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 year-end updates



(TSE : 4883)

Modalis therapeutics Corporation

March 25, 2026

MODALIS

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MODALIS

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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,

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Updated

Major updates since the last report (Aug 2025 version)

P7, P20	Updated corporate info
P42-44	Updated IP position
P60-62	Newly added details of the technical partnership with Broad regarding muscle tropic capsid technology.
P26, 29, 36, 61	Newly added DMD disease model mice study data
P78, 101-102	Updated along with the business progress
P107-109	Added info of most recently announced finance

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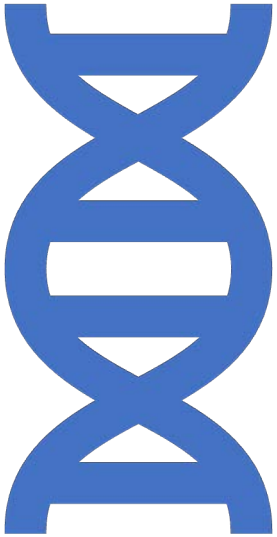
Updated

Outline of the strategy

- Adopt a business strategy with MDL-101 as the lead program
- Prioritize research and development for neuromuscular diseases where know-how can be repurposed, starting with MDL-201.
- For central nervous system diseases, resume development contingent on determining delivery methods and securing resources. Research continues.

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1. Corporate Overview
2. Gene Therapy, Gene Editing
3. CRISPR-GNDM® and its advantages
4. Pipeline
5. Growth Strategy
6. Risk Information

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1. Corporate Overview

Updated

Corporate Overview (As of December 31, 2025)

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

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)
Business	Drug Development
Capital stock	1,728 million yen
Outstanding share	87,484,098 shares of common stock
Number of employee	21 (including 8 Ph.D.) (5 in Japan, 15 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 Value Highlights

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

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

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

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

Experienced team with deep knowledge of platform

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

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

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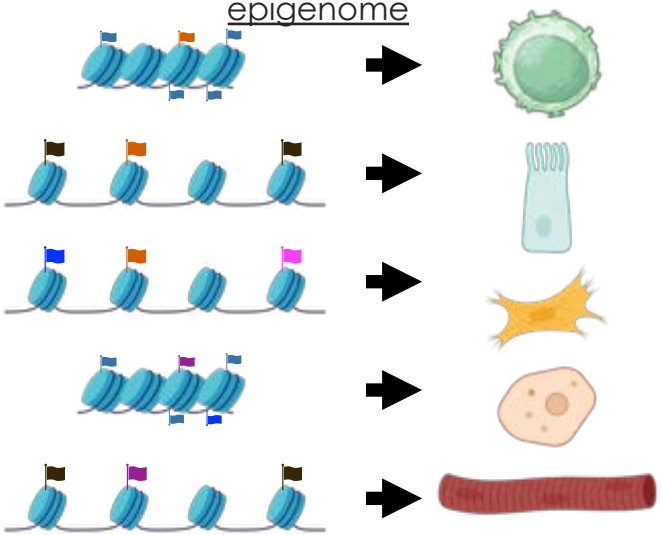
Epigenome

The mechanism by which genes determine when, where, and how much they are transcribed, thereby creating diversity in cells and their functions

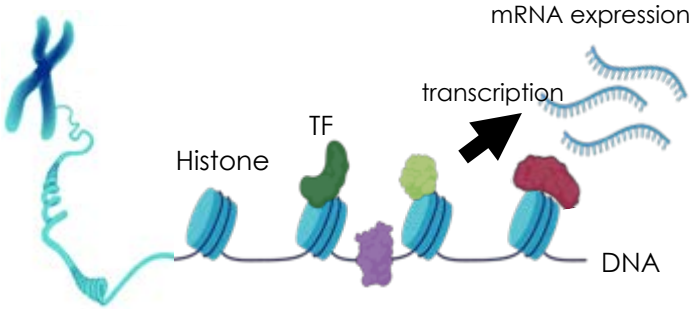


37 trillion cells
20,000 genes
200 cell types
Over 100 organs
Yet just one set of blueprints

Cellular diversity is governed by the epigenome



RNA is transcribed from DNA





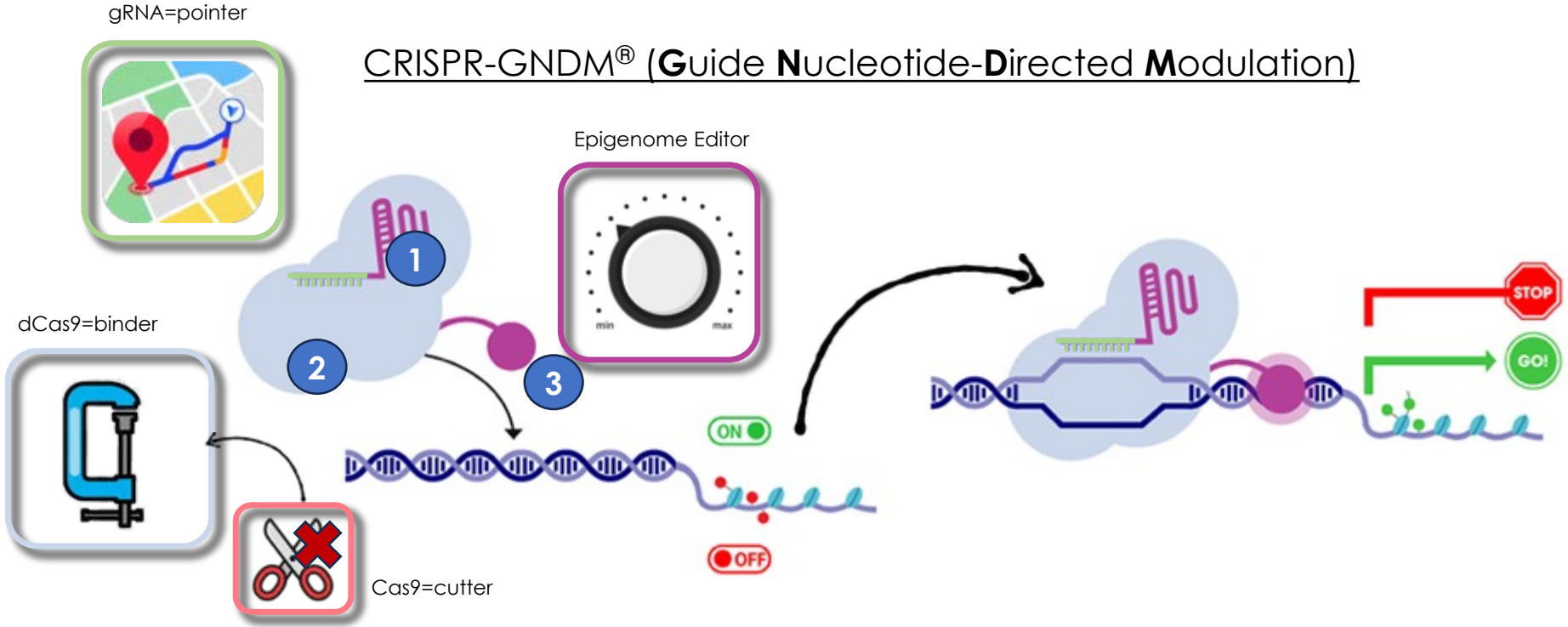
The epigenome regulates gene expression like a conductor But what if that regulation were to break down….

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CRISPR-GNDM®

GNDM restores the controls target protein expression through epigenetic regulation

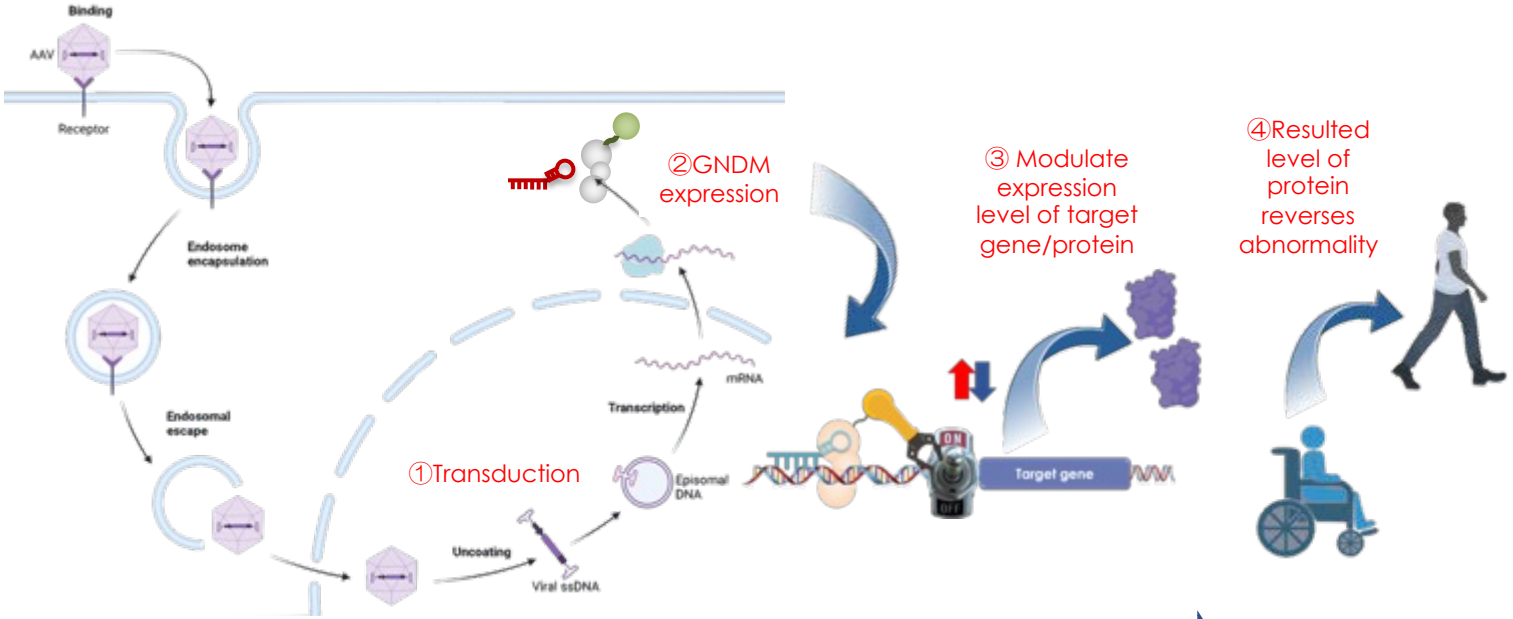


CRISPR-GNDM® consists of: ① a "guide RNA (gRNA)" for positioning, ② 'dCas9' as the binding device to DNA, ③ an "editor" for editing the epigenome, enabling precise control over gene expression on and off.

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Delivery of GNDM to the target

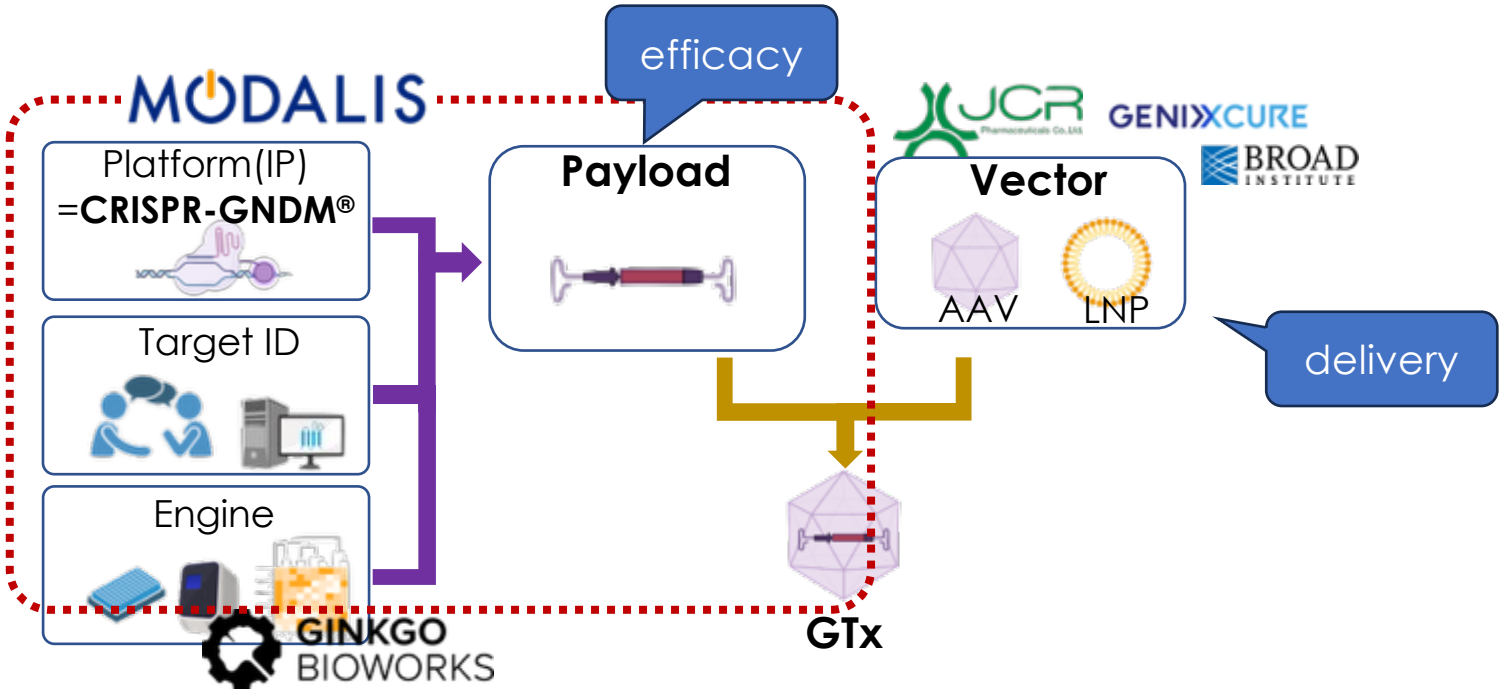
Packed in a vector, GNDM is delivered to target cells and selectively controls the expression of the target gene



