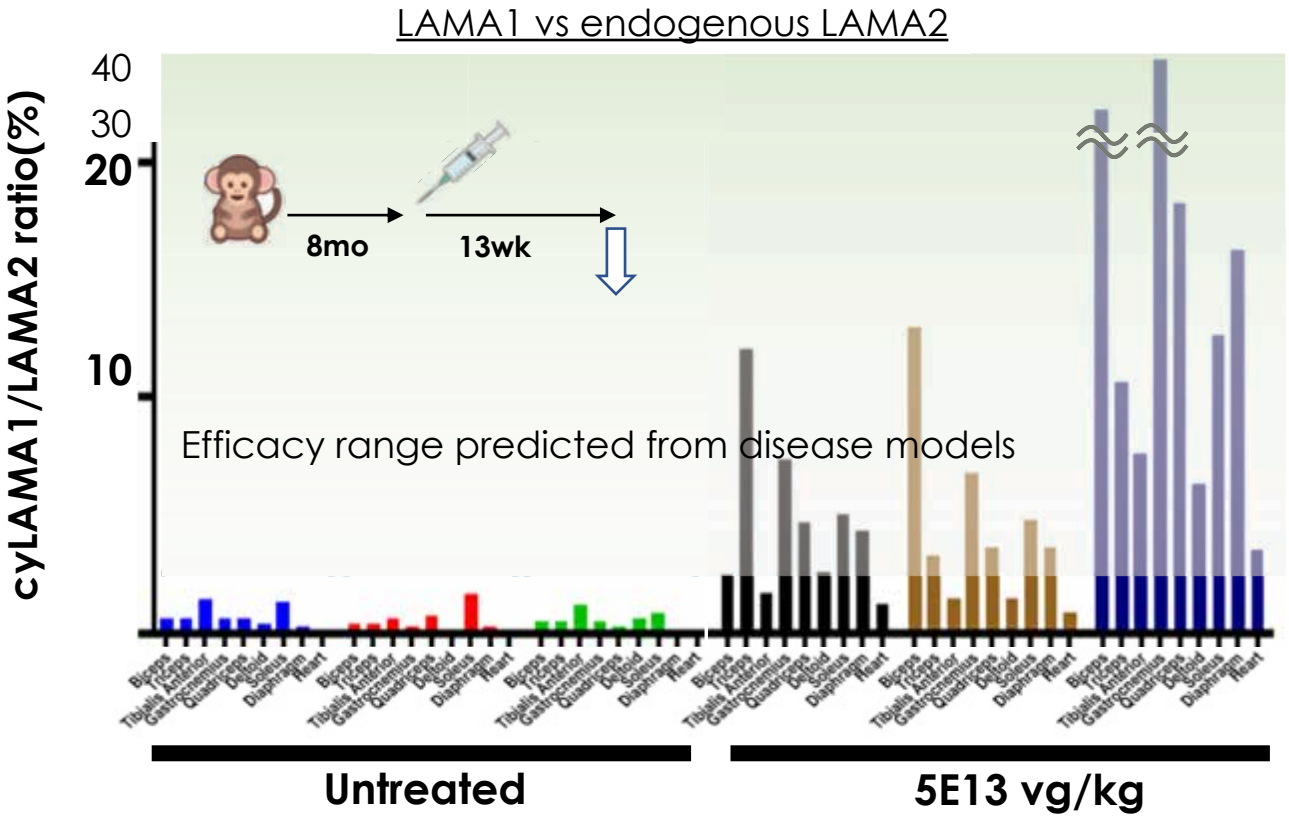
# Monkey data suggesting efficacy in humans

LAMA1 expression confirmed at levels above those associated with symptom improvement in monkeys

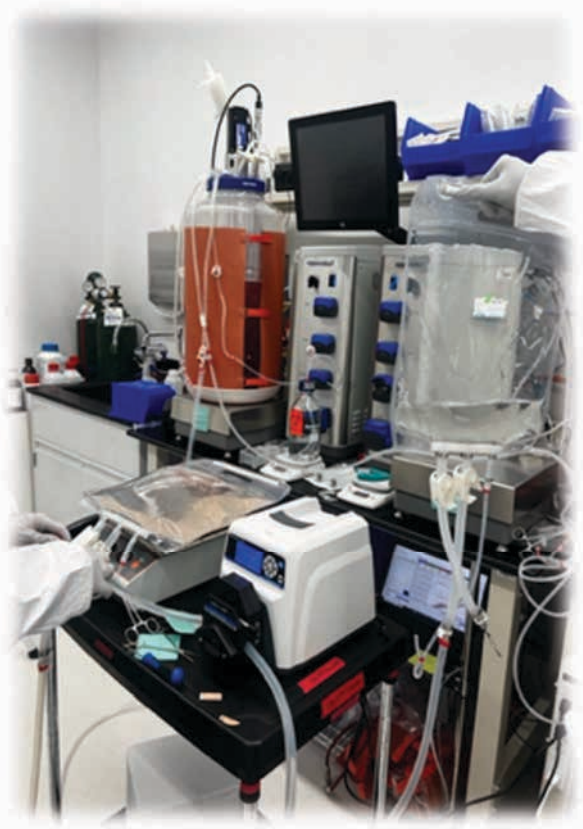


## Manufacturing

Established a manufacturing process for the engineered capsids and scale up achieved successfully

- Manufacturing process adapted to modified capsids
- Achieves reasonable production efficiency, yield, and quality
- Establishment of analytical methods also carried out in parallel
- Manufacturing plan for samples required for clinical use

GMP Manufacturing through strategic alliance with a CDMO







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NEW

# Muscle tropic Capsid

Acquired license for MYOAAV capsids from the Broad Institute

- Modified capsid with excellent muscle selectivity
  - Achieves increased efficacy and/or reduced dosage (= improved safety)
- Manufacturing method established independently by our company
  - Practical yield and quality achieved
  - Scale-up completed
  - Manufacturing for GMP production underway at CDMO
- License terms within reasonable conditions
  - Modalis will pay license fees to the Broad Institute as progress is made

MODALIS

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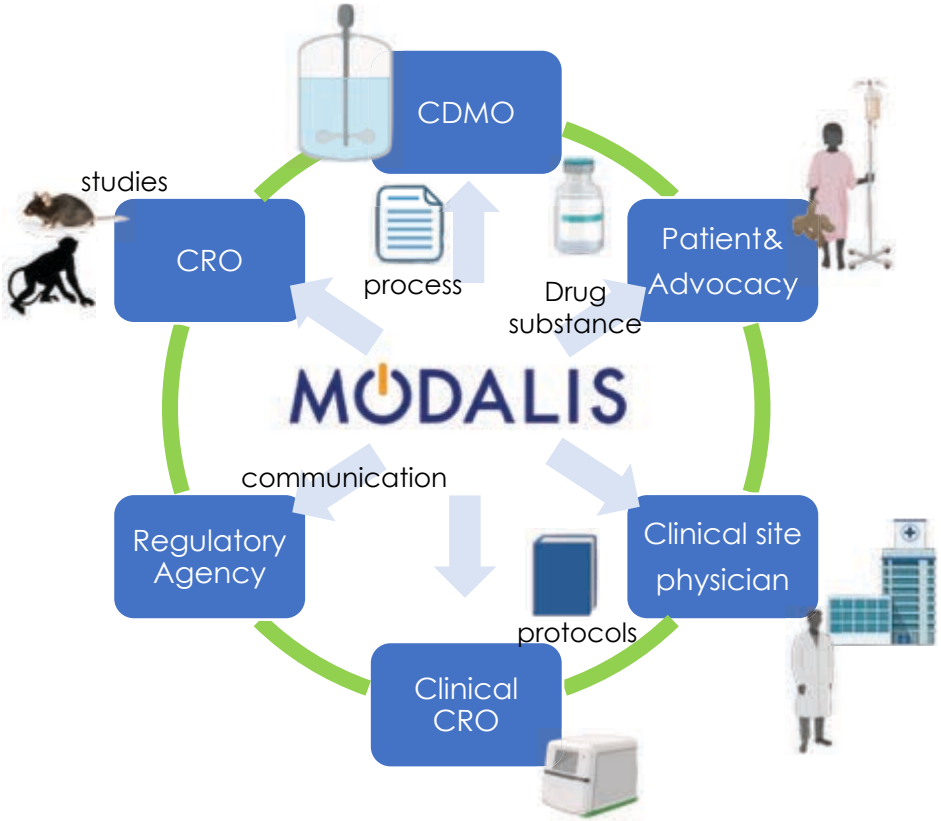
BROAD INSTITUTE

# Alignments for the clinical trial

Modalis has set up the network for the clinical trial and is working with them



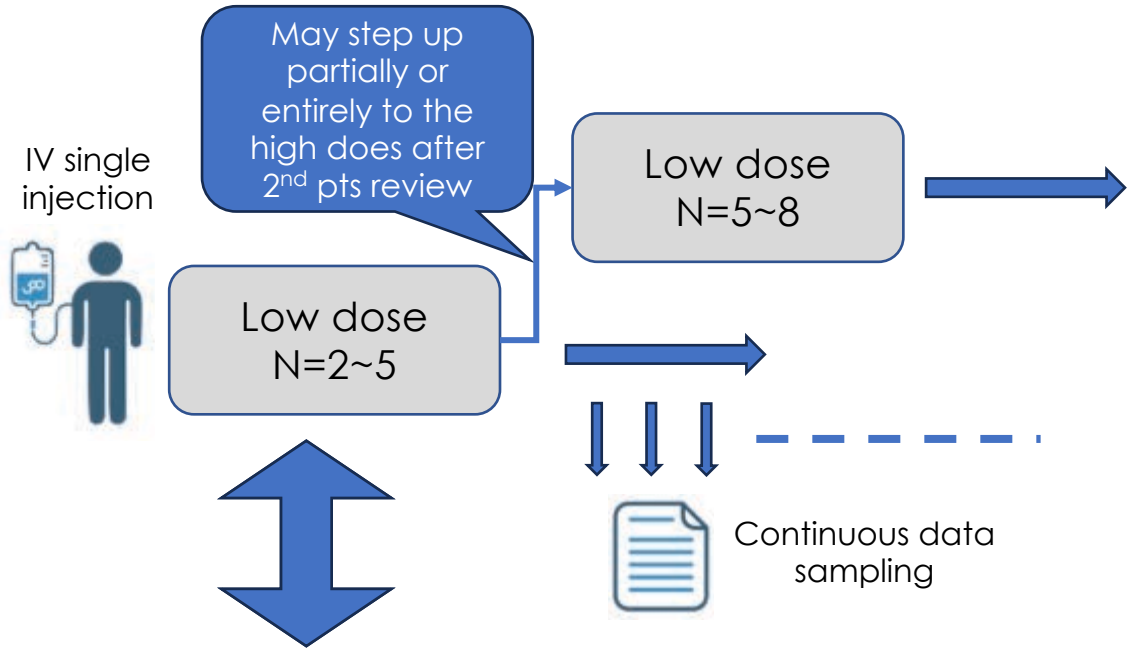

Updated

# Design of the FIH trial

Phase 1/2, open-label, dose-escalation study

Summary of MDL-101-001 phase 1/2 Open-Label Dose-Escalation Study

- Male or female patients **36 months** of age and younger
- Clinical phenotype and Lama2 gene mutations and/or decreased LAMA2 staining in muscle consistent with LAMA2-CMD
- Stable background medications
- No independent ambulation or sitting




Comparison with Natural History Study in the US, France, and Netherland (NCT06354790, NCT04299321, NCT06132750)





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New

# Summary of MDL-101 for LAMA2-CMD

Resolve technical obstacles for IND. The remainder is GLP toxicity testing and GMP

- Achieved so far
  - ✓ Confirmed efficacy in mice disease model and target engagement in NHP with the muscle tropic capsid version MDL-101
  - ✓ Completed a juvenile NHP study that confirmed comparable or better LAMA1 expression than adult NHP study
  - ✓ Confirmed long term expression of GNDM and LAMA1 in disease model mice
  - ✓ KOL meetings and drafting clinical synopsis and protocol
  - ✓ Presented development updates of MDL-101 as a late-breaking abstract at ASGCT
  - ✓ Received Pre-IND response from FDA (June)
  - ✓ Established a feasible manufacturing process with reasonable yield and quality
  - ✓ Initiating GLP tox study
  - ✓ Received follow up question to the preIND response
  - ✓ ODD and RPDD designations approval (Sep, Oct)
- Next steps:
  - ☐ Continue IND enabling GLP tox and PK/PD
  - ☐ Pilot productions and GMP campaign
  - ☐ IND filing





60

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# MDL-101 is potentially the first epigenome-editing therapeutic program to enter the clinic

01

CRISPR-GNDM efficiently targets and upregulates LAMA1 gene

02

STRONG ANIMAL POC CONFIRMED IN MICE *IN VIVO* INCLUDING FUNCTIONAL IMPROVEMENT

03

THE PROCESS TO MANUFACTURE THE MOLECULE WITH MUSCLE-SPECIFIC VECTOR HAS BEEN ESTABLISHED WITH FEASIBLE PRODUCTIVITY, YIELD AND QUALITY

04

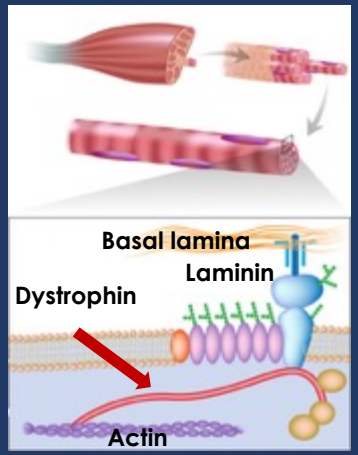
THE INJECTION OF THE PRODUCT DID NOT CAUSE DETRIMENTAL SAFETY ISSUES IN MICE AND NHPS