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MODALIS' core competence and collaboration

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



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MODALIS's value proposition and corporate policy

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



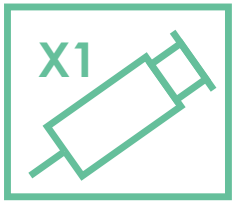
Every life deserves attention

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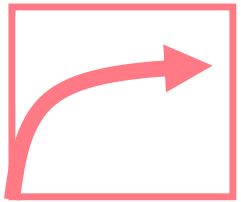
CRISPR-GNDM®'s advantages

A single injection provides long term disease modifying effect

Potential benefits of CRISPR-GNDM® Technology



Single dose
Doesn't require
Repeated dosing



Long-lasting
Sustained effect
for years or decades



Disease Modifying
Not just to reduces
symptoms but
gives cure

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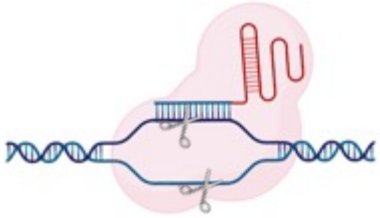
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Non-cleaving CRISPR = CRISPR-GNDM®

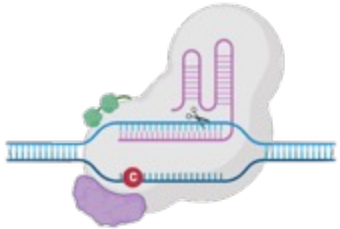
Enables treatment of genetic disorders by controlling epigenetic ON/OFF switch

GTx Technologies

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



Permanent Removal



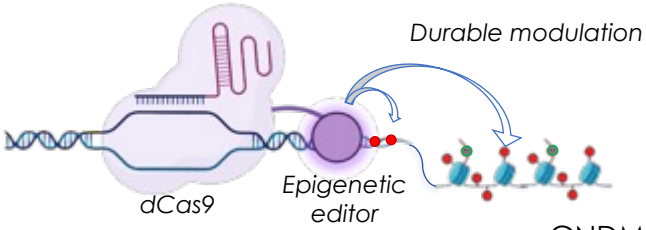
Permanent Replacement



Temporal silencing

Epigenome Editing(CRISPR-GNDM®)

Bind without cleaving
No DNA damage



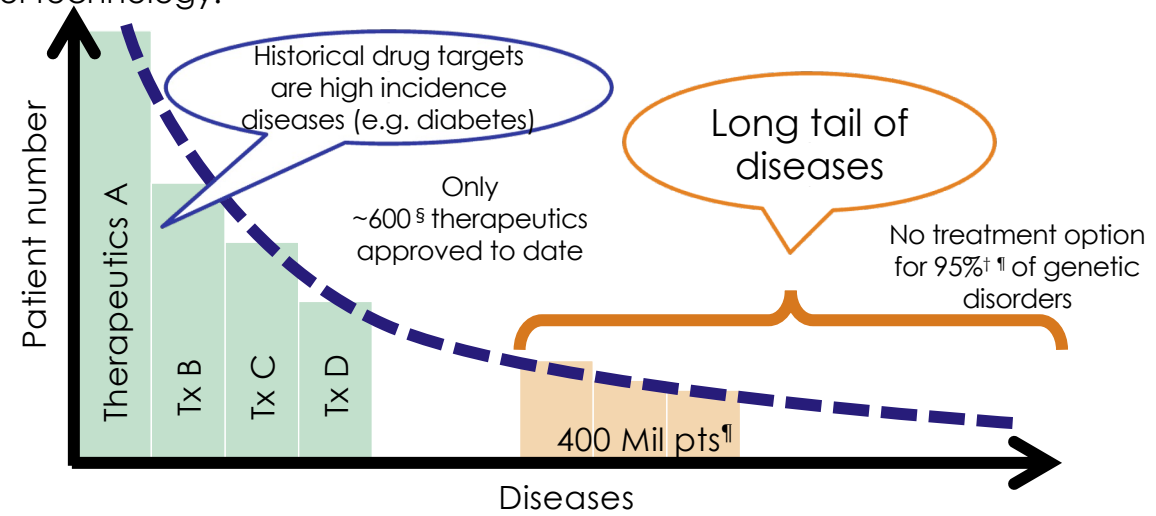
GNDM=Guide Nucleotide Directed Modulation

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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

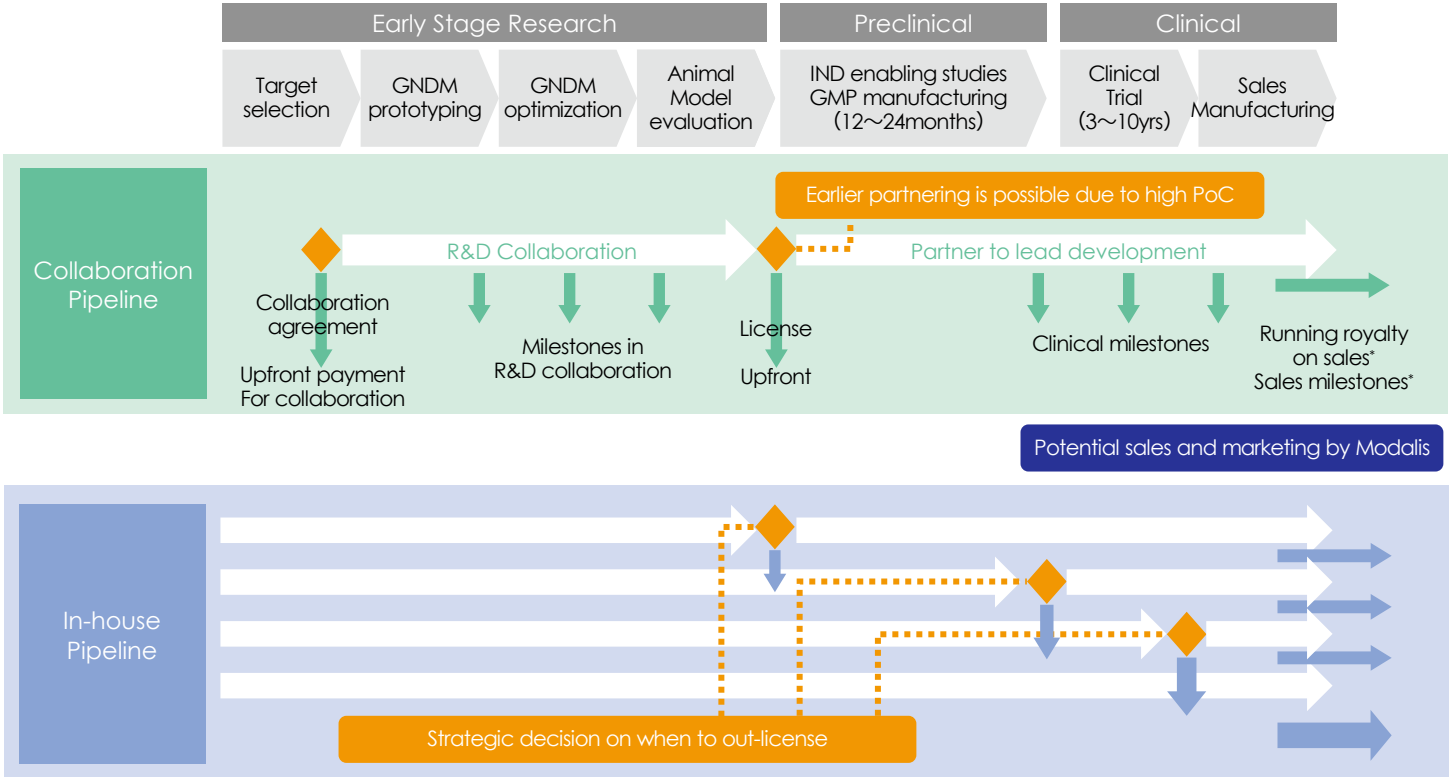
reference: *21st Century Cure Act, #NIH GARD †innovation.org ¶GlobalGenes.org
§Active therapeutics of 491 NME, 106 BLA, 17 cellular and gene therapy products @FDA as of 2019.7.22 Source from KEGG

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MODALIS

Business Model

Hybrid of own pipeline and collaboration pipeline

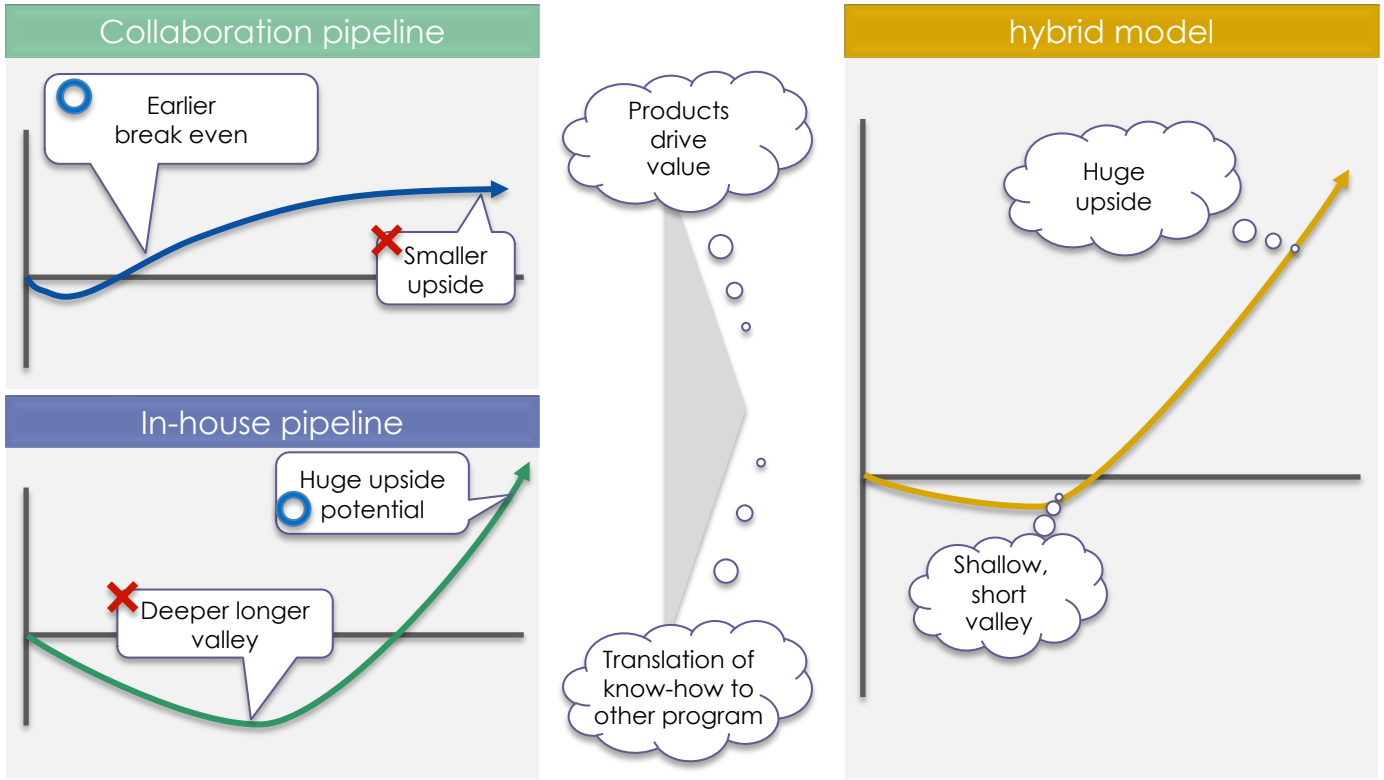


* future plan

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Modalis is pursuing a hybrid model

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

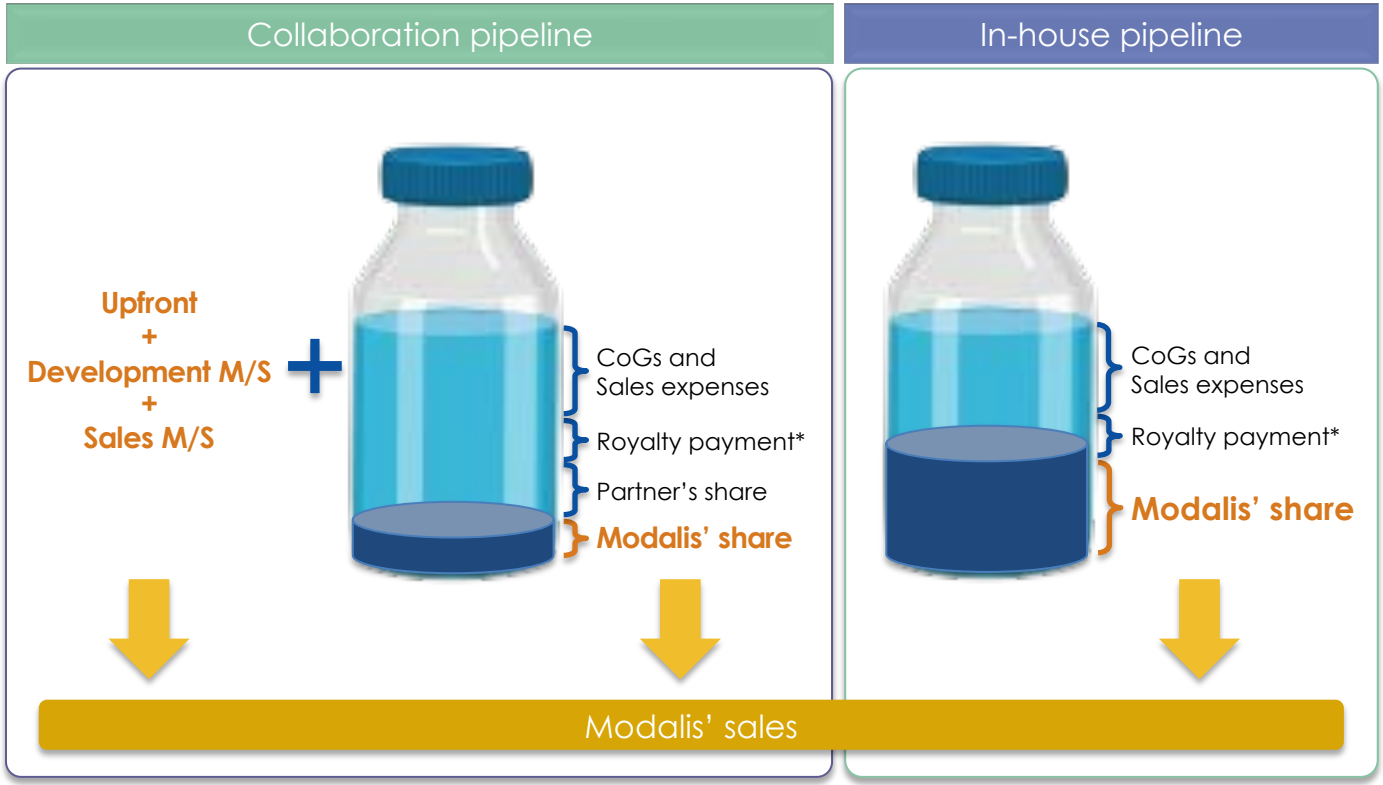


* The above is only an image and does not suggest or guarantee our future performance.

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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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Updated

Management Team and Board of Directors

Seasoned team

Executive Officers

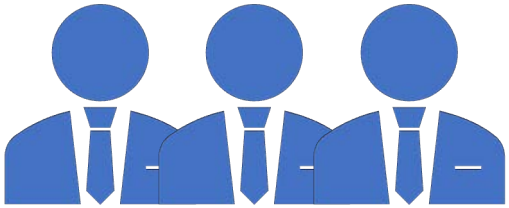
Haru Morita Co-founder, President, CEO, and Chair of the board
- REGiMMUNE, Founder, President and CEO
- Y's Therapeutics, Booz Allen and Company, Kyowa-KIRIN

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

Yuanbo Qin PhD: VP Neuromuscular Diseases rations
- Yale University, Harvard Medical School

Seth Levy PhD: VP Operations and Business Development
- Brammer Bio/ThermoFisher Scientific, Sanofi Genzyme.



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)

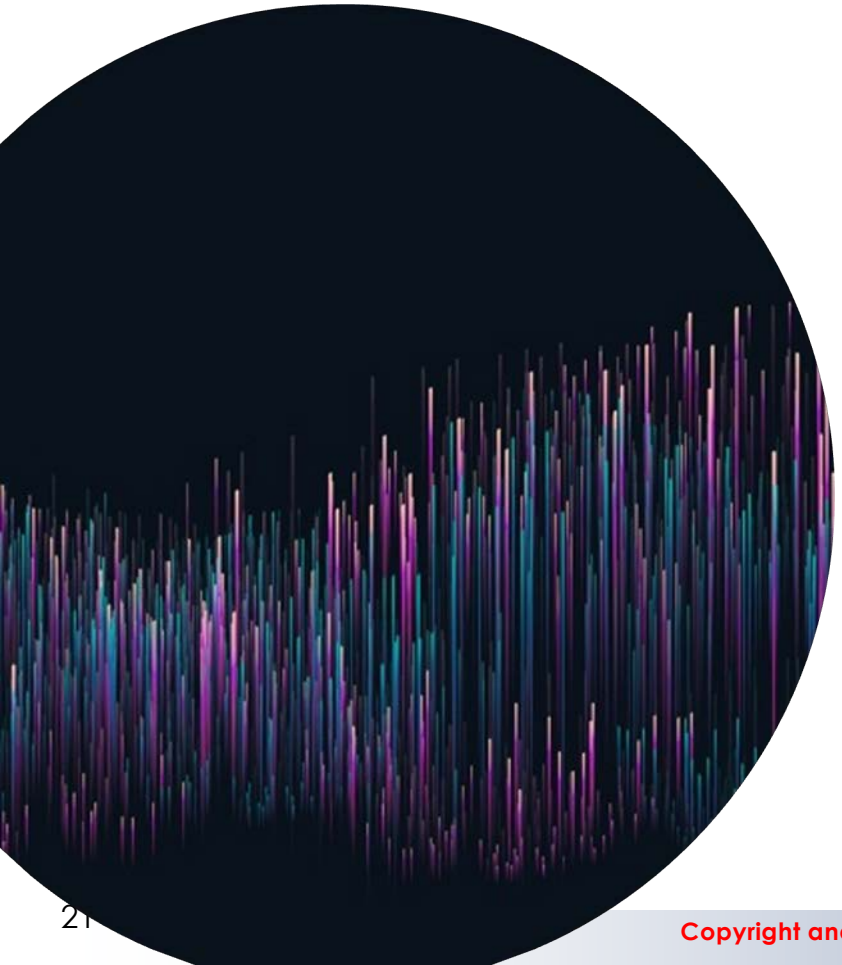
Joseph S. McCracken DVM Board member
- Roche Head of Global license, Genentech, Sanofi

Eisaku Nakamura Board member, Audit committee
- Corporate Auditor (D. Western Therapeutics, Solasia, Luca Science)
- Marubeni, BioSite Capital, Activus 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)

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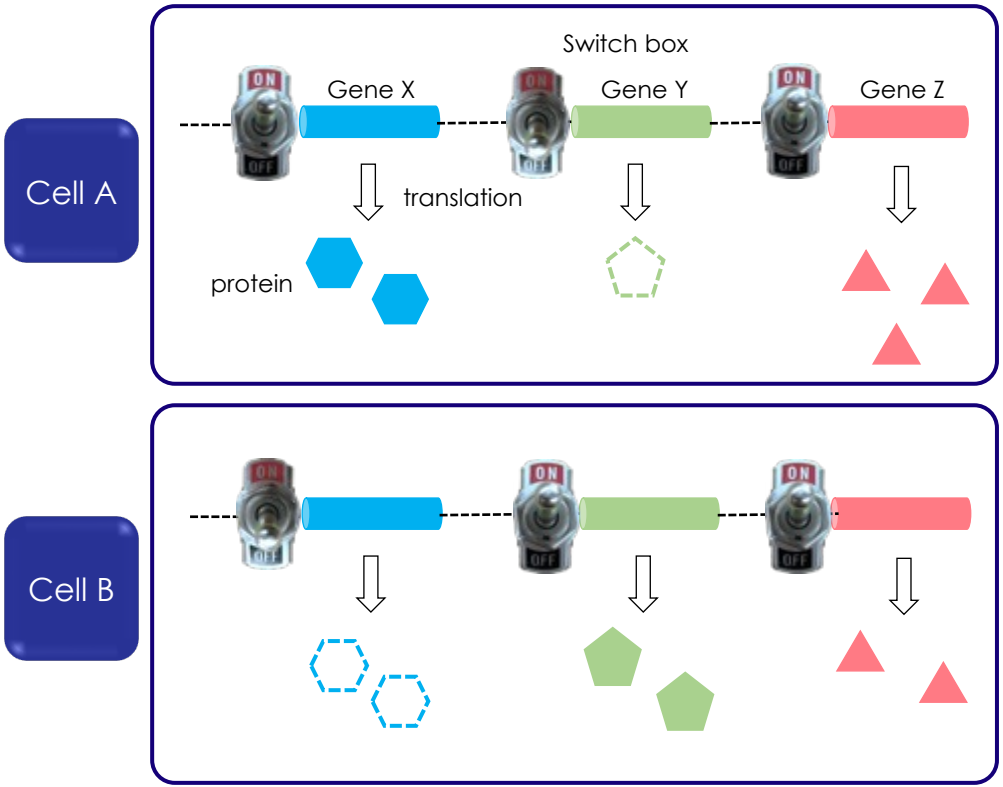


2. Gene Therapy and Gene Editing

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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

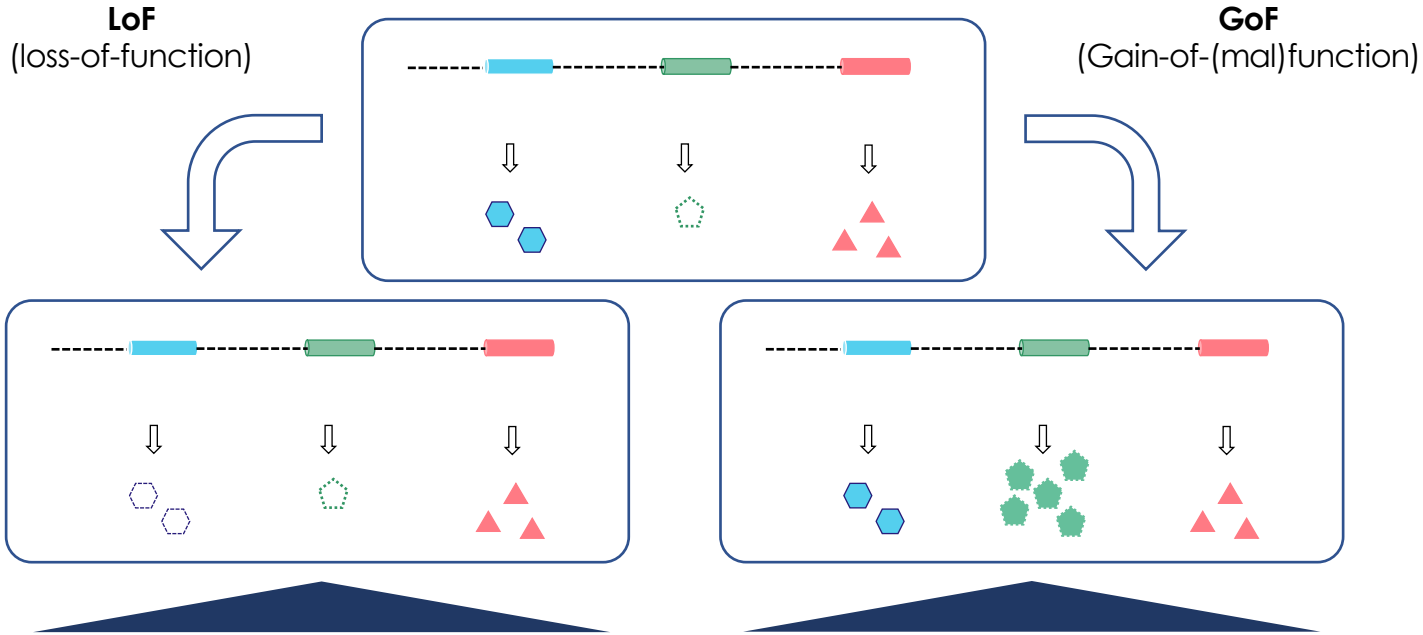


- There are **37.2 Trillion cells** in our body
- **200 cell types** in our body have the same DNA code despite differences in appearance and function
- Differences in cell types and their states are controlled by ON / OFF switches of the expression of **20,000 genes** coded by **3 billion bases of DNA**

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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

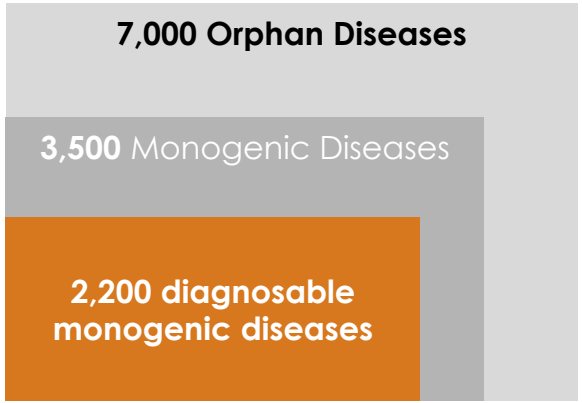


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Untapped opportunities in monogenic disorders

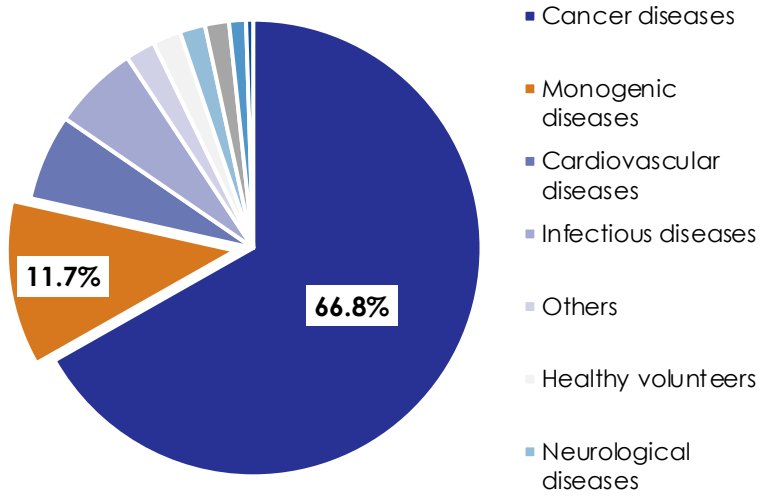
Only limited number of drugs are approved or in clinical development for monogenic disorders

Monogenic Disease



Source: Discovery Medicine

Breakdown of GTx clinical trials (1989~ Worldwide)