# 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





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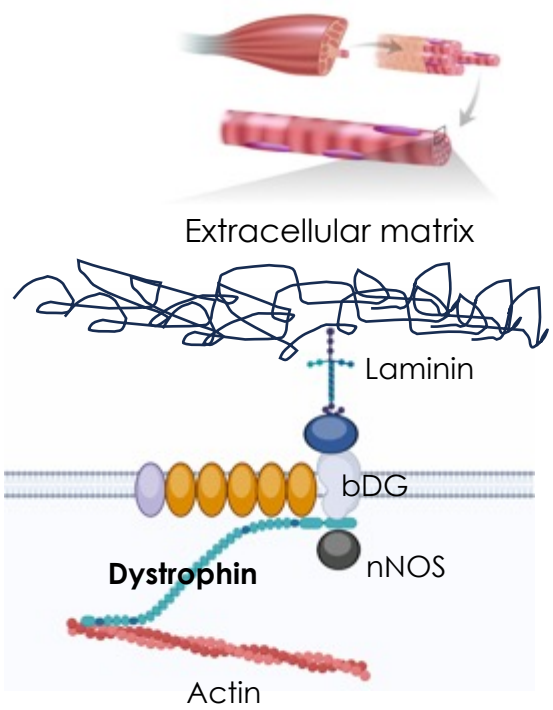
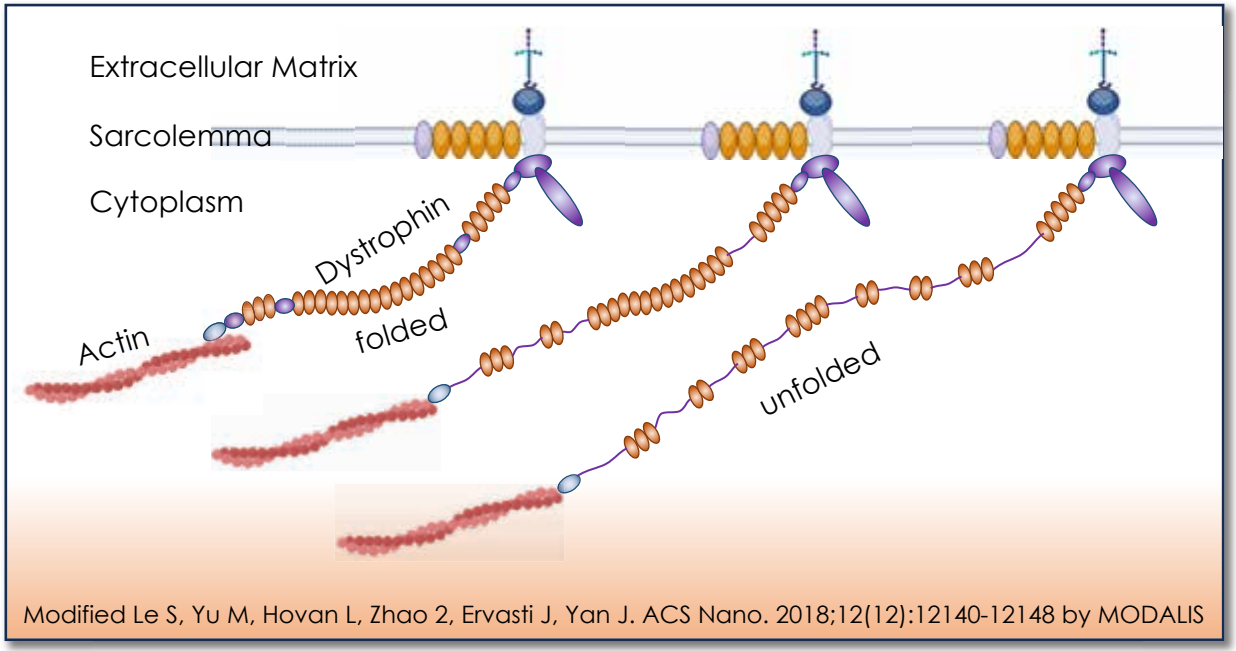
# Dystrophin's function

Functions as a shock absorber and signal transmitting molecule in muscles

**Dystrophin location**




**Dystrophin stretches and contracts to connect the cell membrane and actin**





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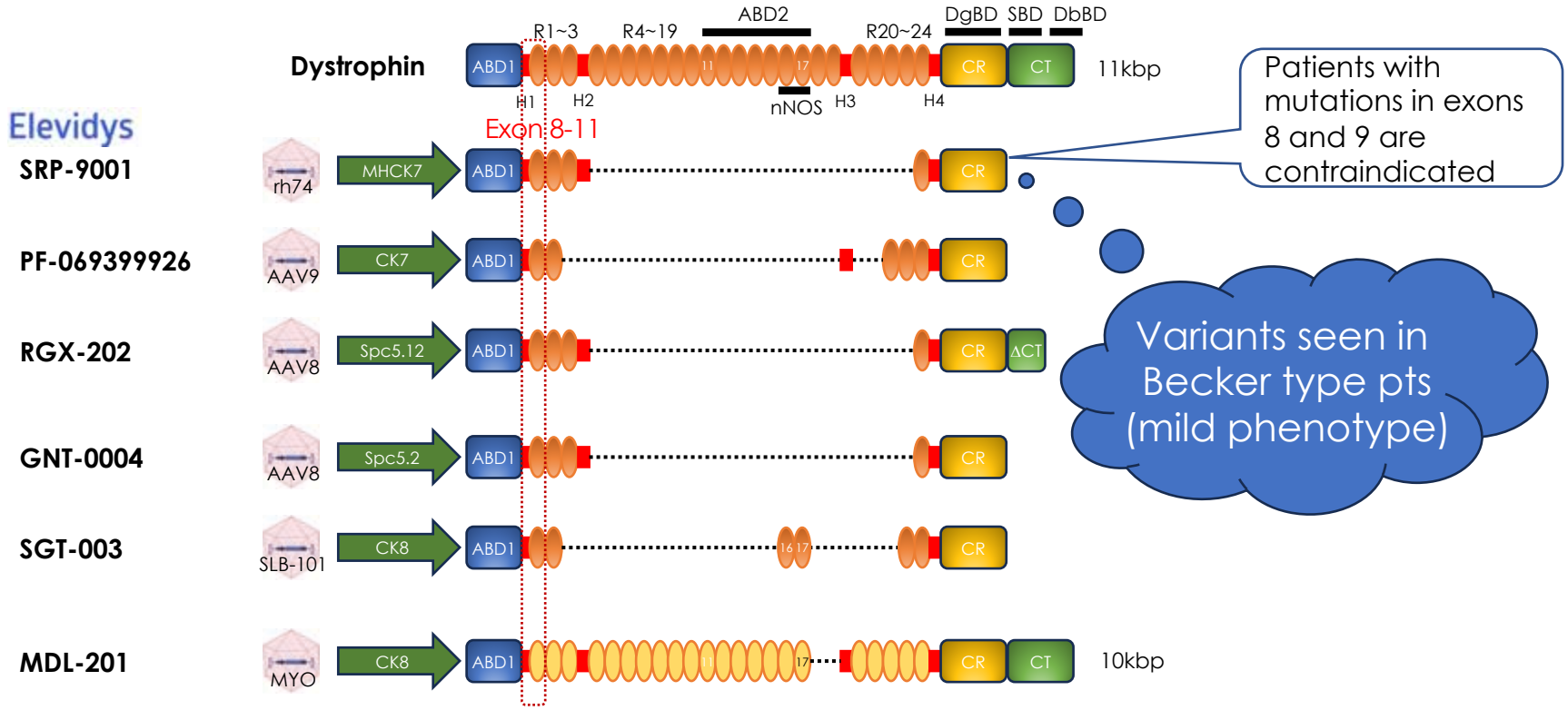
# micro-Dystrophins payload comparison

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

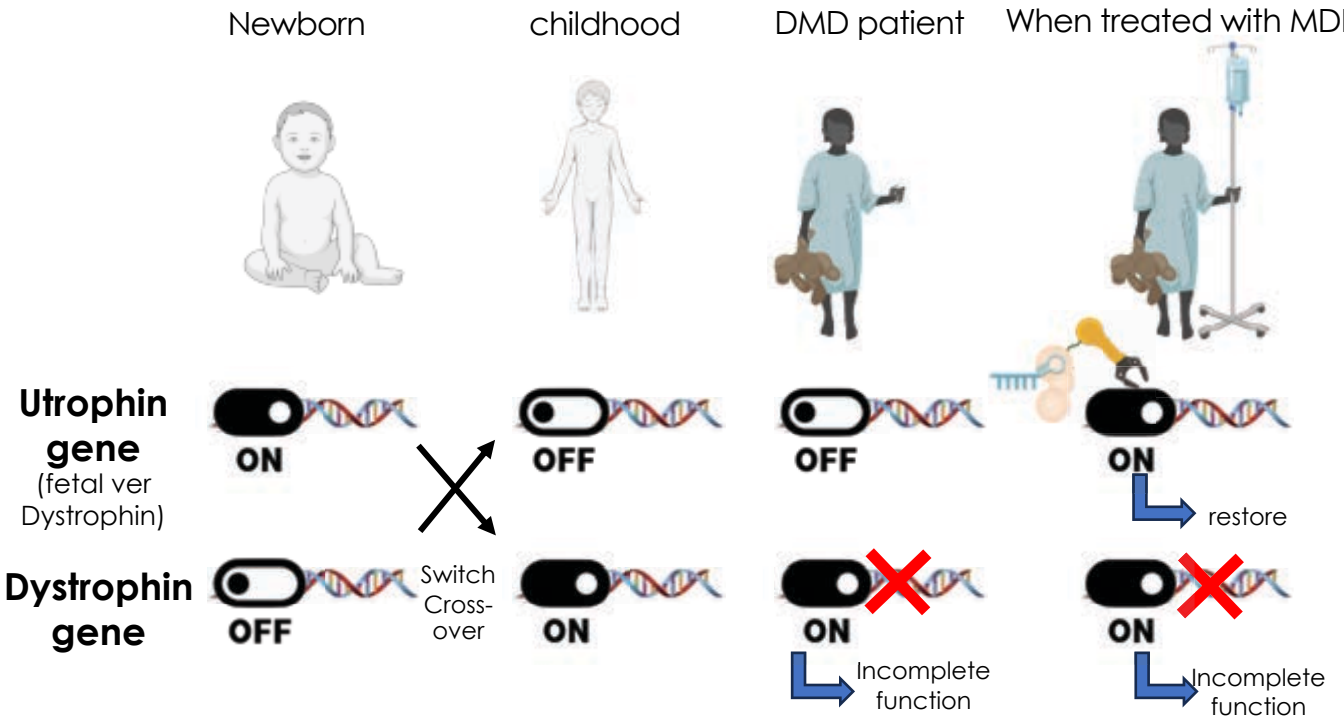
**Dystrophin/Utrophin and mini-Dystrophin structure**

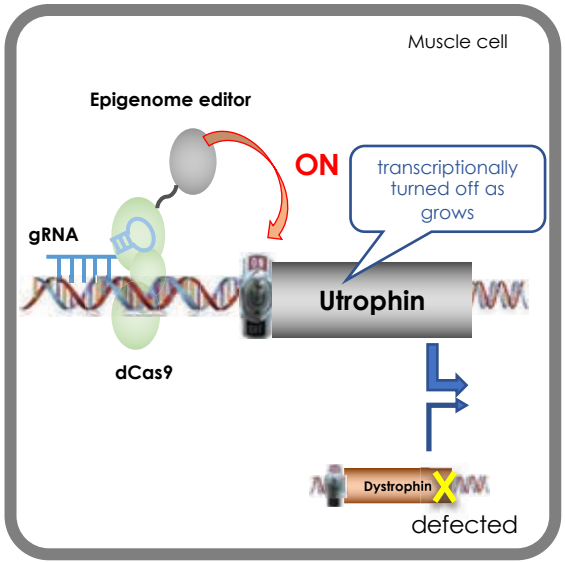



Modified from Crudele &Chamberlain, 2019

# 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





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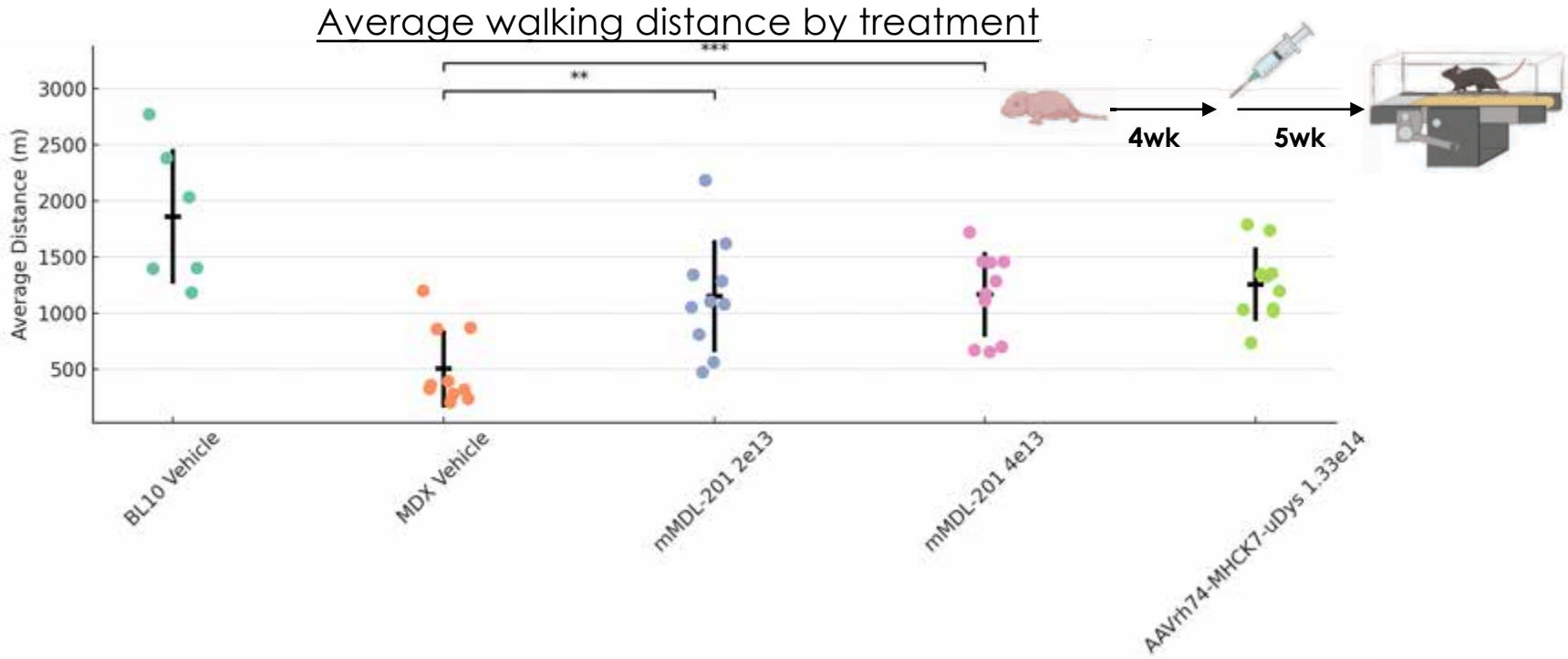
NEW