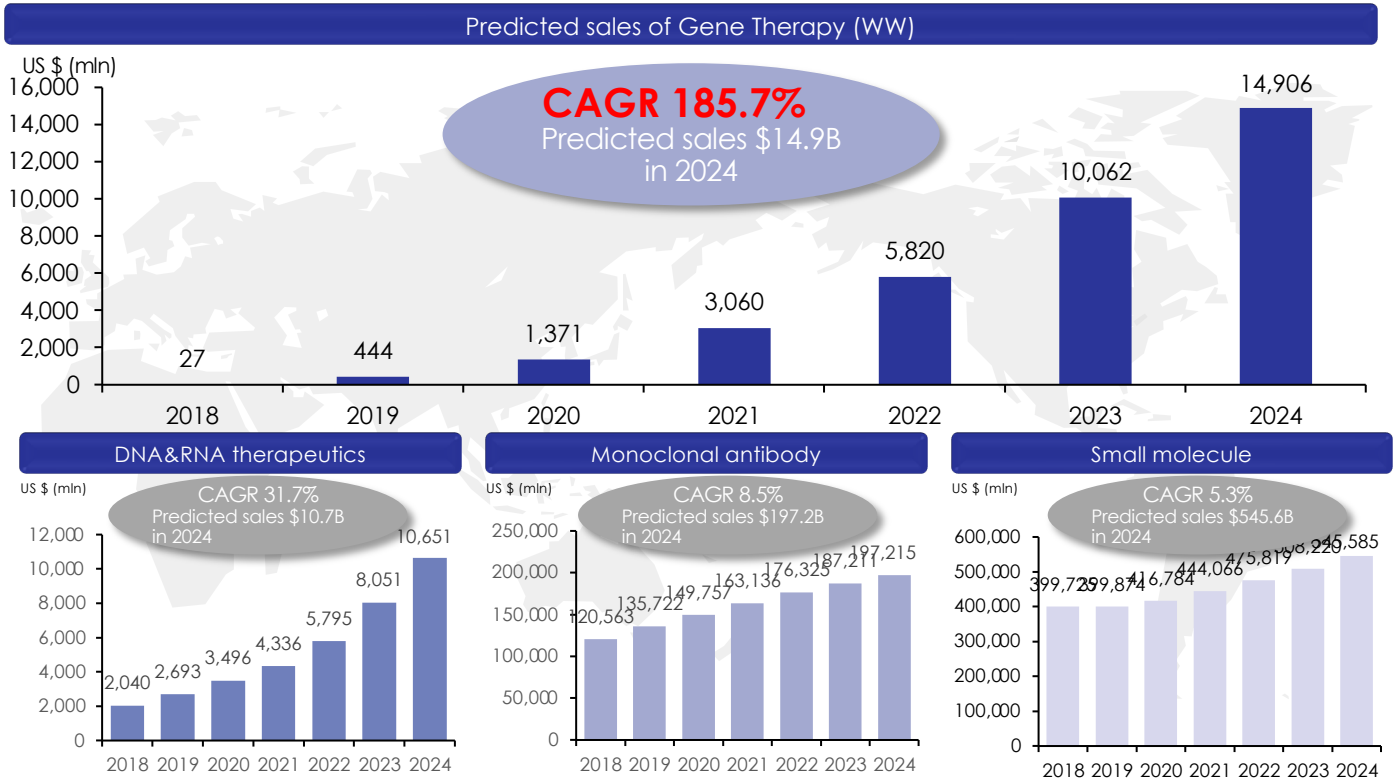


Source: The Journal of Gene Medicine (2019)

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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

Approval Status of GTx

Itvisma has received approval for expanded indications for SMA

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	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]
Itvisma	2025	$2.6M	SMA	Novartis	Over 2yrs SMA patients Approx. 1000s ~10k patients in US	~$10B[#2]

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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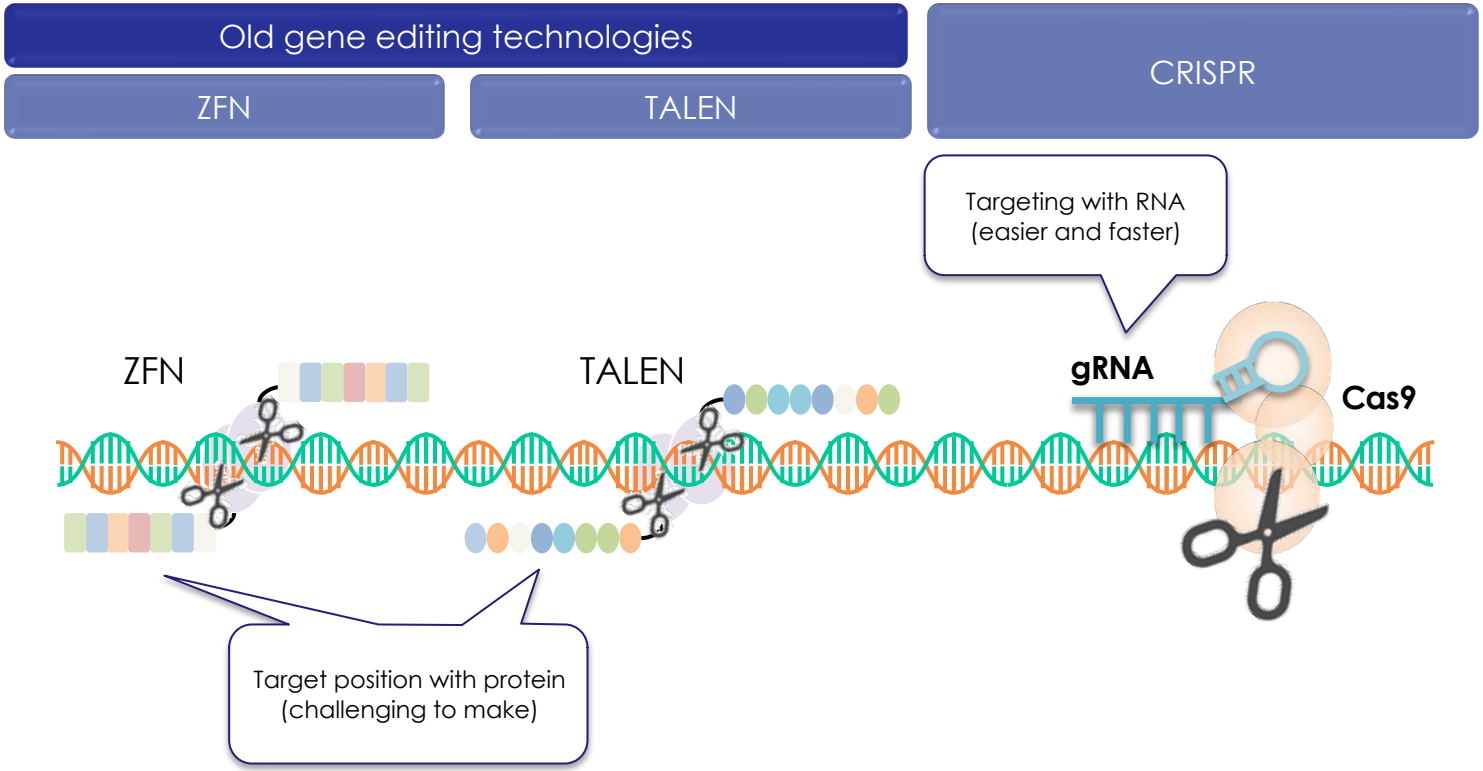


3. CRISPR-GNDM® and its advantages

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CRISPR is a novel gene editing technology

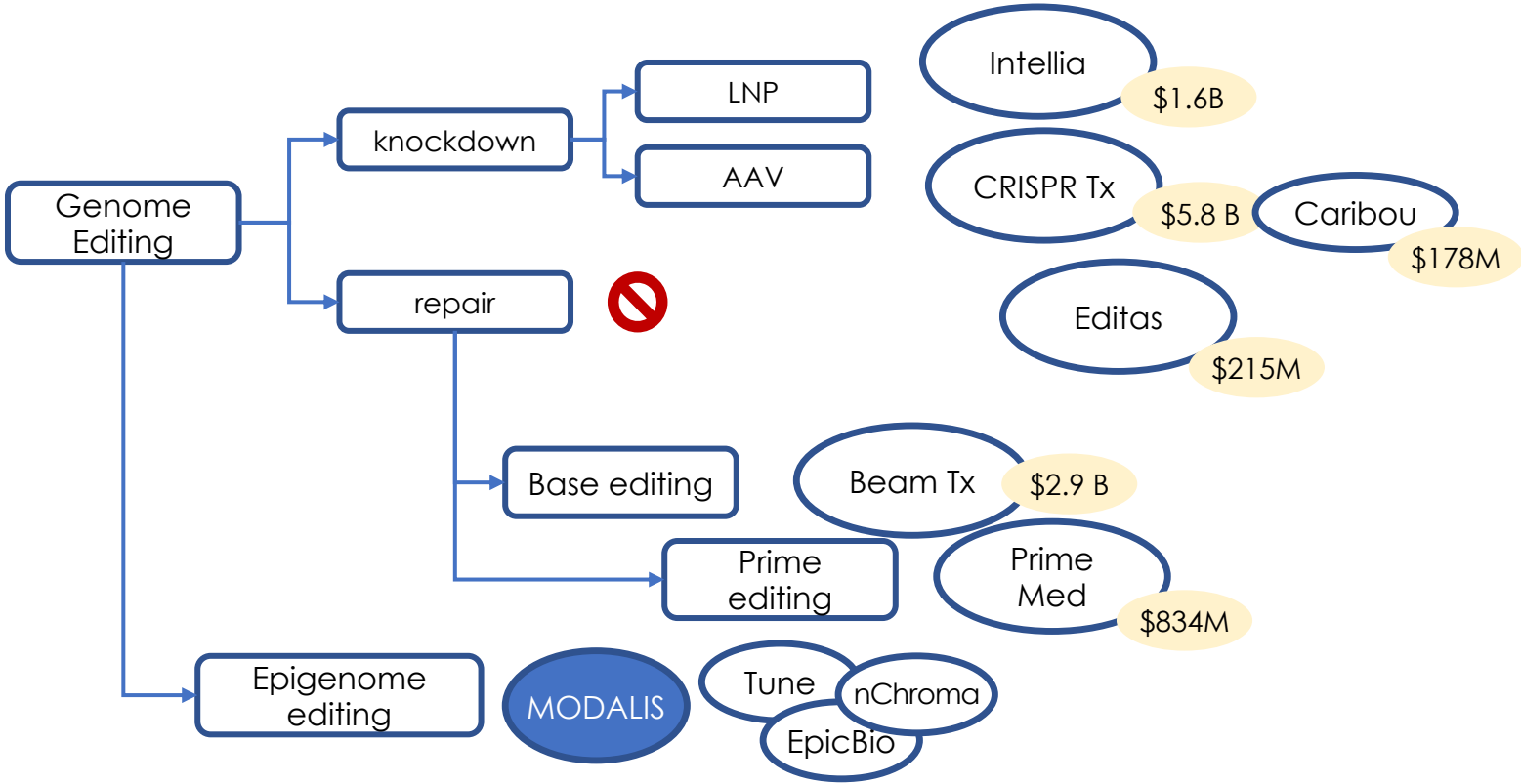
Faster and higher throughput due to limited variable region which is easily synthesizable as gRNA



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Genealogy of CRISPR based Technology and major players

The whole CRISPR area has been expanding, but the repair by simple editing has been found difficut



Note: The yellow circle shows the market capitalization as of the closing price at the end of Feburuary 2026.

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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®

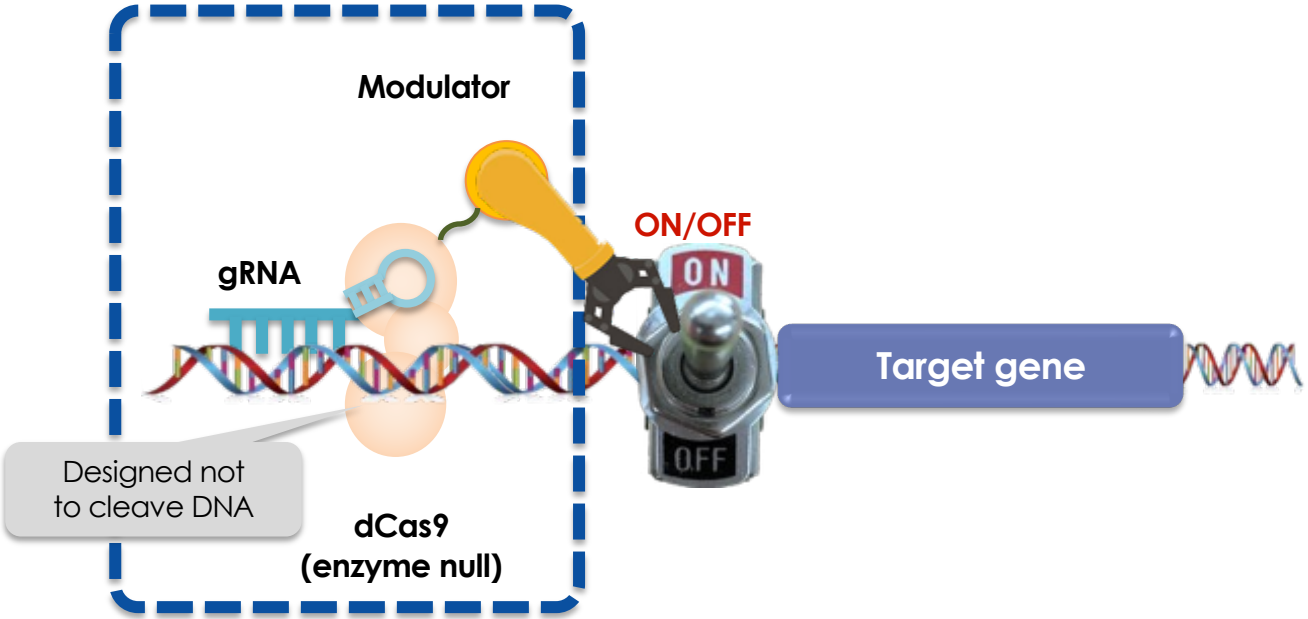
*Source: Interview on Future Human "Fresh Off Her Nobel Prize Win, Jennifer Doudna Predicts What's Next for CRISPR"

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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

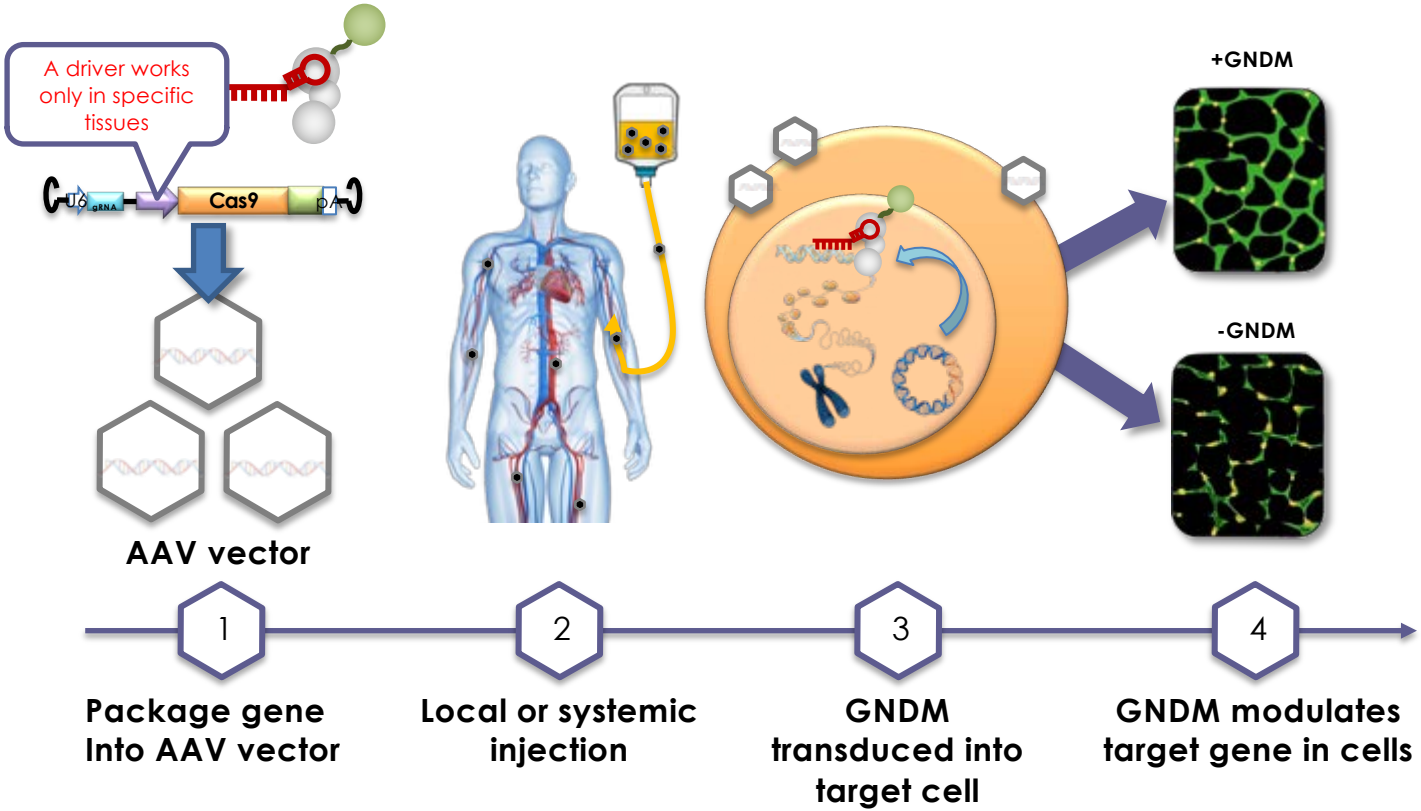


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Delivery of CRISPR-GNDM® to target

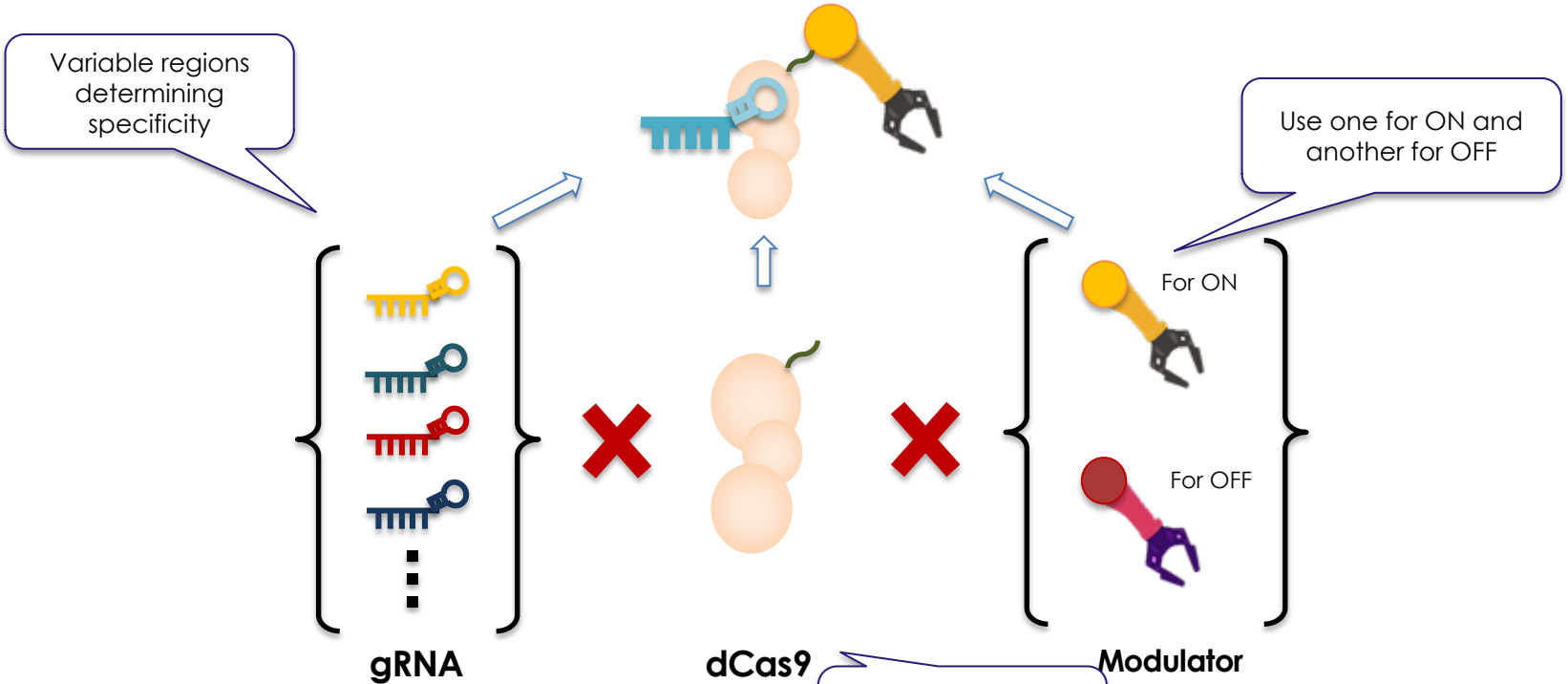
Use AAV vector to deliver GNDM to target cell



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GNDM is scalable

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



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

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



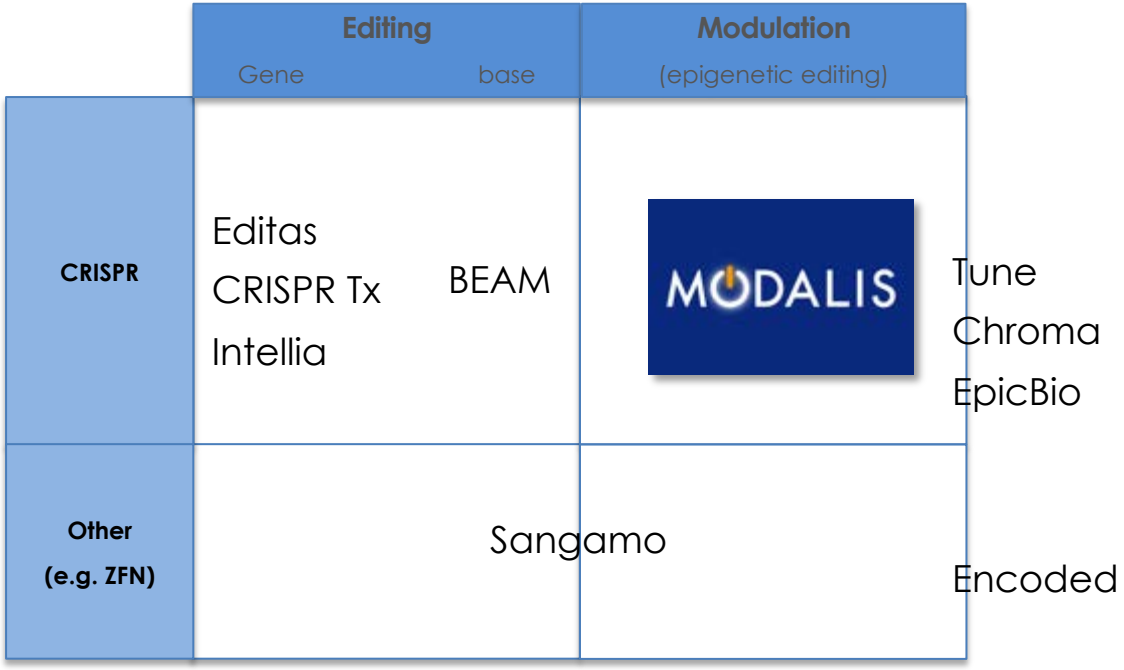
	Conventional Gene therapy	Gene Editing	ASO siRNA	CRISPR-GNDM
Precise targeting	Yes	Yes	Delivered to off-target tissues	Yes
Durability	Years	Permanent	Require repeated injection	Years
Applications	LoF ONLY	Mostly GoF	GoF only	**LoF and GoF**
Target gene limitation	Limited to small size genes	Limited to 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

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Positioning in the CRISPR and genome editing space

Modalis is uniquely positioned within the CRISPR field



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Updated

Epigenome editing competitive landscape

The field is gaining more traction and MODALIS is uniquely differentiated from the other epigenome companies

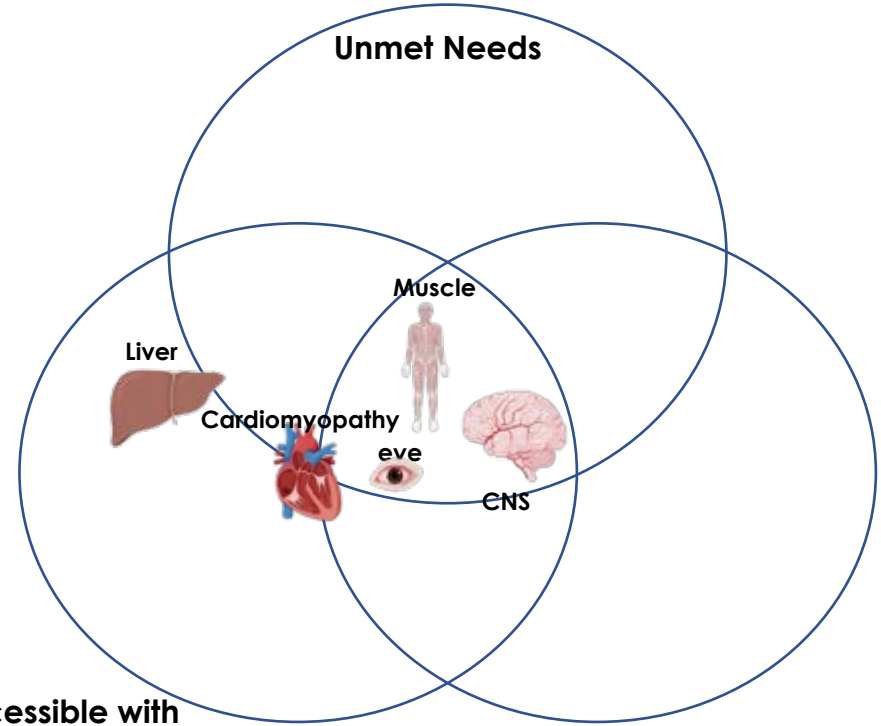
Company	Year Founded	Funding	Platform	Pipeline/Target indication	Stage of Development
MODALIS	2016	Public	CRISPR-GNDM x AAV	MDL-101 for LAMA2-CMD **Gene activation**	IND enabling
Tune	2020	Series B ($175M, 2025)	DNMT-KRAB fusion dCas9 x LNP	Une-401 for HBV **Gene suppression**	**CTA approval from Hongkong, 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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Focused area