# 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).





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# MDL-201 potentially is a best-in-class DMD gene therapy that surpasses micro/mini-dystrophin approaches

01

Utrophin retains functional domains that are absent in µ-dystrophin

02

MDL-201 shows higher functional improvement than µ-Dystrophin in mouse pathological models

03

MDL-201 shares the same platform as MDL-101, on which much experience has been accumulated





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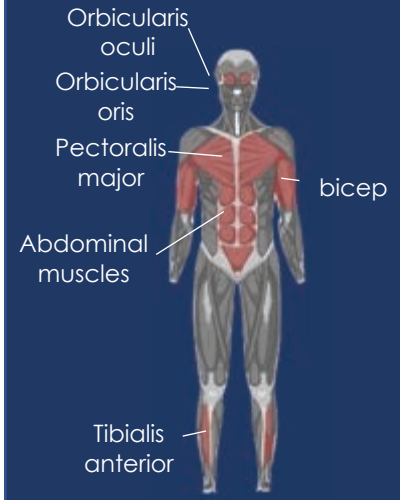
# Facioscapulohumeral Muscular Dystrophy (FSHD)

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<br>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





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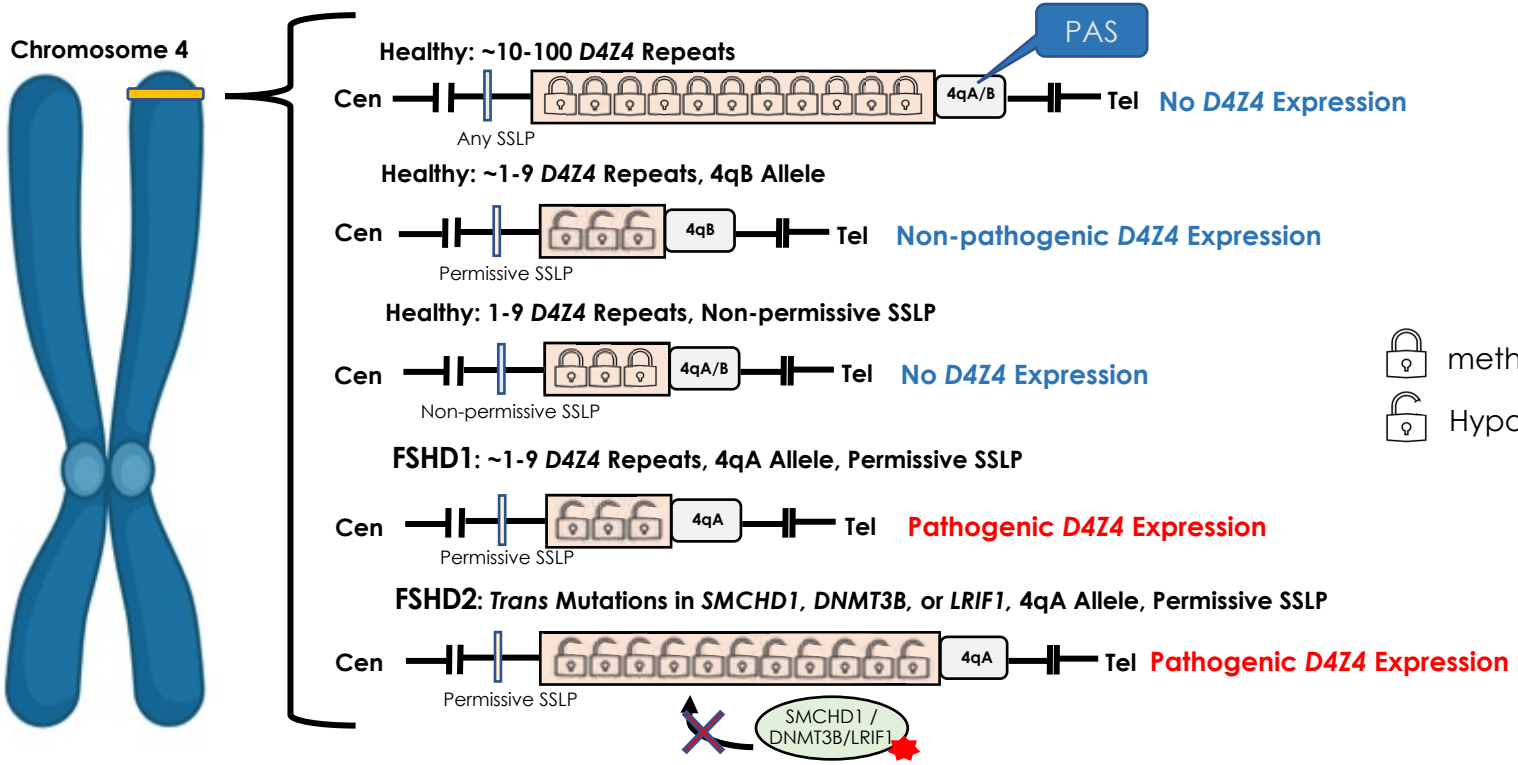
# FSHD disease mechanism

Inappropriate expression of toxic Dux4 in skeletal muscles




DeSimone et al. 2020, *Dis Model Mech*

SSLP: Simple Sequence Length Polymorphism PAS: polyadenylation signal





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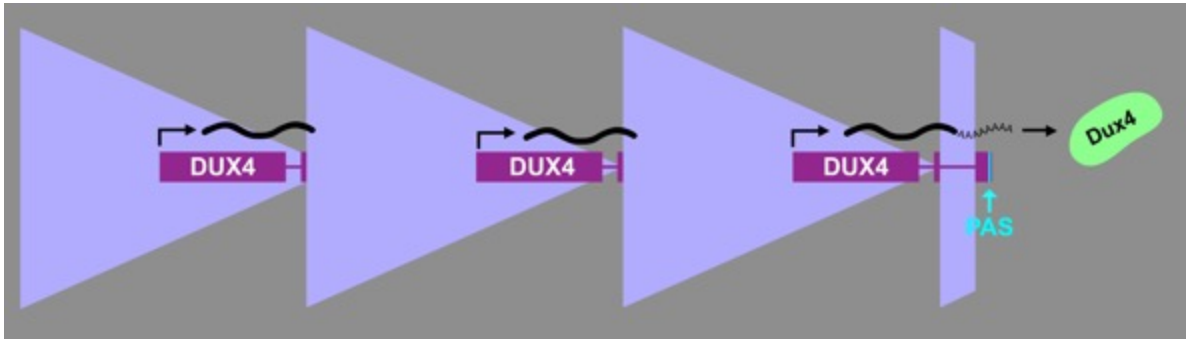
# Why Epigenome editing makes sense for treating FSHD?

DUX4 Gene in the Last D4Z4 Repeat Codes for a Pathogenic Protein




- Each D4Z4 repeat contains a copy of the DUX4 gene, put the **polyadenylation signal(PAS=stabilizer)** is absent, so any transcribed RNA is unstable
- The DUX4 gene in the final repeat can read through the end of the array and incorporate a PAS(if the 4qA haplotype is present), resulting in synthesis of the pathogenic protein
- Dystrophy is presumably caused by the **cytotoxicity of the DUX4 protein**
- 1)The size of the array, 2)the presence of a nearly identical array on chromosome 10, and 3) the presence of individual D4Z4s spread across the genome makes traditional CRISPR-Cas9 gene replacement, base-editing, and indel approaches untenable
- Using a CRISPRi approach to inhibit expression of all D4Z4s is a more plausible approach





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Following the SOLVE FSHD–Sponsored XPRIZE Healthspan Bonus Prize, SOLVE FSHD itself has also decided to provide research and development grants



*"I prefer not to sit in the stands, but to be on the court to solve this disease that is so very close to my heart."*

Chip Wilson
Founder of SolveFSHD and Lululemon

- Selected lead gRNA and filed patent application
- Restarted MDL-103, a drug candidate for the treatment of FSHD
- Aiming to conduct clinical trials after verification using animal models in collaboration with universities and other research institutions

71 Source: Solve FSHD website



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# Myotonic dystrophy type 1(DM1)

extension of CTG repeat in 3' UTR of DMPK gene

| **MDL-202**<br><br>Potential to be the first-in-class and the first DM1 treatment | | | |
|---|---|---|---|
| | **Prevalence** | **1-4.8 in 10,000**<br>(1 in 2,300*) | DM is the most common muscular dystrophy among adults of European ancestry |
| | **Disease onset** | DM1 can occur from birth to old age | Age at onset is between 20 and 70 years (typically onset occurs after age 40) |
| | **Disease Burden** | muscle weakness and wasting (atrophy), myotonia | DM causes weakness of the voluntary muscles, although the degree of weakness and the muscles most affected vary greatly according to the type of DM and the age of the person with the disorder |
| | **Cause of disease** | Microsatellite expansion in 3' UTR of DMPK gene | Extended CTG repeat capture MBNL1 protein which is essential for normal splicing |
| | **Market size** | **$2.2B #**<br><br>By 2032 | $80M market as of 2022 without any treatment but is expected grow |

*Source: Myotonic Disease Foundation # DelveInsight (including both DM1 and DM2)





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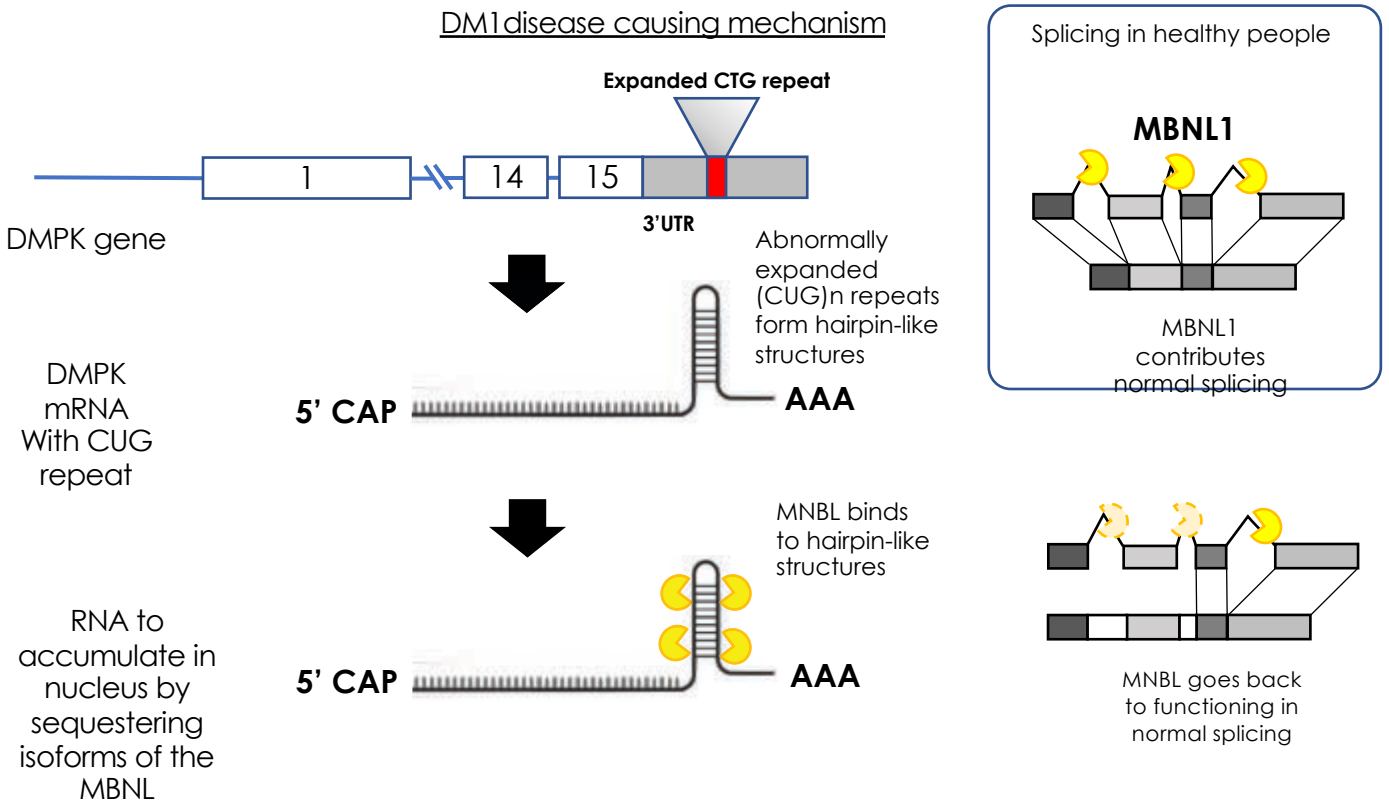
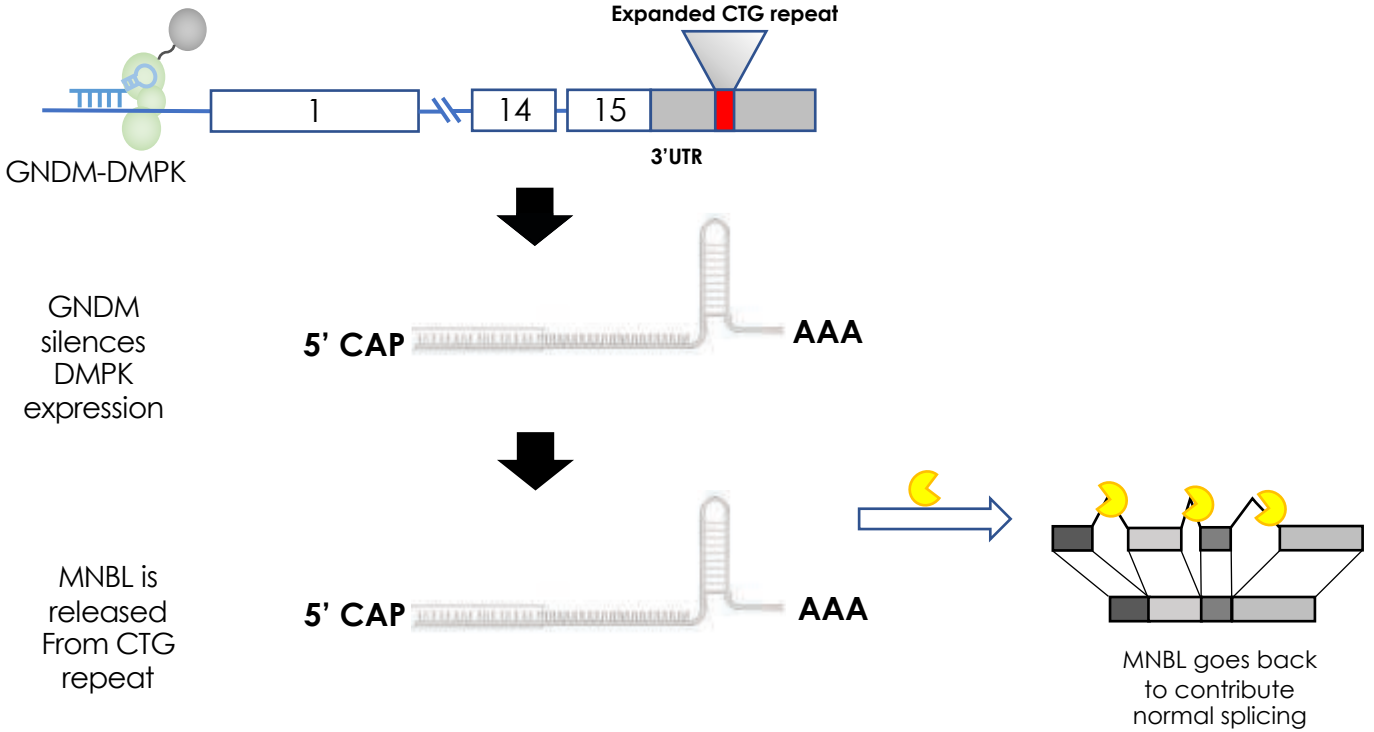
# DM1 is caused by abnormal splicing rooted from CTG extension in 3'UTR of DMPK gene