Muscle and CNS are the areas with huge unmet medical needs

Target selection for Modalis' gene therapies





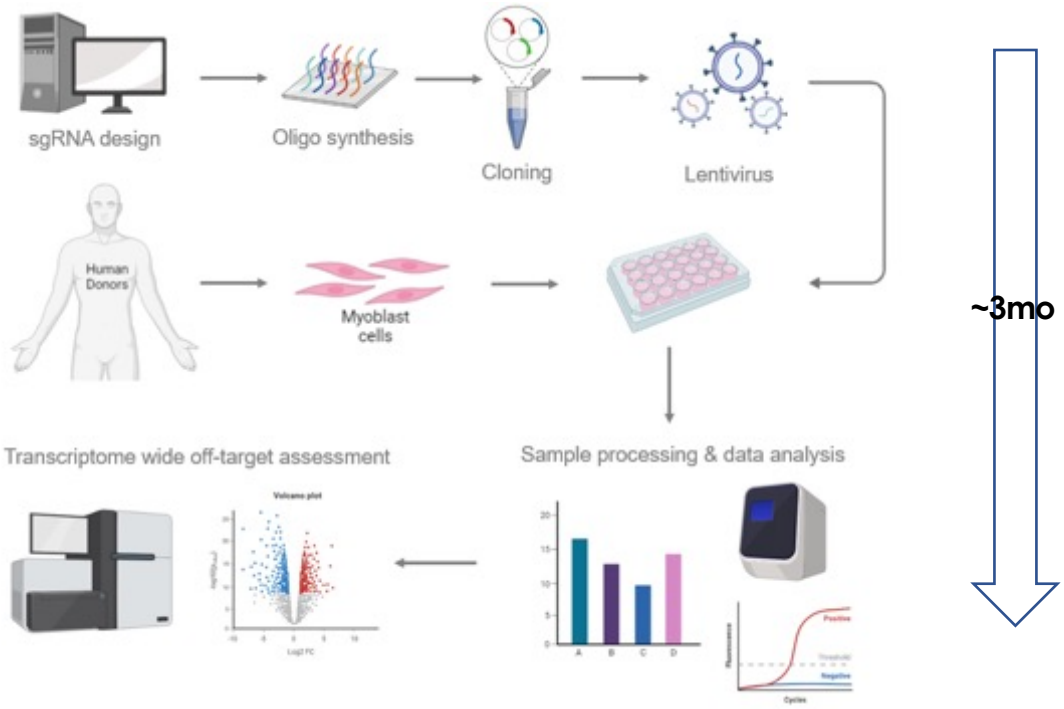
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MODALIS

The Making of GNDM Products

CRISPR-GNDM® technology enables efficient and rapid generation of candidate compounds

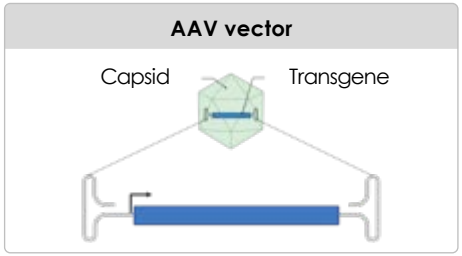
Lead candidate screening in human primary myoblast cells



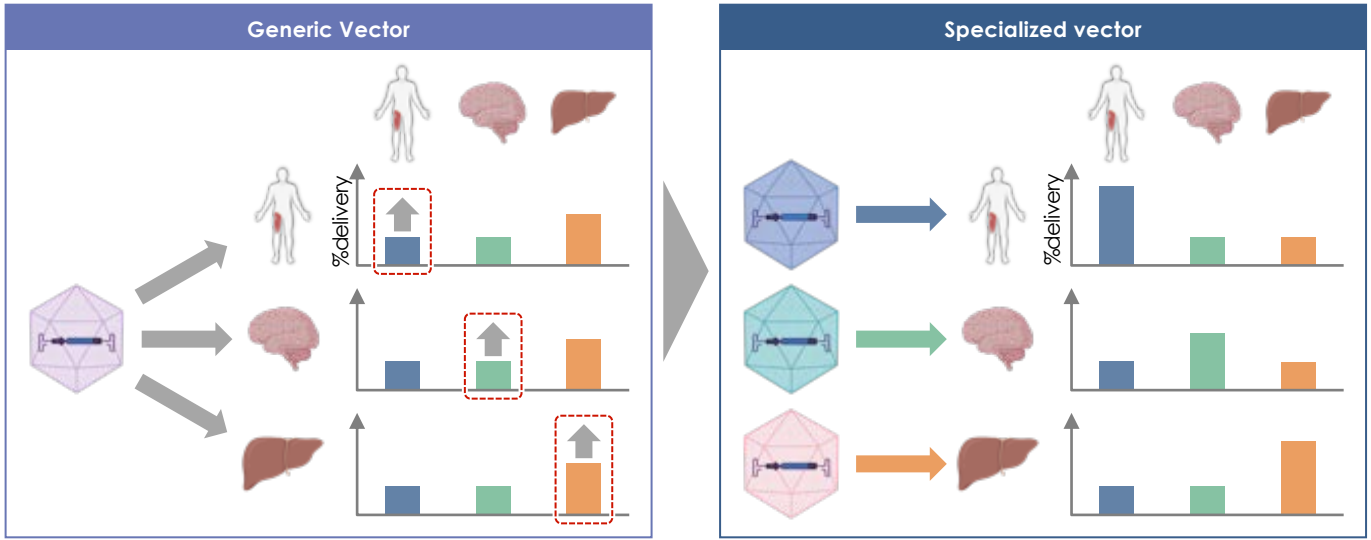
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Innovation through Tissue-Selective Vectors

increases delivery to the target tissue while minimizing toxicity in non-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

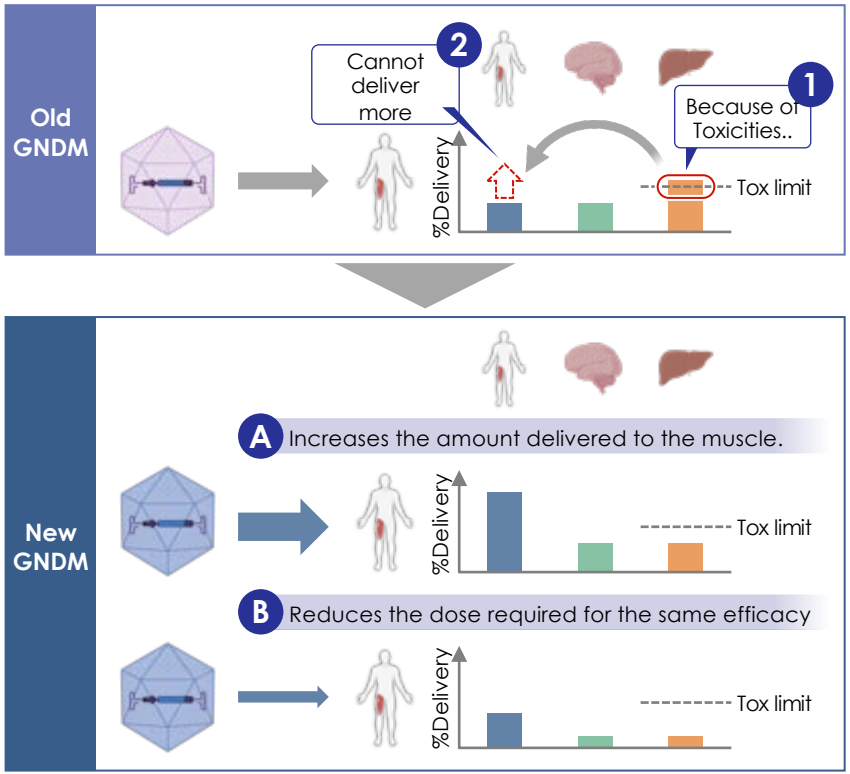


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Impact of the New Capsid on Our Pipeline

Enhancing drug efficacy, reducing toxicity and cost

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

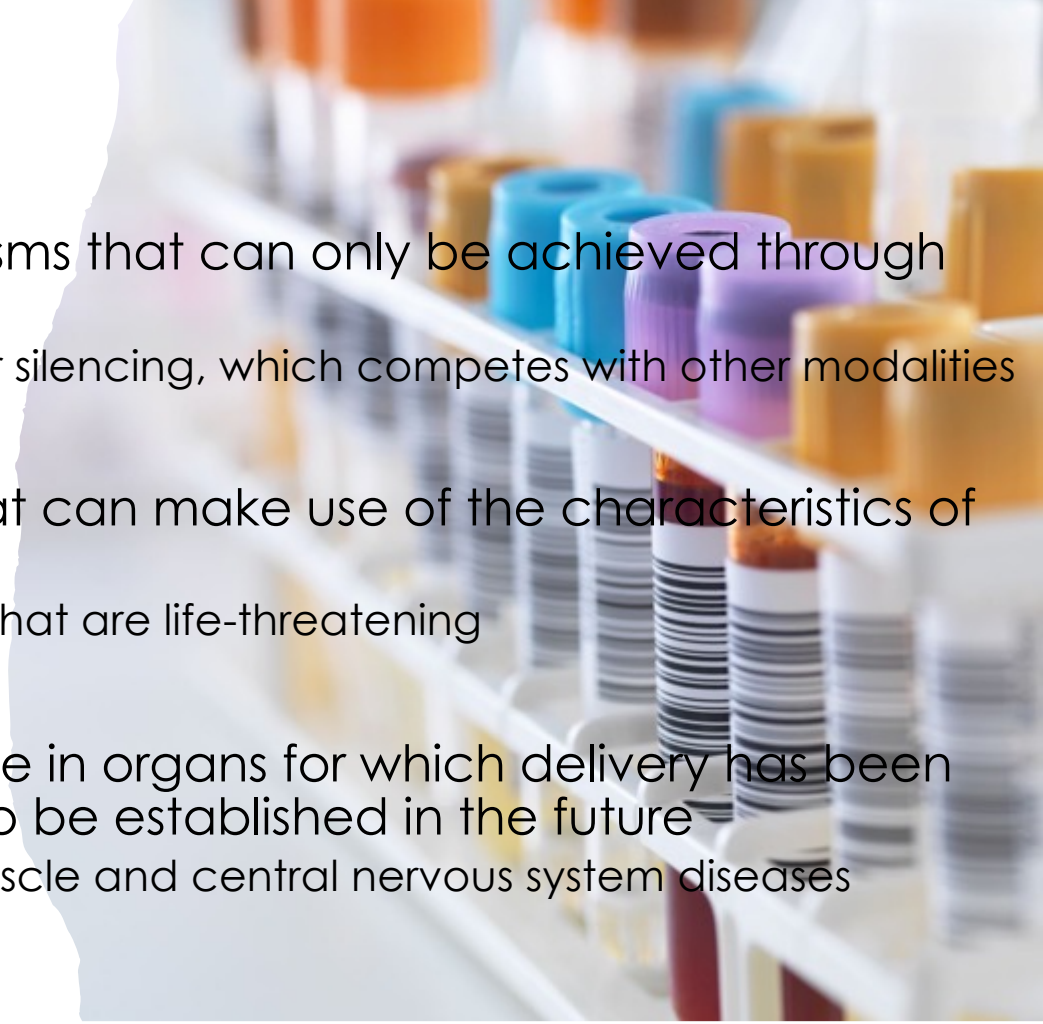
- By shifting to specialized capsids, the transduction efficiency to the target organ can be increased, which can

- **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.

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Essentials of Technology Strategy



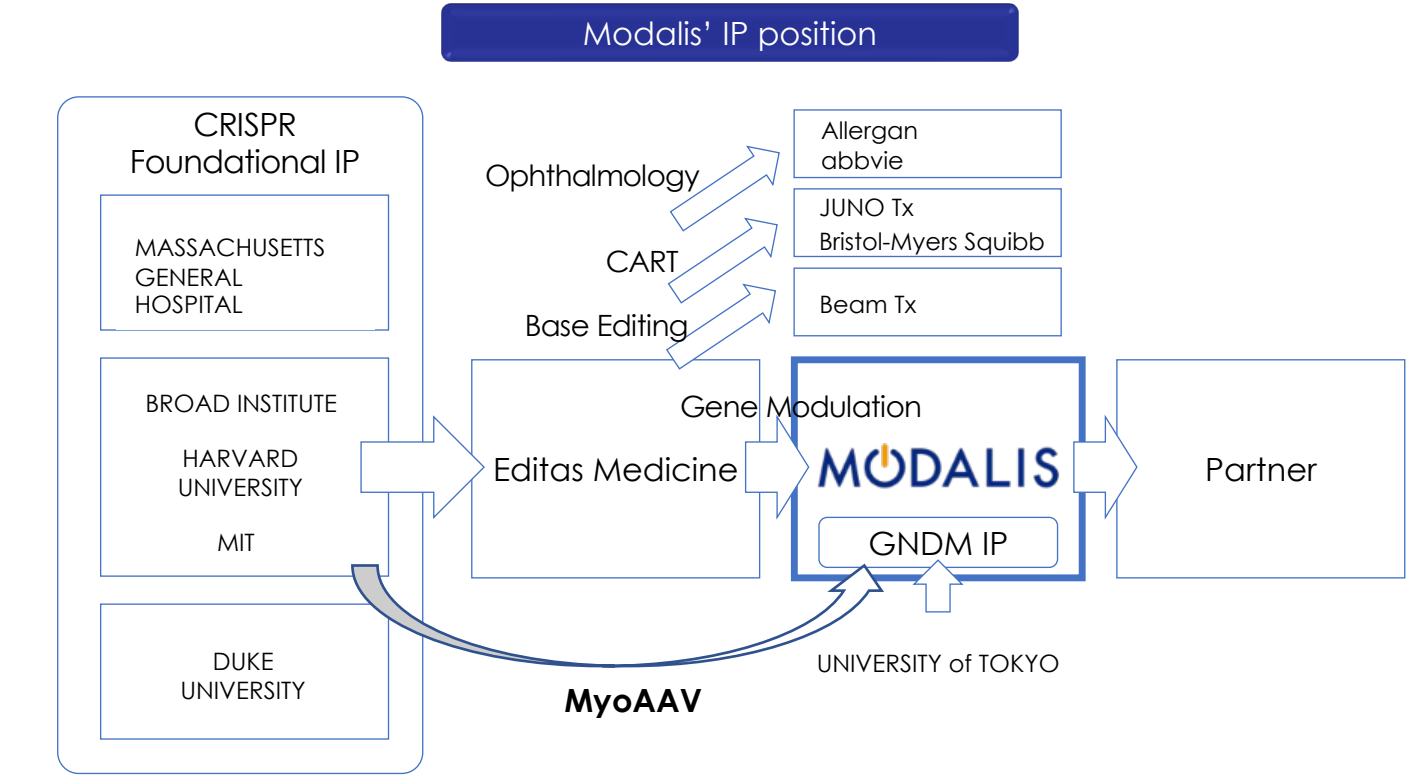
- Focus primarily on mechanisms that can only be achieved through epigenome editing
  - Prioritize gene activation over silencing, which competes with other modalities
- Focus on disease groups that can make use of the characteristics of gene therapy
  - Aim to solve severe diseases that are life-threatening
- 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

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Updated

Intellectual Property position

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



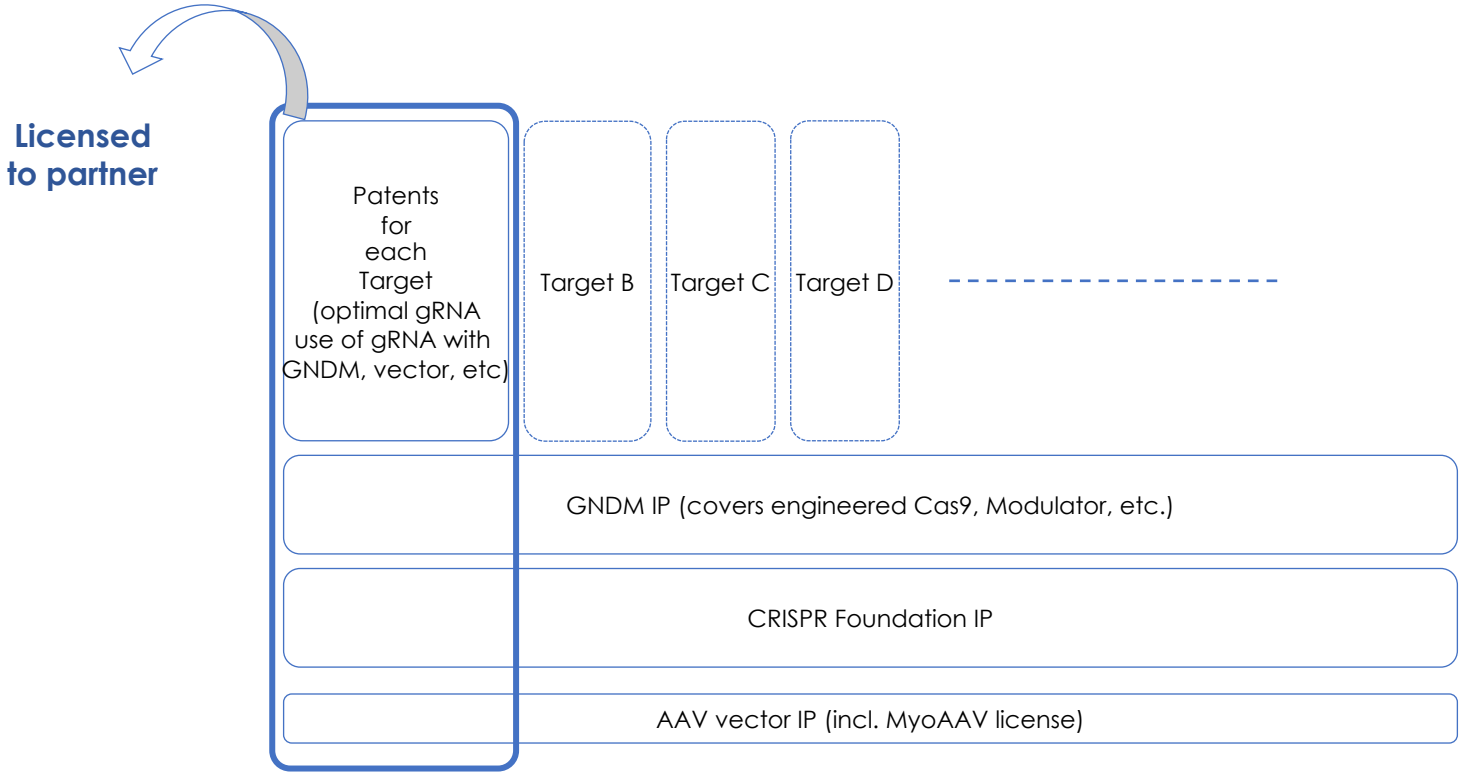
Source： disclosed information by each company

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Updated

Intellectual Property Structure

Each product will be protected by multiple layers of IP



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Updated

Progress on IP

Three patents were granted in Japan in 2025

- Patent “Method for Treating Muscular Dystrophy Targeting the LAMA1 Gene” related to **MDL-101,** the lead program drug for LAMA2-CMD, registered in Japan (Patent No. 7641644) (March)
- Patent related to **MDL-103**, targeting the DUX4 gene for the treatment of facioscapulohumeral muscular dystrophy (FSHD), registered in Japan (Patent 7736329) (September)
- Patent related to **MDL-104**, a therapeutic agent for tauopathies including Alzheimer's disease, “Therapeutic method for Alzheimer's disease targeting the MAPT gene” (Patent 7749244) registered in Japan (October)

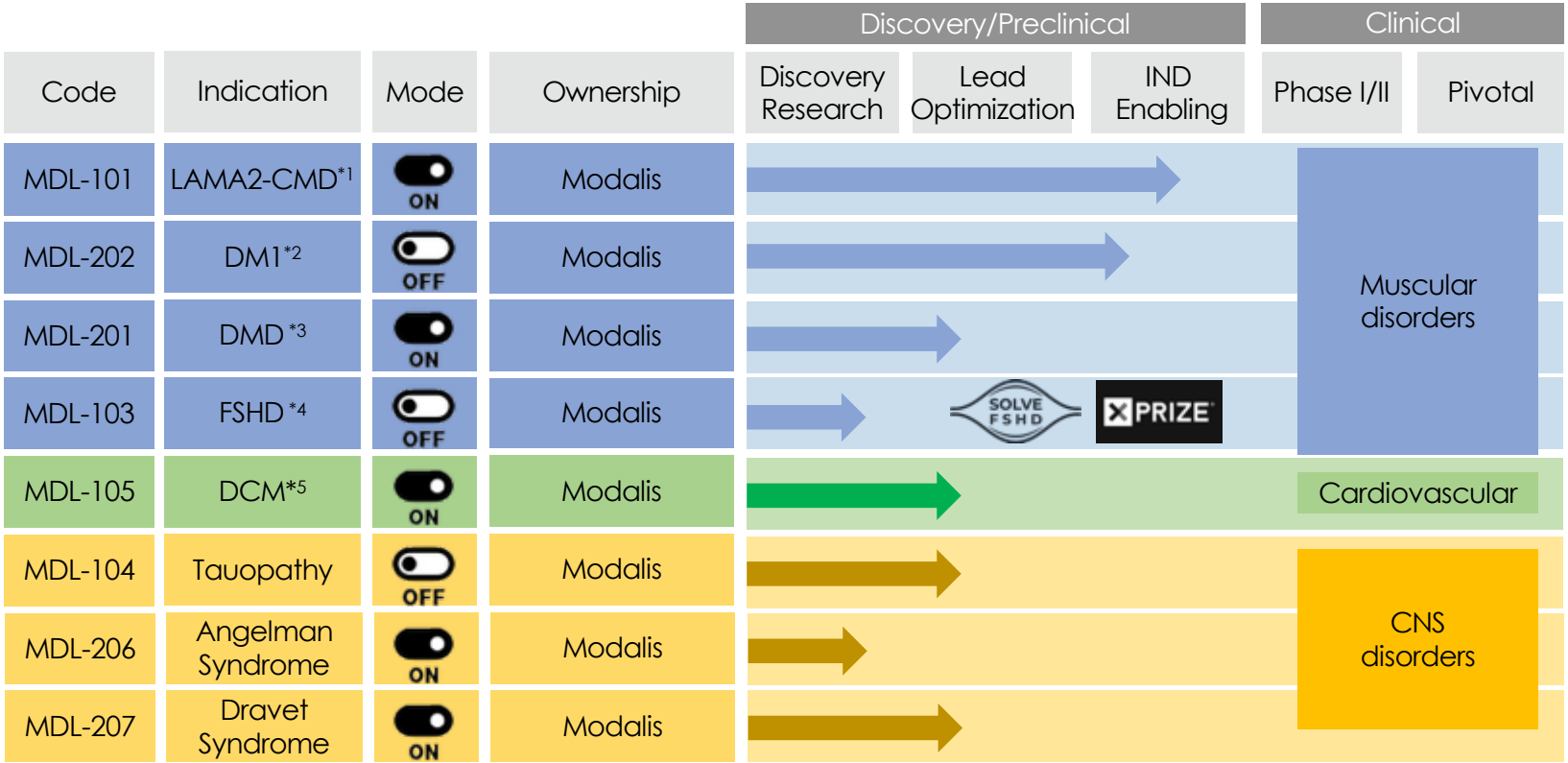


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4. Pipeline

Current Pipeline at Modalis Therapeutics



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

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All muscle programs share the same platform as MDL-101

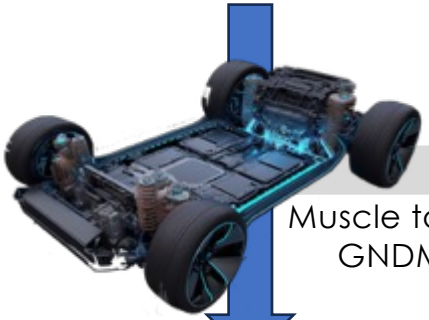
Other muscle programs can be achieved with relatively lower risk and effort











Muscle targeting AAV
GNDM platform



MD-101



MDL-202



MDL-201



MDL-103

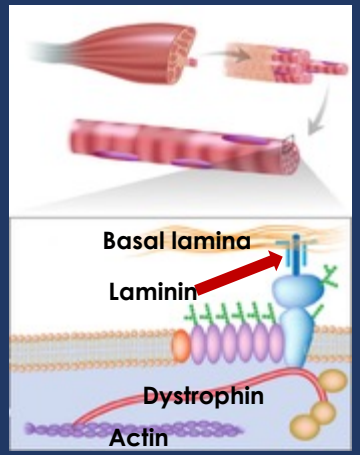
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LAMA2-CMD (aka CMD1a)

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)

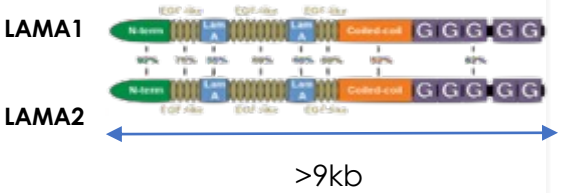
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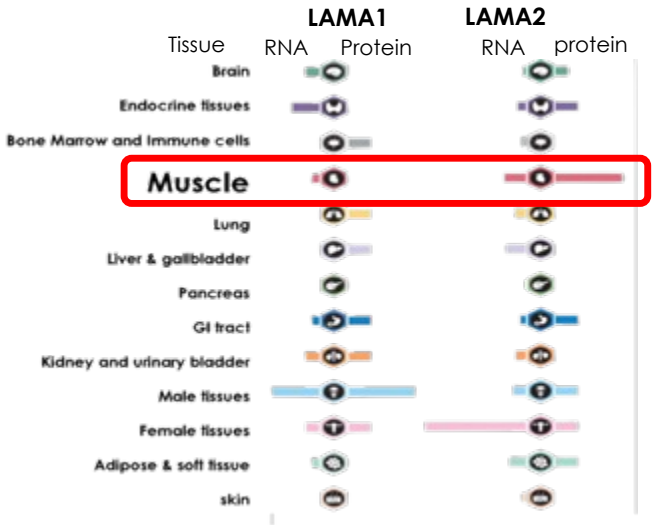
Mechanism of Action of CRISPR-GNDM®

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

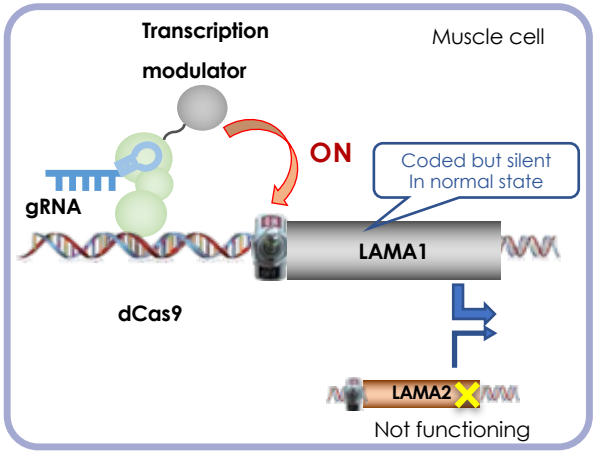
Protein structure of LAMA1 and 2



Exspression pattern of LAMA1and 2 by tissues



CRISPR-GNDM® targeting LAMA1



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Updated

Publication

Preclinical trial data for our MDL-101 published in *Human Gene Therapy*

Efficient LAMA1 Gene Activation by Epigenome Editing as a Therapeutic Approach for LAMA2-CMD

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

Modalis Therapeutics, Inc., Waltham, Massachusetts, USA.