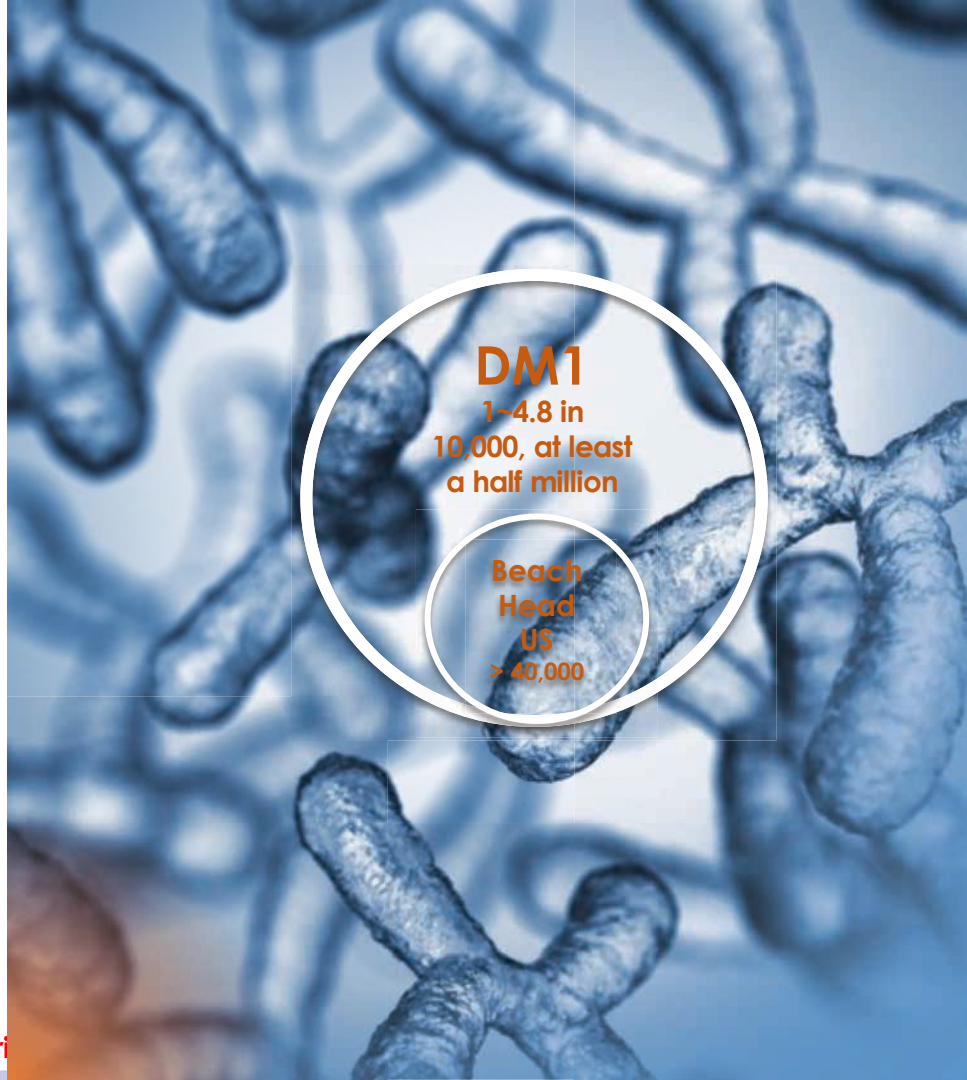
# MDL-202 silences DMPK expression and release splicing protein MNBL to function properly in muscle cells

MDK-202's mechanism of action



## DM1 has relatively large prevalence in muscular disorders

- Prevalence was estimated at 1 in 8,000-10,000, but recent population-wide screening estimated: mutation prevalence of 4.8 in 10,000 individuals
- DM1 can affect newborns to older adults
- US>40,000 individuals (Japan>10,000)




Source: Marta Pascual-Gilabert, The myotonic dystrophy type 1 drug development pipeline: 2022 edition

# MDL-202 offers a feasible and fastest path to the clinic

01

Modalis has candidate Myo tropic AAV-based molecules confirmed in NHP

02

Modalis has established a manufacturing process available for large-scale production

03

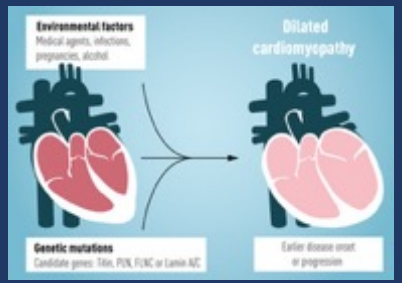
Modalis had INTERACT and PreIND meetings and knows what is required for IND

# Dilated Cardiomyopathy (DCM)

*A condition in which the heart becomes enlarged*

## MDL-105

Potential first-in-class precision medicine targeting DCM caused by TTN truncated variant mutations




| | | |
|---|---|---|
| **Prevalence** | **1 in 250-2,500#** | • ~20% of DCM is estimated to be caused by TTN variant<br>• Half is by truncated variant |
| **Disease Onset** | Middle age around **20-60 yo** | |
| **Disease Burden** | Five-year survival rate is about **50%*** | • Without treatment, the 1-year survival is 70%–75%, with a 5-year survival of as low as 50%<br>• Patients goes to a heart transplantation |
| **Disease Causing Gene** | Mutation in **TTN, MYH7, MYBPC3** | |
| **Commercial opportunity** | **>$300M** | • Estimated to grow at CAGR=4.1% and reach $421M by 2027# |

Source: picture MayoClinic *https://doi.org/10.1111/joim.12944 #Global Industry Analysts, Inc





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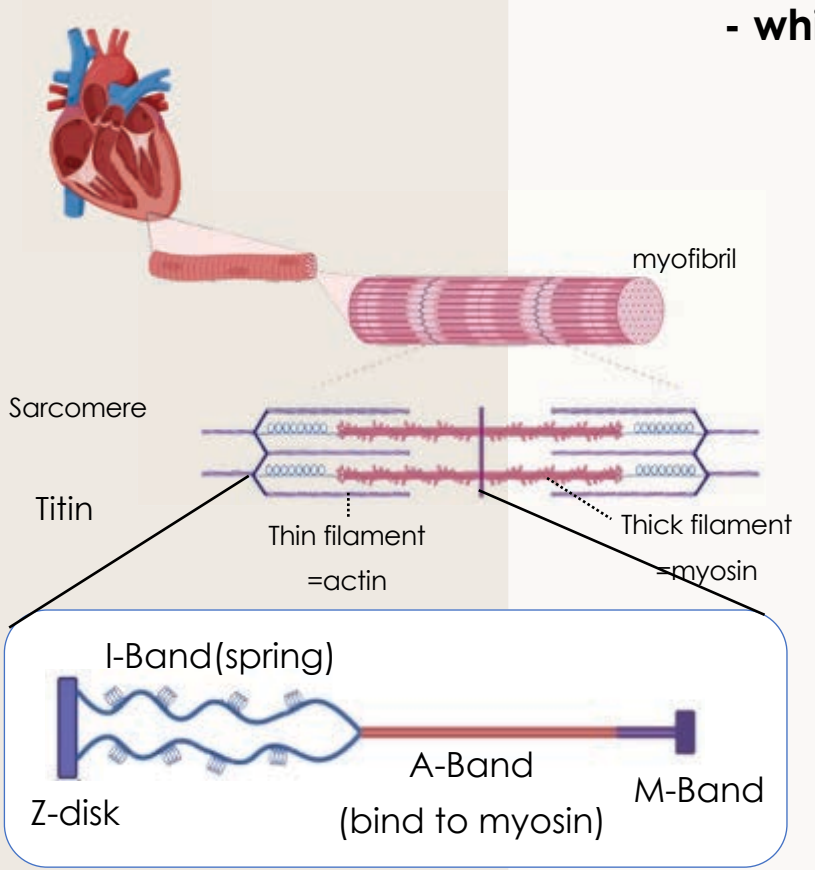
# TTN is the largest human protein - which is too large for AAV packaging

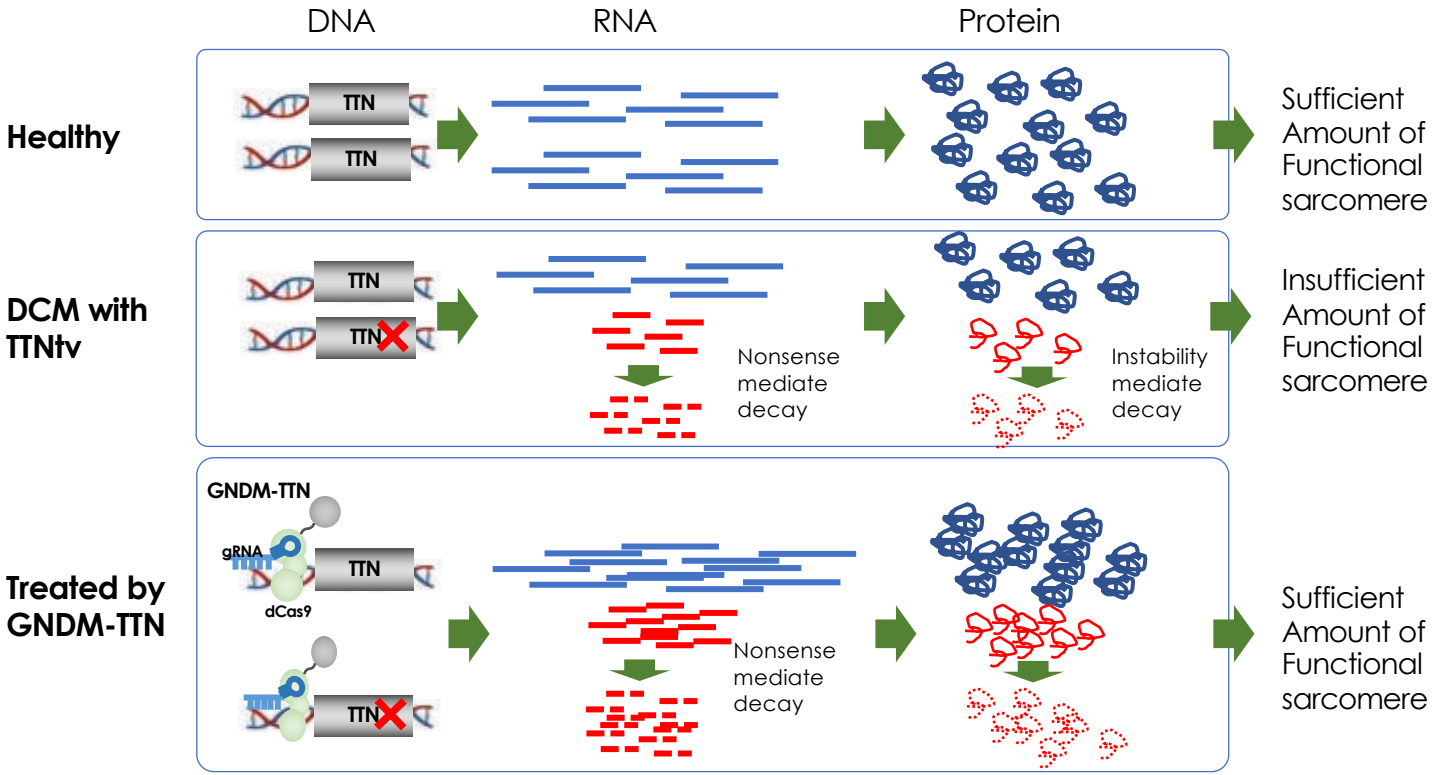



- **Largest** human protein
  - 35,000 amino acids /17kb
  - 363 exons
  - Acts as spring in sarcomere
  - Tension during relaxation
- **Abundant** in human body
  - Third most abundant protein in muscle next to myosin and actin
  - Adult human contains approximately 0.5 kg of titin
- **~90% mutations** are truncated variant (TTNtv)

# MDL-105 returns TTN protein levels to normal through transcriptional activation of TTN

Restore normal sarcomera levels by boosting TTN

*Working hypothesis of GNDM based DCM therapy*





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## Why GNDM for TTN?

- TTN mutations are “definitive” for DCM (ClinGen)
- TTN mutations are associated with 15-23% of DCM cases
- TTNtv is a haploinsufficiency rather than dominant negative
  - produce non-functional protein
- No direct approach to target TTN has been reported as too big to treat

Targeting TTN by GNDM is a unique and differentiated approach





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# Status of Development of MDL-105

- Achievements so far
  - Human gRNA screening completed
    - Filed patent
  - Introduced mice disease model
    - The model is not reproduced in our hands
  - Initiated animal PoC study
    - With muscle tropic capsids
  - Discussion on the strategy with CV experts

- Next steps
  - Explorer disease models that can evaluate molecule s with
  - Explorer funding including partnership opportunities
  - Reconsider timing of PreIND contingent on identifying and pursuing disease model study and funding.

## **Tauopathy** (incl. Alzheimer's Disease)

Neurodegenerative disorders caused by misfolding of the tau protein

| **MDL-104**<br><br>Potentially best-in-class molecule by silencing Tau expression | | | |
|---|---|---|---|
| | **Prevalence** | **1 in 9 above 65*** <br>55 million in ww | 60-80% of cognitive disorders |
| | **Disease Onset** | Progressed in **6-8 yrs** | Slow and chronic progression, depending on the individual |
| | **Disease Burden** | progressive disease beginning with mild memory loss | possibly leading to loss of the ability to carry on a conversation and respond to the environment. |
| | **Disease Causing Gene** | Multiple causes have been proposed but not yet known | APO-E, PSEN1, PSEN2 and many other gene mutations reported<br>All mutations are associated with Aβ hyperactivity |
| | **Commercial opportunity** | **$4.2B** in 2022# | Estimated to grow to $15.6B by 2030# |

Source: * Alz.org (for Alzheimer Disorder) #Grand View Research





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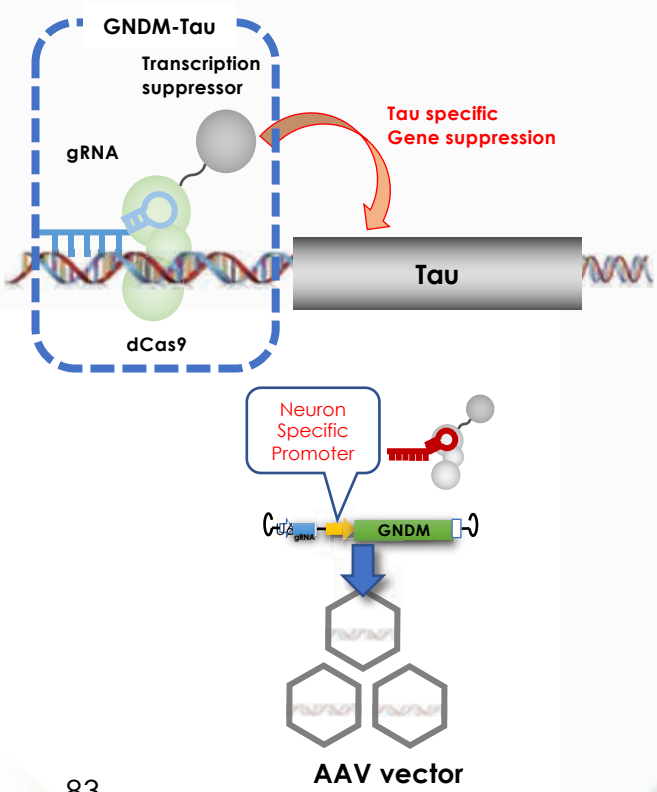
# MDL-104 suppress Tau at transcription level

MDL-104's mechanism of action




- Reversing the pathogenic conditions of Tauopathy by partial or full suppression of Tau gene that leads to reduction of Tau protein in the brain
- GNDM-Tau, driven by neuron specific promoter delivered by AAV9 or alternative capsid
- ICM (intra-cisterna magna) injection to achieve efficient brain delivery and to avoid high-dose AAV related toxicities

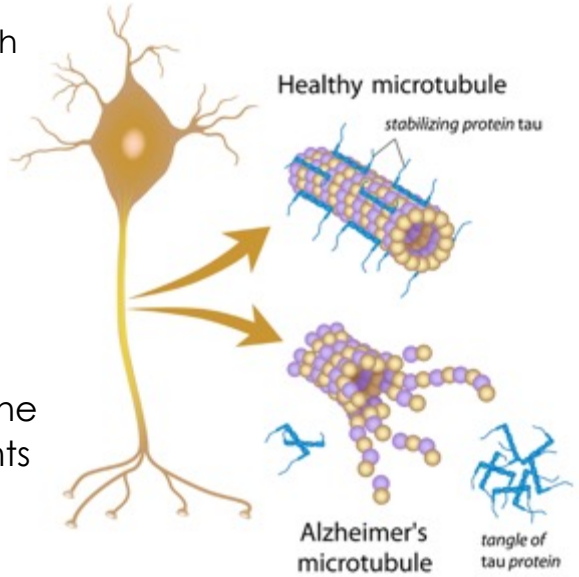
# AD and FTD are our primary choice for the initial indication but multiple potential diseases

| | Prevalence | Target in Brain | Major symptom | Progression |
|---|---|---|---|---|
| **AD** | 1 in 9 above 65<br>1 in 3 above 85 | cortex and hippocampus | memory, movement, language, judgment, behavior, and abstract thinking | 6-8yrs |
| **CBD** | ~5 in 100k<br>low in Asian | multiple areas of the brain | Balance, Memory, muscle control, speech | 6-8yrs |
| **PSP** | 5-17 in 100k | Basal ganglia and brain stem | movement, control of walking (gait) and balance, speech, swallowing, eye movements and vision, mood and behavior, and thinking (Perkinson-like symptom) | ~7yrs |
| **FTD** | 2-10% of dementia | frontal and temporal lobes | apathy, change in personality, lack of inhibition, obsessive behavior | ~8yrs |
| **AGD** | 18.8% to 80% of PSP<br>41.2% to 100% of CBD | Limbic system | cognitive decline, personality changes, urine incontinence and cachexia | 3 months |
| **Chronic traumatic encephalopathy** | 0.79% of population | Various | depression, explosivity, short-term memory loss, executive dysfunction and cognitive impairment | Decades |
| **Post-encephalitic parkinsonism** | Unknown | Substantia nigra | Parkinsonism | Unknown |
| **Subacute sclerosing panencephalitis** | 2:10,000 people infected with measles | cortical atrophy, white matter lesions | personality changes, mood swings, depression, muscle spasms, seizures, loss of vision, and dementia | 4 yrs |

AD: Alzheimer's Disease
CBD:Corticobasal degeneration
PSP: progressive supranuclear palsy
FTD: Frontotemporal dementia
AGD: Argyrophilic grain disease

## Tau is a center of attention in treating Alzheimer diseases

- Tau correlates with clinical symptoms and neuronal loss in Alzheimer's disease and other primary tauopathies.
  - Tau aggregates and tangles are thought to induce neuronal degeneration, synaptic loss and cell death
  - Tauopathies include a range of high value and orphan clinical diseases
    - AD (Alzheimer's Disease)
    - FTLD (Frontal Lobar Degeneration)
    - PSP (Progressive Supranuclear Palsy)
    - CBD (Corticobasal Degeneration)
    - Pick's disease
- Tau is likely to be a better target than Aβ because the tau burden correlates better with clinical impairments than does the Aβ burden
- Tau knockout has few adverse effects
- Therefore, reducing total Tau expression is a logical therapeutic strategy




*Source: Congdon EE*, Nature Review Neurology 2018 "Tau-targeting therapies for Alzheimer disease"





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# Status of Development of MDL-104

- Achievements so far
  - Evaluation of the human version molecule with hTau and humanized Tau mice
    - Robust Tau suppression is confirmed both in Cortex and Hippocampus.
  - Initiation of biodistribution study in NHP
  - Discussion on target indications with KOLs
    - Alzheimer's disorder (AD) and/or Frontotemporal dementia (FTD)

- Next steps
  - Explorer delivery methods including CNS tropic capsids
  - Reconsider timing of PreIND and IND contingent on identification of delivery tools and funding.

hTau mouse（mMAPT knockout, hMAPT transgenic)
humanized MAPT mouse （aka MAPT（H2.1）-GR = mouse MAPT replaced with human MAPT gene)





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# Angelman Syndrome

CNS disorder caused by impaired UBE3A gene expression

**MDL-206**

Potentially first-in-class treatment by unsilencing UBE3A gene expression

| | | |
|---|---|---|
| **Prevalence** | **1 in 10,000 to 20,000** | • 60,000 patients WW (2017)<br>• 20,000 in US |
| **Disease Onset** | typically diagnosed at **6 to 12 months** | Seizures may begin at 2 to 3 years. |
| **Disease Burden** | Developmental delay | small head, specific facial appearance, intellectual and developmental disability, speech impairment, balance and movement problems, seizures, and sleep problems |
| **Disease Causing Gene** | Mutation in maternal allele of **UBE3A** | 5-26% has unknown mechanism |
| **Commercial opportunity** | **$330M** 2017 | US, EU, and Japan |

Source: Orpha.net

Angelman syndrome Market and Epidemiology forecast (delveinsight.com)





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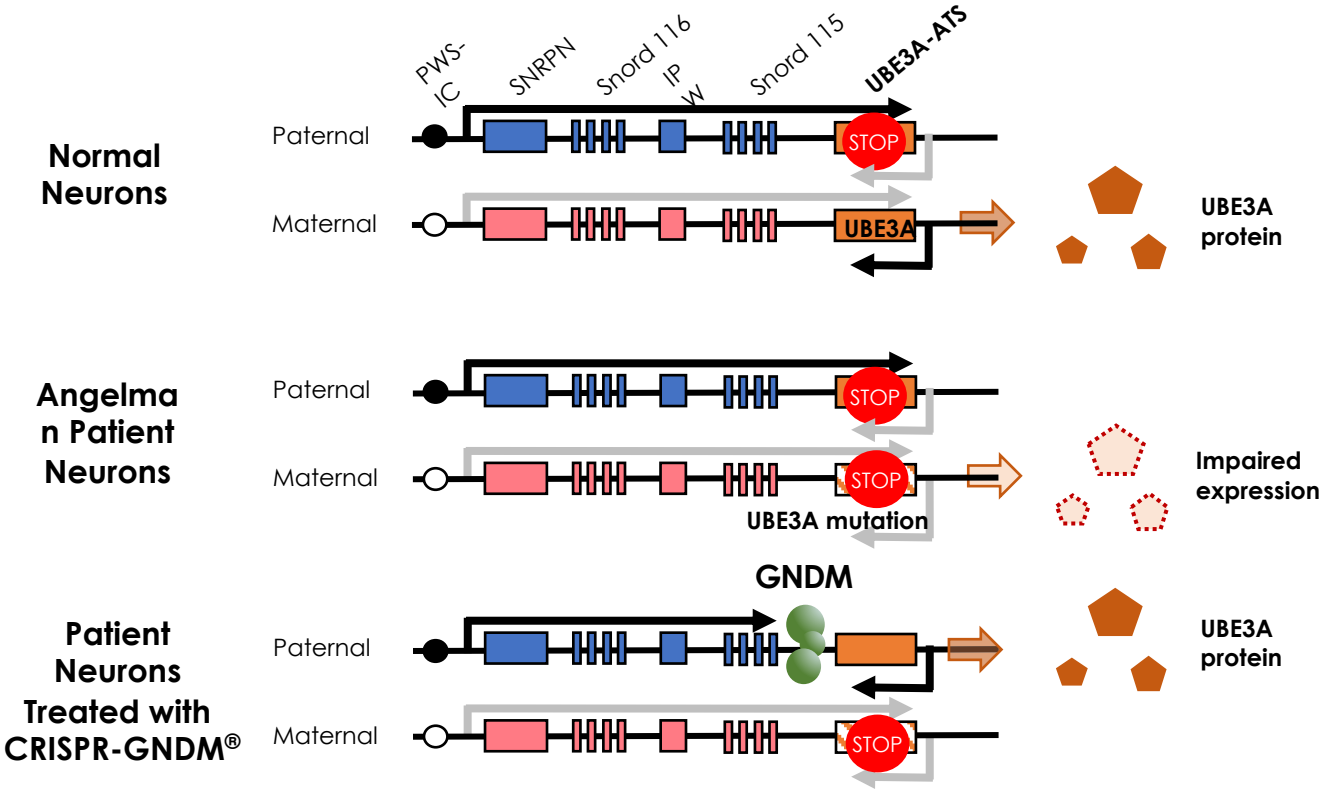
## What is Angelman syndrome?

- Angelman syndrome (AS) is a rare neuro-genetic disorder that occurs in **one in 15,000 live births** or **500,000 people** worldwide.
- It is caused by a loss of function of the **UBE3A gene** in the 15th chromosome derived from the mother.
- Angelman syndrome shares symptoms and characteristics with other disorders including **autism**, **cerebral palsy** and **Prader-Willi syndrome**.
- People with AS have developmental problems that become noticeable by the **age of 6 – 12 months**. Other common signs and symptoms usually appear in early childhood like **walking and balance disorders**, **gastrointestinal issues**, **seizures** and **little to no speech**.

Source: Angelman Syndrome Foundation

# By blocking ATS transcript, GNDM un-silences UBE3A expression



# Status of Development of MDL-206

- Achievements so far
  - Animal PoC established with disease mice model
  - Up-regulates the UBE3A gene by GNDM based molecule is confirmed with UBE3A heterozygous mice

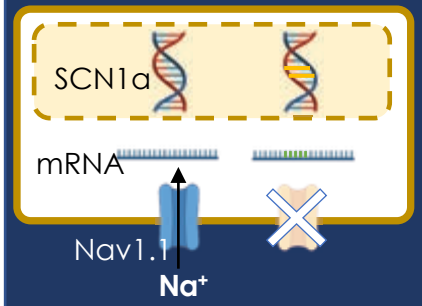
- Next steps
  - Verification of superiority over approaches using other modalities
  - Planning and validation of clinical development strategies, including route of administration, capsid modifications, etc.
  - In parallel, partnering efforts to fund the program

# Dravet Syndrome

*A type of epilepsy caused by haploinsufficiency mutation in SCN1A gene*

## MDL-207

Potential to be the best-in-class and first precision medicine for Dravet Syndrome




| | | |
|---|---|---|
| **Prevalence** | **1 in 20,000-40,000*** ~10,000 in US | |
| **Disease Onset** | Seizure starts between **1 and 5 yo** | |
| **Disease Burden** | **10-20%** of DS patients pass away before reaching adulthood | • SUDEP (sudden unexpected death in epilepsy patients)<br>• status epilepticus (SE).<br>• Autism-like spectrum (ASD)<br>• Attention deficit hyperactivity disorder (ADHD) |
| **Disease Causing Gene** | **SCN1A** | • Haploinsufficiency of SCN1A |
| **Commercial opportunity** | **$500M+** | • Currently with no curable drugs<br>• The market is estimated to grow at CAGR of 9.6% # driven by new therapeutics |

Source: *Epilepsy foundation #Technavio





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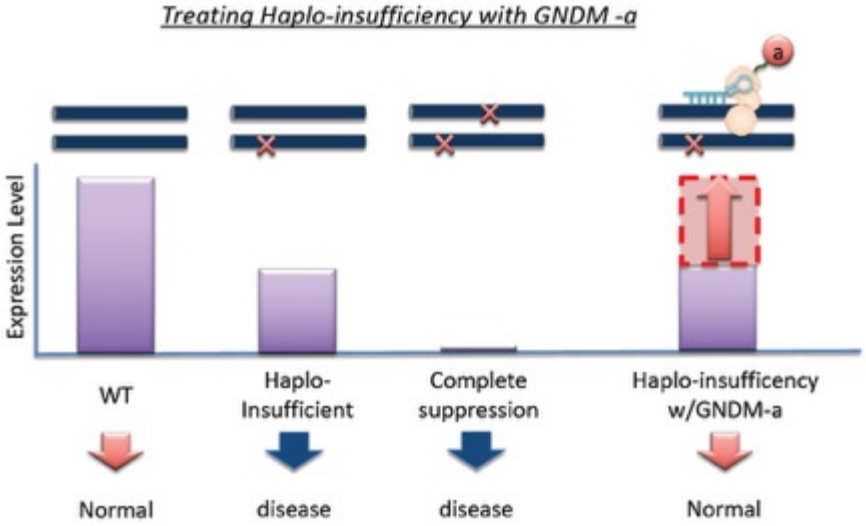
# A simple solution is to double up SCN1a protein expression




| Company | Modality | MOA | Route | Stage | IND |
|---|---|---|---|---|---|
| Enoded Therapeutics | AAV-ETN (regulatory element) | • Overexpress regulatory element for Scn1a<br>• Upregulate endogenous Scn1a expression specifically in GABAergic inhibitory neurons | ICV | IND cleared | 2021 |
| E-Rare | Adenovirus-Scn1a | • Restore Scn1a mRNA and Nav1.1 protein levels | ICV | Preclinical | TBD |
| UCL | Lentivirus-Scn1a | • Restore Scn1a mRNA and Nav1.1 protein levels | ICV(?) | Preclinical | TBD |
| OPKO | AntagoNAT | • Binds to the DNA and removes an endogenous repressor of SCN1A<br>• Restore Scn1a mRNA and Nav1.1 protein levels | IT | Preclinical | TBD |
| PTC therapeutics | Small molecule (nonsense reading through) | • Read through premature nonsense stop signals on mRNA and allow the cell to produce a full-length, functional protein (not specific to Scn1a) | Oral | Phase 2 (pending?) | N/A |
| Stoke Therapeutics | ASO (TANGO) | • Reduce non-productive mRNA and increase productive Scn1a mRNA via modulation of splicing<br>• Increase in the levels of mature mRNA and Nav1.1 protein | i.c.v. | Preclinical | 2020 |

Updated

# Patents related to MDL-101, 201 and 202 were granted and registered in major countries

- LAMA1 patent
  - Treatment method for muscular dystrophy targeting LAMA1
  - JP7641644, **US17/635,608**
- UTRN patent
  - METHOD FOR TREATING MUSCULAR DYSTROPHY BY TARGETING UTROPHIN GENE
  - JP7069426, US11473071, CN113271982
- DMPK patent
  - METHOD FOR TREATING MUSCULAR DYSTROPHY BY TARGETING DMPK GENE
  - JP7565620 , CN 113785066B





93

Updated

# Achievements of the programs and coming milestones

| | Achievement so far | Coming milestones |
|---|---|---|
| MDL-101 LAMA2-CMD | • Animal PoC<br>• Target engagement in monkeys<br>• Pre-IND response<br>• Process Development and **Scale up** completed<br>• ODD (Sep) and RPDD (Oct) received<br>• Data presentation (**Most recently at SciFam (Aug)**) | • GLP-Tox<br>• GMP manufacturing<br>• IND (**2026**) |
| その他 | • Established animal PoC<br>  • MDL-201 (DMD): **Confirmation of superiority in functional improvement over the benchmark with disease models**<br>  • MDL-202 (DM1)<br>  • MDL-104 (Tauopathy)<br>  • MDL-205 (Angelman syndrome)<br>  • MDL-207 (Dravet syndrome)<br>• MDL-103 (FSHD): **Received grant from xPrize and SolveFSHD**<br>• MDL-105 (DCM)<br>• Research collaboration with JCR in CNS<br>• Collaboration with Ginkgo Bioworks, GenixCure | • Additional readout of MDL-201<br>• **Data presentation at (6th Next Generation Genome Editing Summit)**<br>• Explore optimal capsid and route of administration for CNS program<br>• Allocation of development funds through partnering and grants<br>• Animal PoC<br>• Continuing Research and Moving to Next Steps |





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# 5. Growth Strategy

# Diversified pipeline with their own missions

Pioneer the gene modulation With highly suitable indications

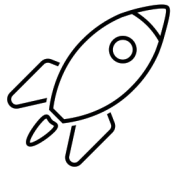
**MDL-101**

Expand technology opportunity with products for larger opportunity

**MDL-201, 202**

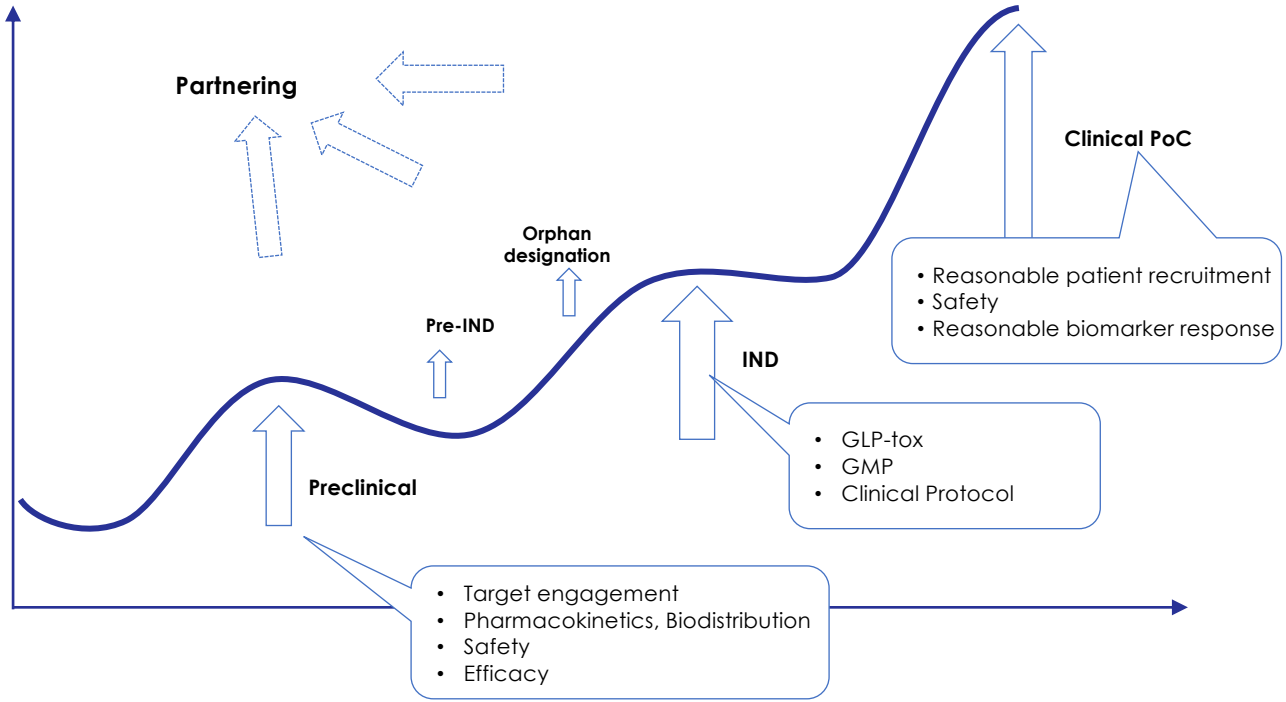
Further approach to challenging applications

**Other programs**



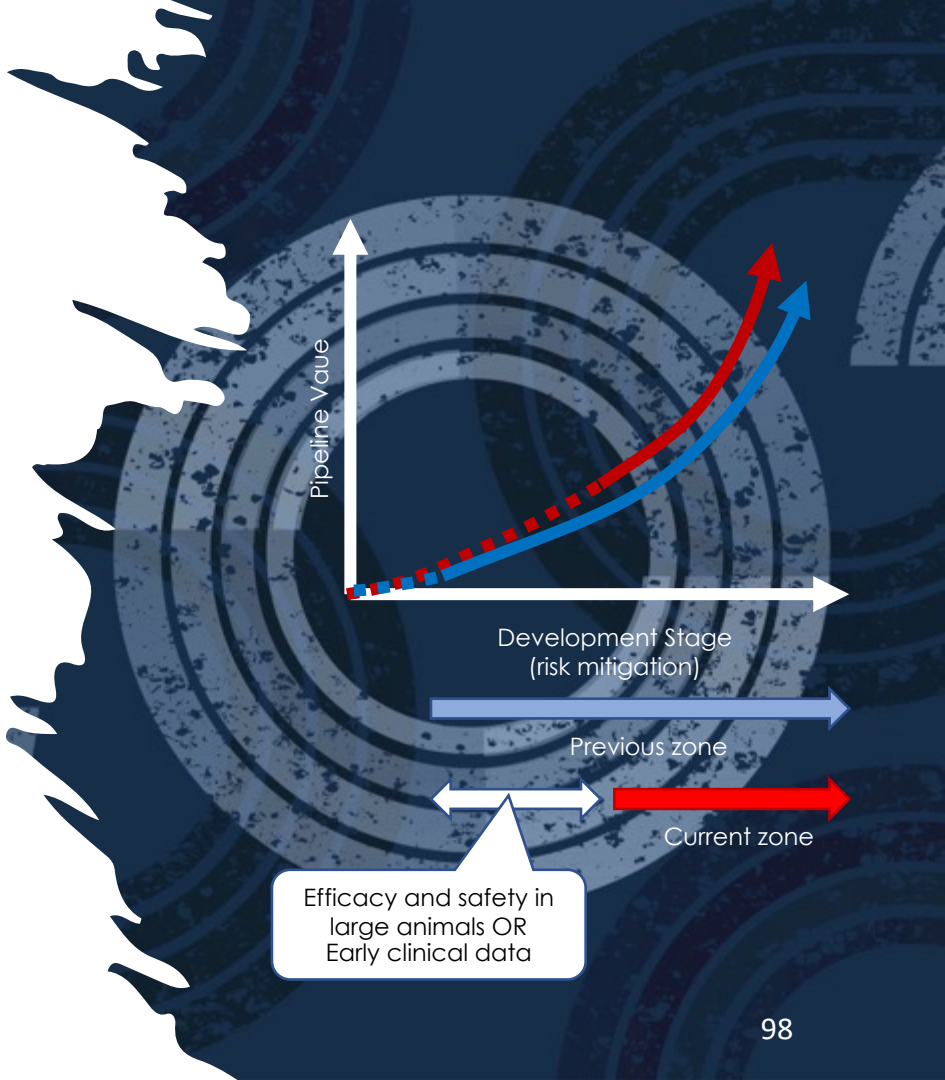
# Future pre-clinical and clinical trials are expected to increase the value of the company.

Expected milestone events and impact on corporate value



# Partnering strategy

- We try to maximize the number of diseases that can be developed by CRISPR-GNDM®. On the other hand, given our limited resources, it is important for us to find partners with whom we can share risk/profit.
- Partnering will be undertaken when conditions and timing are deemed appropriate based on the value and business characteristics of each pipeline.
- Take an open stance on forms of partnering, including licensing, option deals, and co-development
- At the same time, we will negotiate the timing and scheme of the alliance in a manner that allows us to accumulate our own development know-how, with a view to improving the efficiency of future development and maximizing profits.





98

Updated

# Aim of Fundraising
↓
# Funding for the next value inflection point
+
# Next growth

- As a result of the increased partnering hurdles in the biotech industry, P2 or PoC and beyond is a prerequisite.
- Securing funds to reach PoC is key to winterizing through the biotech ice age
- Conversely, if a company is able to reach PoC without partner, in-house sales (= higher profit margin potential) becomes in range
- New Growth Opportunities as MDL-201 and 103 Progress

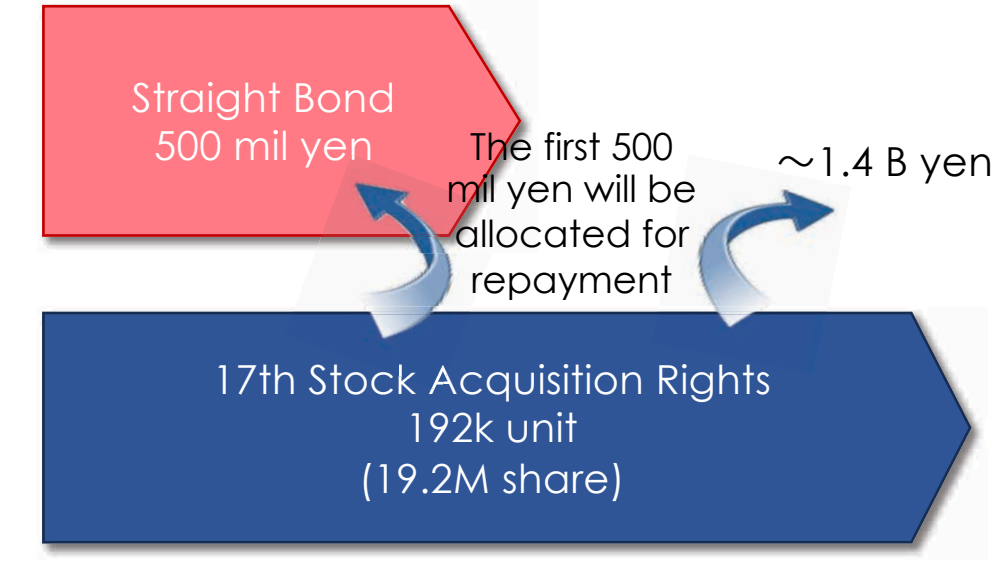


*Source "Biopharma Dealmaking: Time for a Rethink?"* by Lumanity at Swiss HLG Conference 2024

99

## New funding scheme

Funding of approximately 1.4 billion yen, consisting of 500 million yen in SB and 192k MS warrant

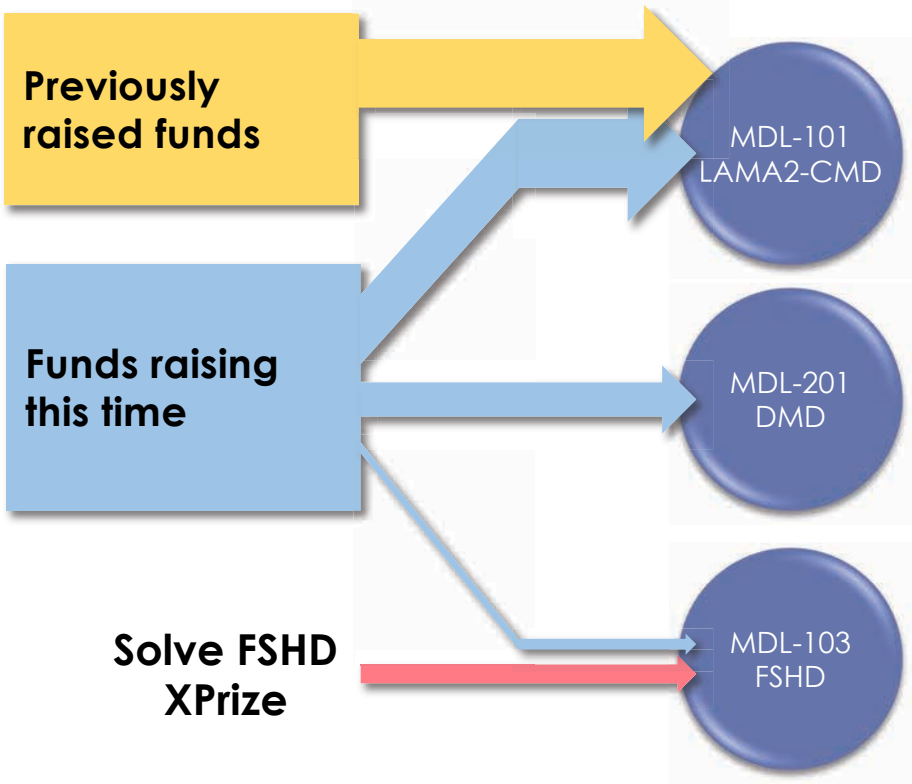



- Additional funding for MDL-101
- MDL-201 development costs
- R&D costs for MDL-103 and other subsequent pipeline products
- Administrative cost

## Allocation of development funds

In addition to MDL-101, we will also deploy MDL-201 and 103 to promote development.

- Together with the funds raised in the previous round, the funds raised will be used, to finance preclinical and clinical proof-of-concept studies for MDL-101
- Also to be invested in the development of MDL-201, a candidate for a large-market pipeline.
- And be used to promote the development of MDL-103 in combination with external grants.





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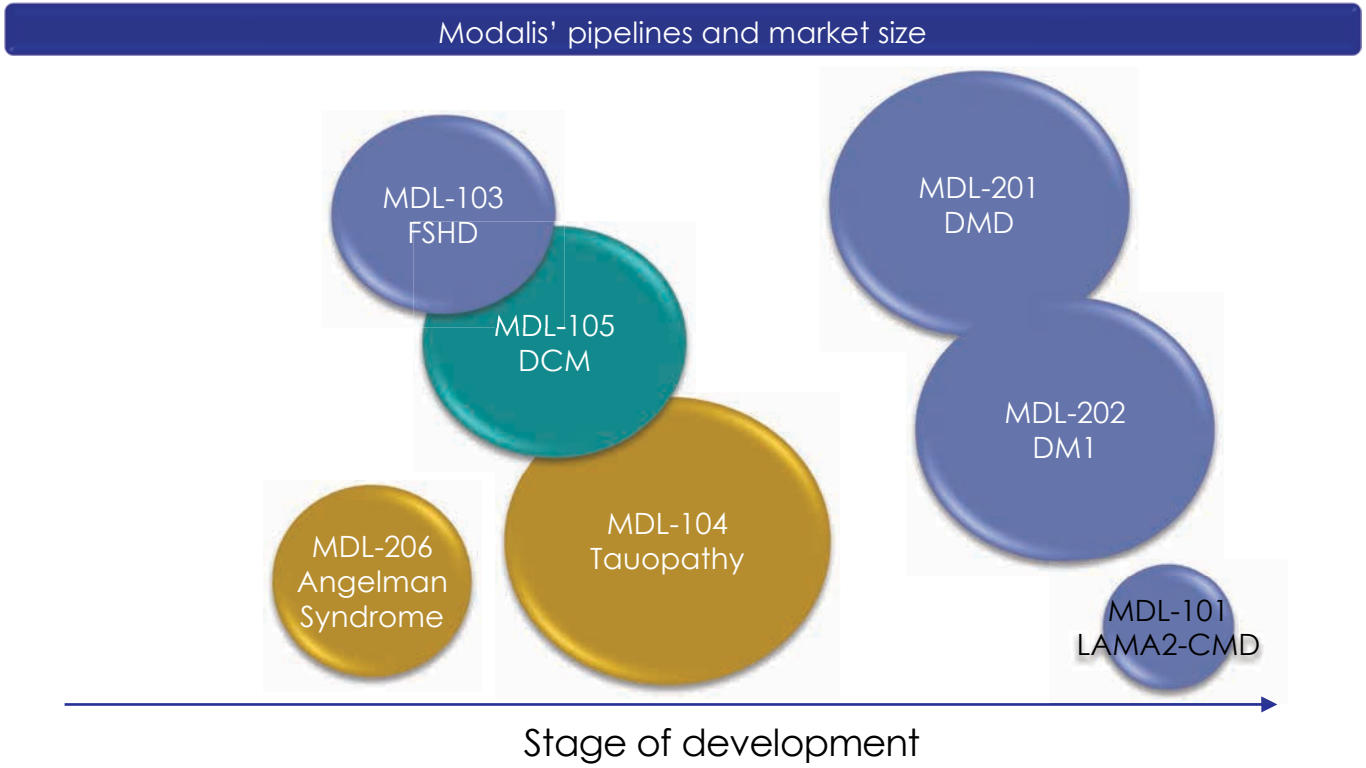
Updated

# 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

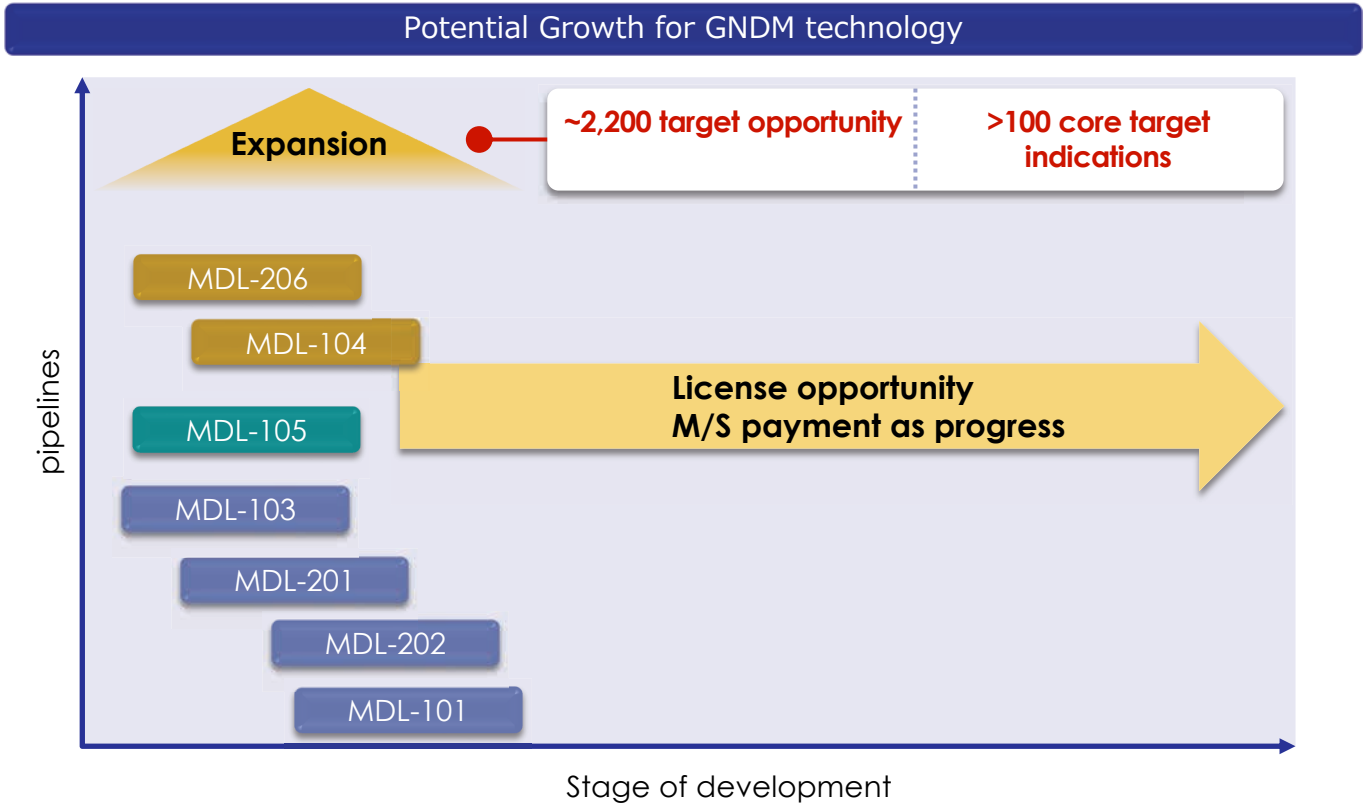




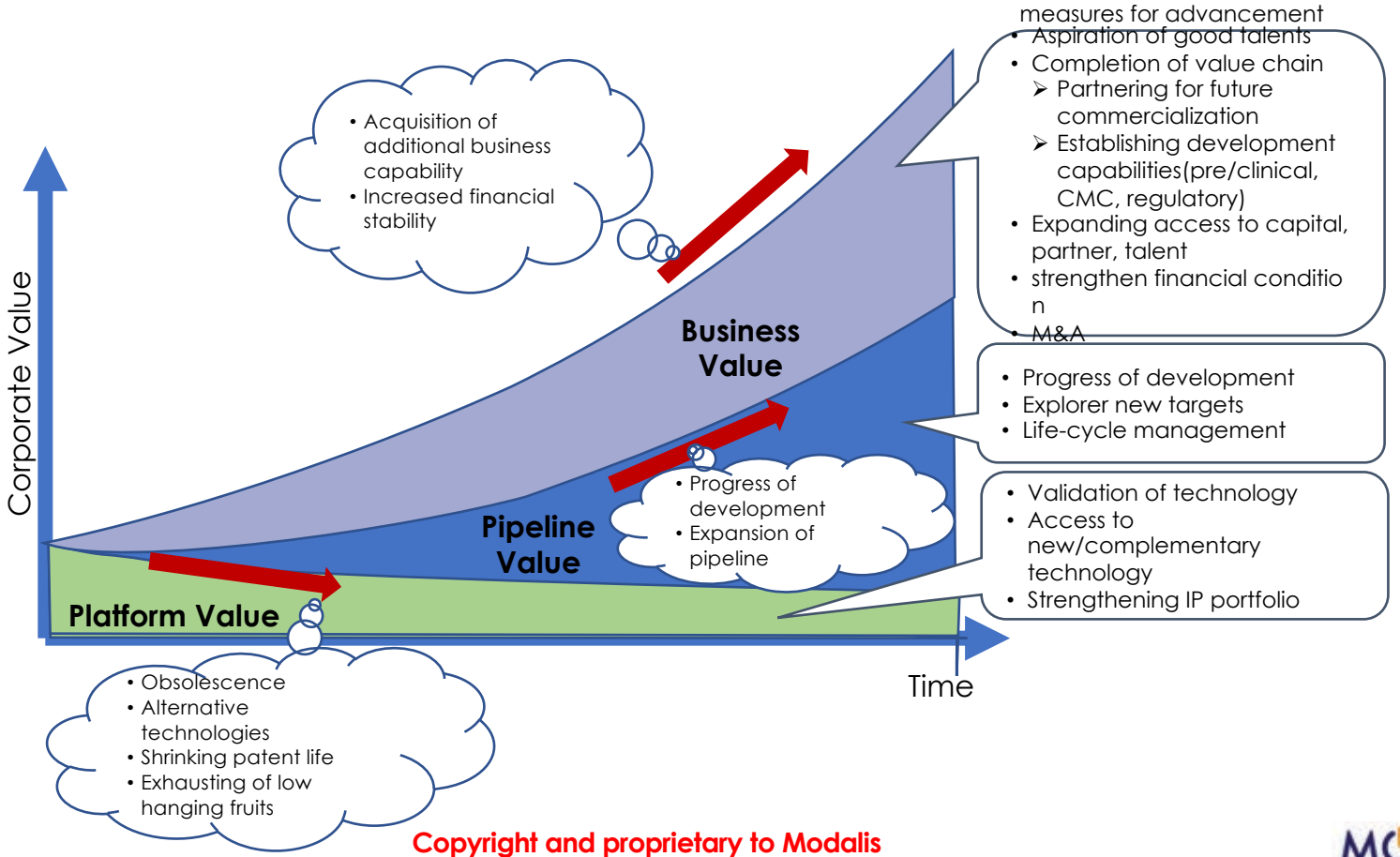
MODALIS

# Growth Strategy

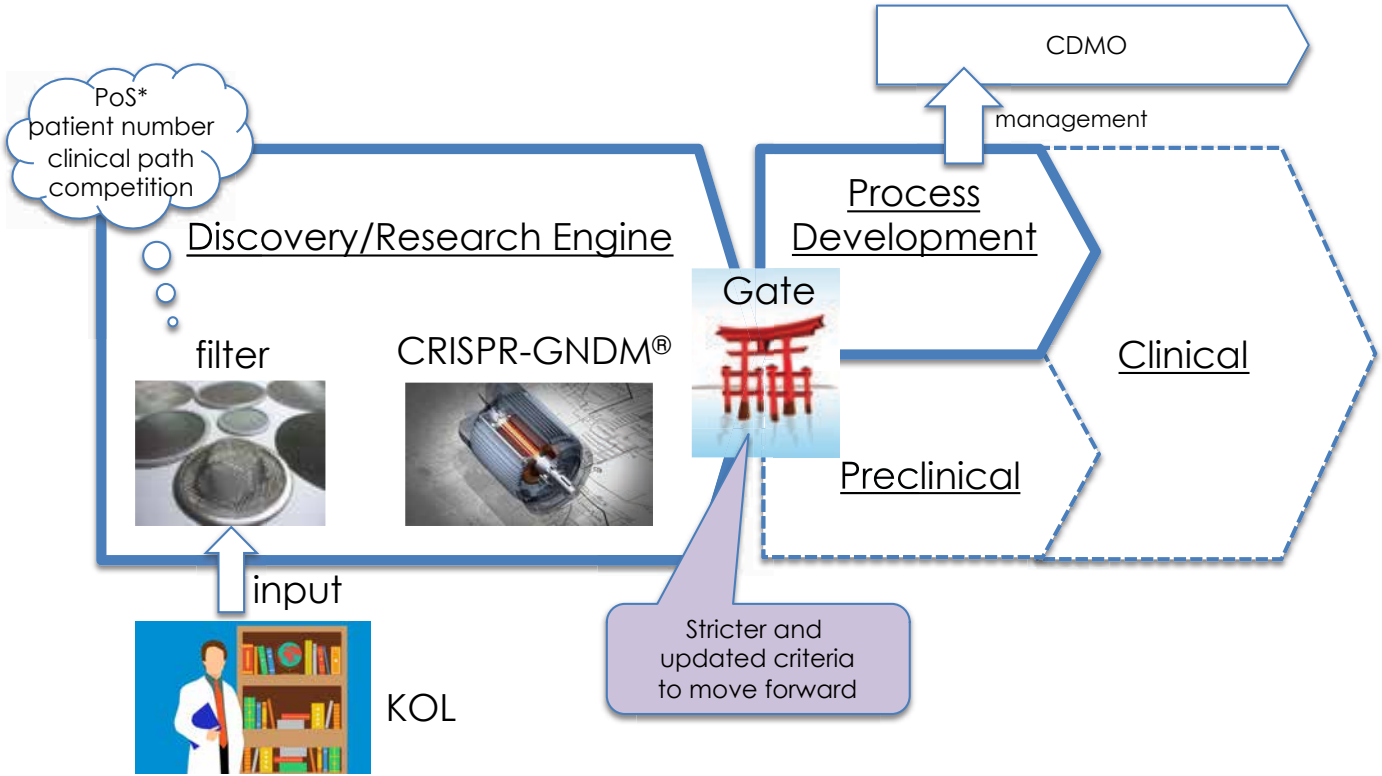
opportunity expands two dimensionally



# Composition of Modalis' value and measures for advance

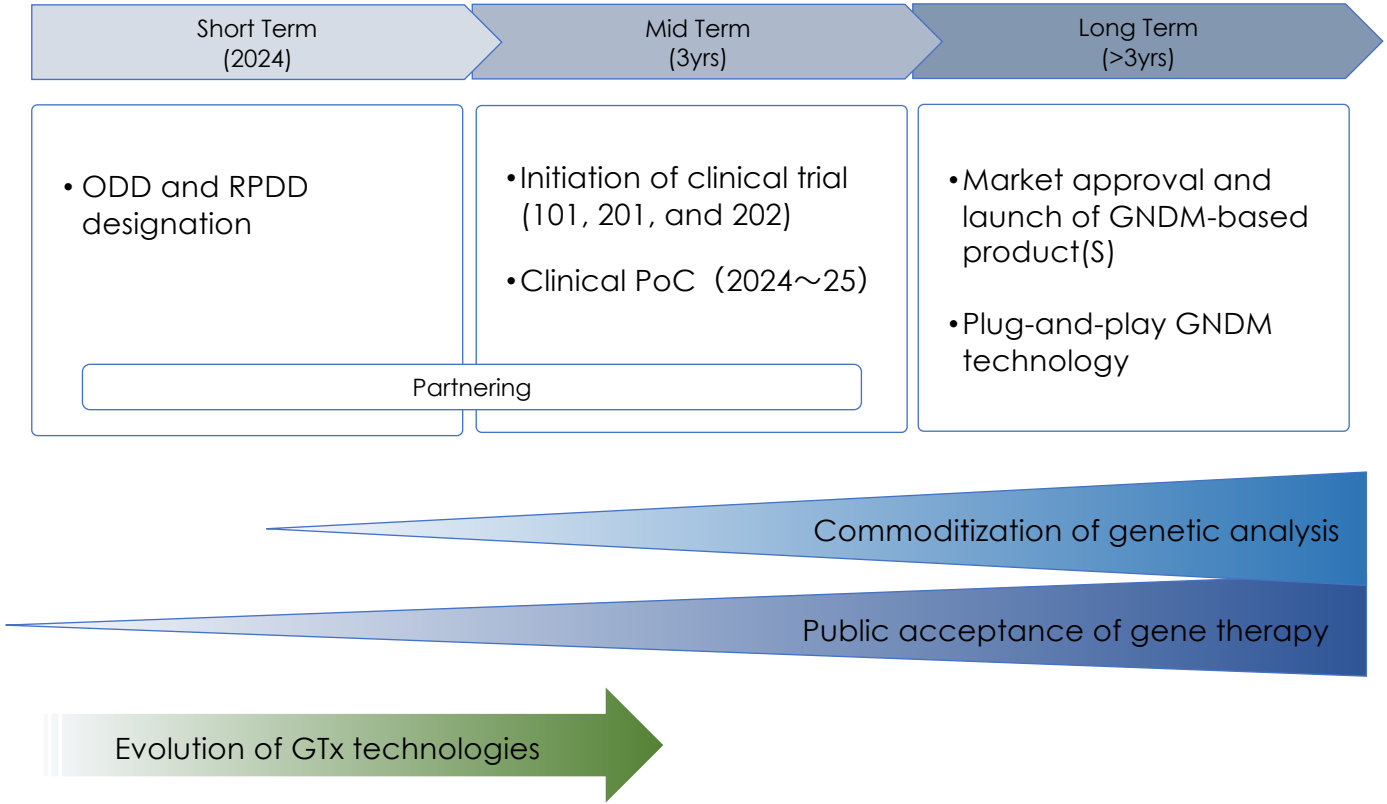


**Upon transition from R to D, which cost time and money, stricter decision is made for higher ROI and better resource allocation.**

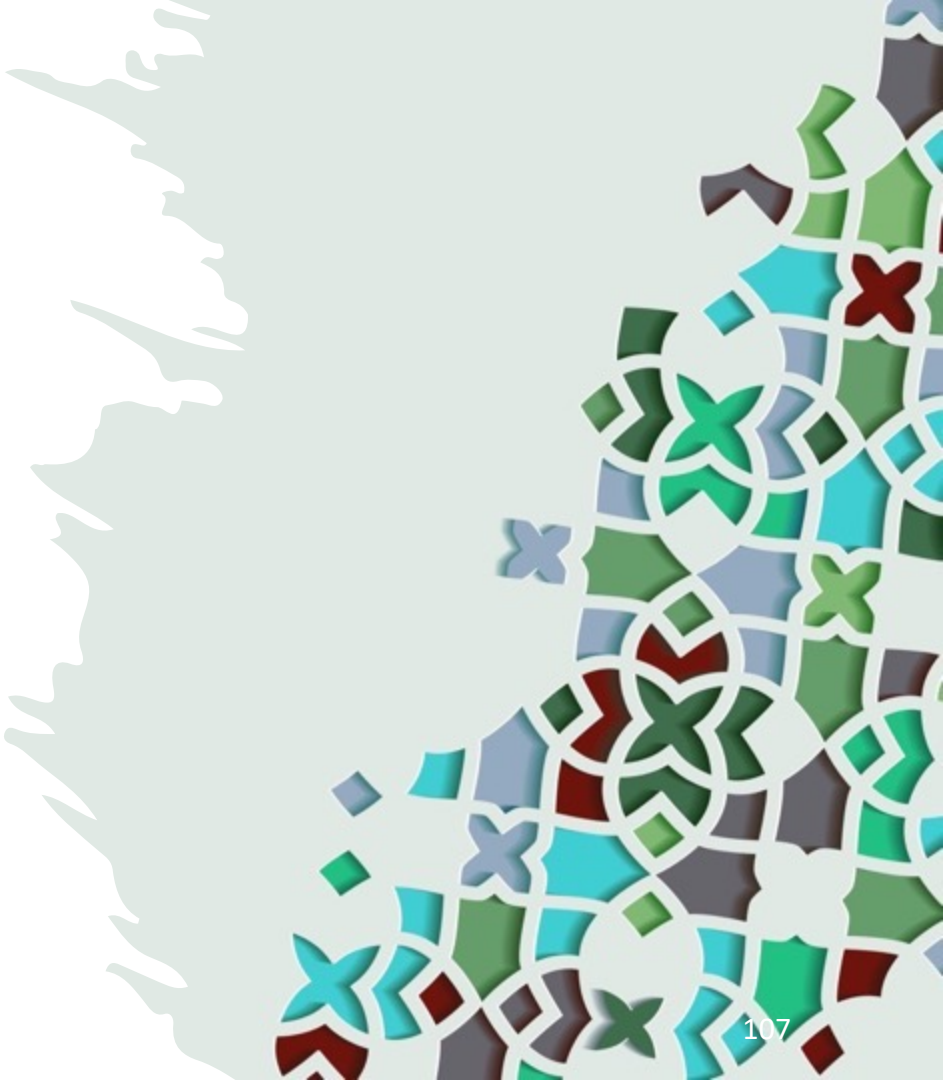



PoS: Probability of success

# The future Modalis envisioned



# 6. Risk infomation





107

# Known Risks and Preventative Measures（1）

| Topic | Main Risks | Probability | Level of Impact | Preventative Measure(s) |
|---|---|---|---|---|
| (1) Risks related to the research and development of gene therapies | The risk of unforeseeable problems developing due to working with cutting-edge experimental medical treatments | Low | High | Constantly monitoring cutting-edge scientific technologies and related businesses, making pertinent judgements, taking appropriate actions |
| | Due to gene editing technology being a field with steady progress and rapid advancement, there is a possibility of new technologies appearing and risk of competing with other modalities | Low | High | Ensuring we are using the most up-to-date version of the underlying technologies in our research and subsequently monitoring new trends in technologies, and adopting necessary technologies as needed<br><br>R&D will be carried out with priority given to pipelines with competitive advantage, and portfolio reviews such as discontinuation decisions will be made as needed for diseases for which competitive advantage cannot be maintained |
| (2) Risks related to the pharmaceutical industry | The risk of failure or decision to suspend development caused by a certain product or technology used in pharmaceutical development | Moderate | High | Regularly reviewing risk mitigation measures and making appropriate modifications to our portfolio when collaborating with partner companies and adding pipelines to our portfolio |
| (3) Risks related to execution of business activities | Due to the fact that execution and related decisions are driven by our partners, there is a possibility development is suspended and the risk of contract cancellation even if there are no failures during development | Moderate | High | Aiming to stabilize for the future and maximize profits through the stratification of our pipelines and strategically adding to our portfolio |
| | The risk of delays in the timeline if appropriate business coordination measures are not made regarding production that is entrusted to external parties, preclinical experiments, etc. | Low | High | Performing appropriate project management, concurrently negotiating with various candidate service providers, and securing a slot to prevent delays in the timeline |

# Known Risks and Preventative Measures (2)

| Topic | Main Risks | Probability | Level of Impact | Preventative Measure(s) |
|---|---|---|---|---|
| (4) Risks related to intellectual property rights | The risk that patents other than the originally introduced license will be required while the basic patent is in a disputed state. | Low | High | Striving to secure patents for each project (including the Company's own patents) and concurrently investigating the introduction of necessary patents |
| (5) Risks related to business performance, financial condition, etc. | The risk that recorded profits will not be stable, since profit is strongly influenced by the license agreements, milestones, etc. | Moderate | High | Using a hybrid model to stabilize for the future and maximize profits through the stratification of our pipelines and strategically adding to our portfolio |
| | The risk of significant events related to the going concern assumption. | Moderate | High | Using a hybrid model to stabilize for the future and maximize profits through the stratification of our pipelines and strategically adding to our portfolio |
| (6) Risks related to the company structure | The risk that we are unable to secure talented individuals who possess technical knowledge or skills for scientific research and development | Low | High | To attract talent, we are engaged in R&D that appeals to potential candidates and creating a favorable working environment in addition to adopting of a restricted stock unit system to recruit competitively |
| | The risk that negative gossip or rumors influence the public credibility of the Company group | Low | Moderate | Misinformation and rumors are taken seriously, and the Company maintains their position by the equitable, fair, and timely disclosure of information |