Epigenome editing technology holds great promise for treating diverse genetic disorders. In this study, we demonstrate epigenetic activation of the *LAMA1* gene for the treatment of *LAMA2*-CMD, a severe congenital muscle dystrophy (CMD) caused by biallelic mutations in the *LAMA2* gene. *LAMA1* is a sister homolog that is known to compensate for the function of *LAMA2*. However, supplementing *LAMA1* or *LAMA2* gene via viral platform is not feasible due to the large size of their coding sequences. Through a single administration of our adeno-associated virus (AAV) vector encoding all the necessary elements for epigenetic activation, we observed significant *LAMA1* gene upregulation and phenotype improvements in mouse disease models. The muscle-tropic AAV capsid exhibited desired vector biodistribution and promising pharmacodynamics with good safety profiles in 2-year-old juvenile nonhuman primates (NHPs). Moreover, administration to 8-month-old infant NHPs demonstrated superior pharmacodynamics compared with 2-year-old juveniles, even at half the dose. Our approach holds broad applicability for a range of loss-of-function genetic disorders and could offer a therapeutic breakthrough where active epigenome offers clinical benefit.

Keywords: gene therapy, epigenetic editing, CRISPR, LAMA1, LAMA2-CMD, MDC1A, AAV

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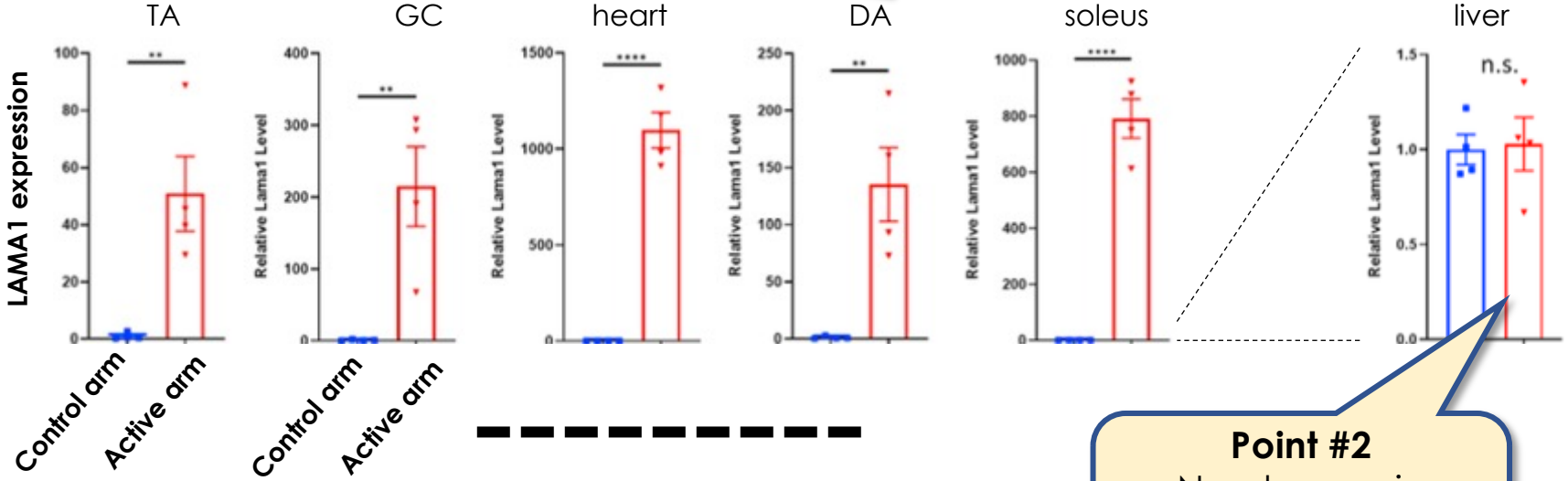
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From the paper

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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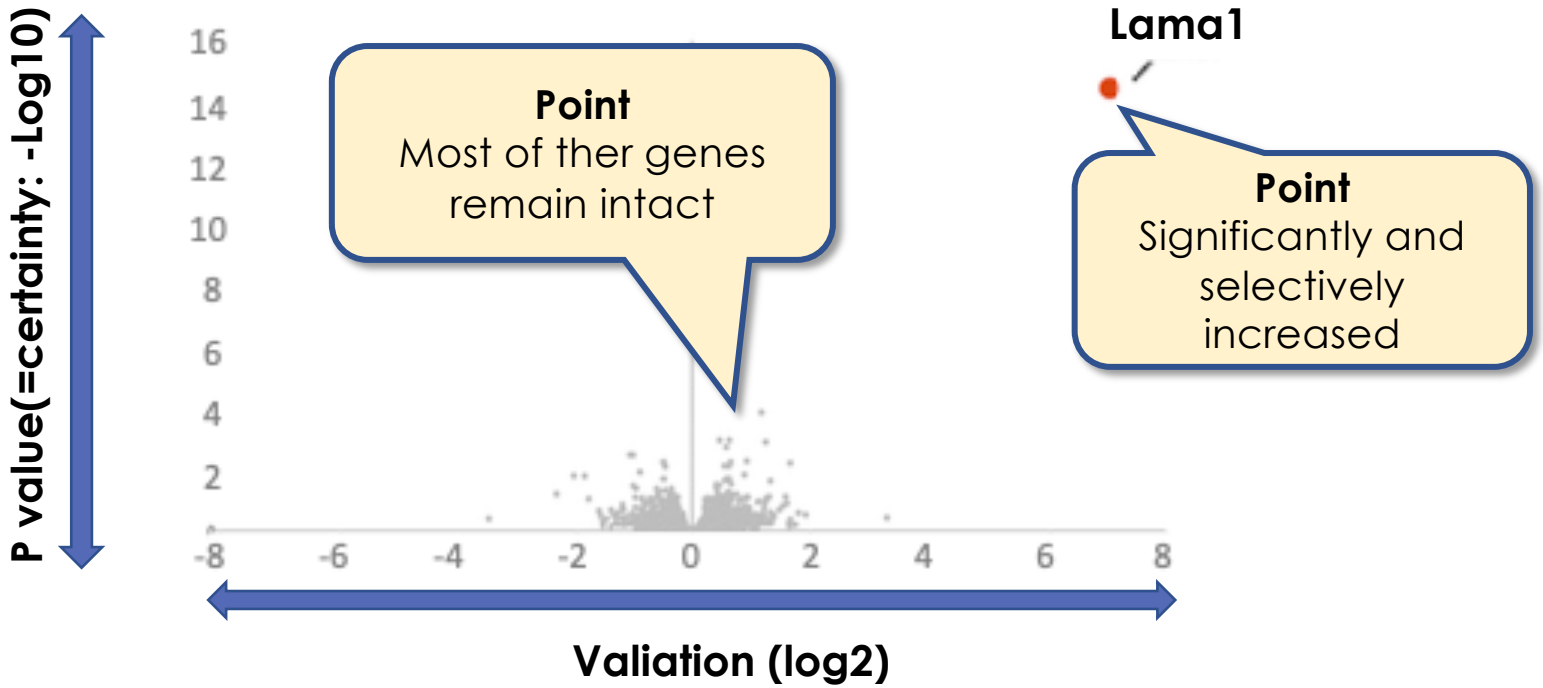
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From the paper

GNDM selectivity

LAMA1 was selectively upregulated as the other genes remain no change

gene perturbation by GNDM-LAMA1 in RNAseq



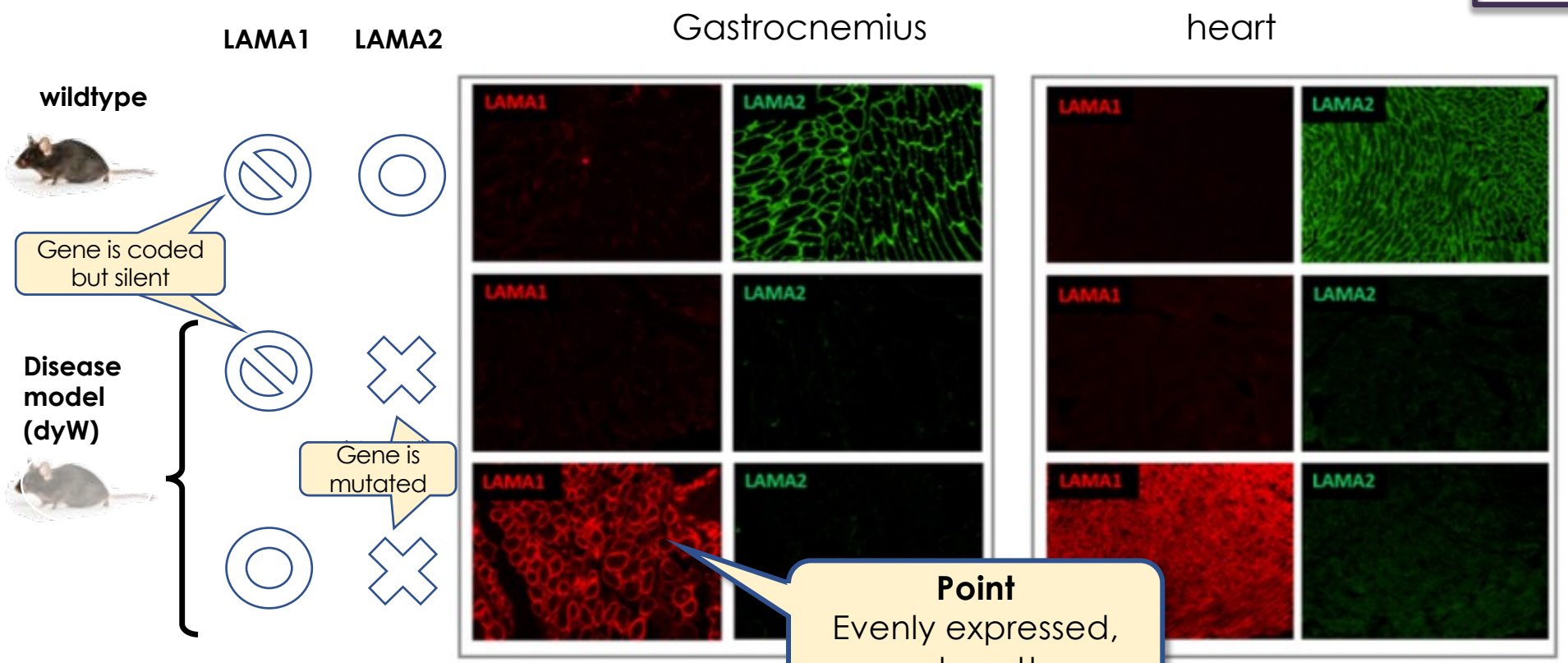
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From the paper

LAMA1 distribution by MDL-101

LAMA1 is uniformly expressed in a wide range of muscle cells



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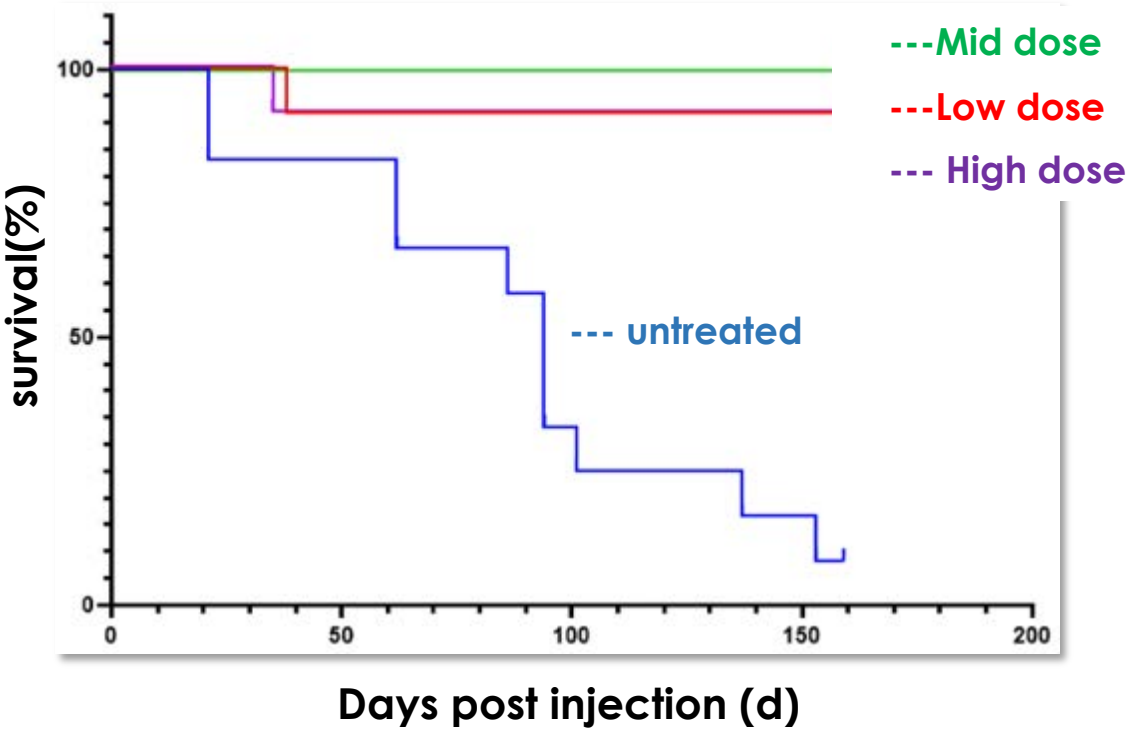
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Survival prolongation effect of MDL-101

Survival rate was significantly improved by administration of MDL-101

Updated

Survival curve of dyW(disease model)mice



Other improvements include:

- **Grip strength**
- **Weight gain**
- **Health deficit**

Details and most updated data will be reported at

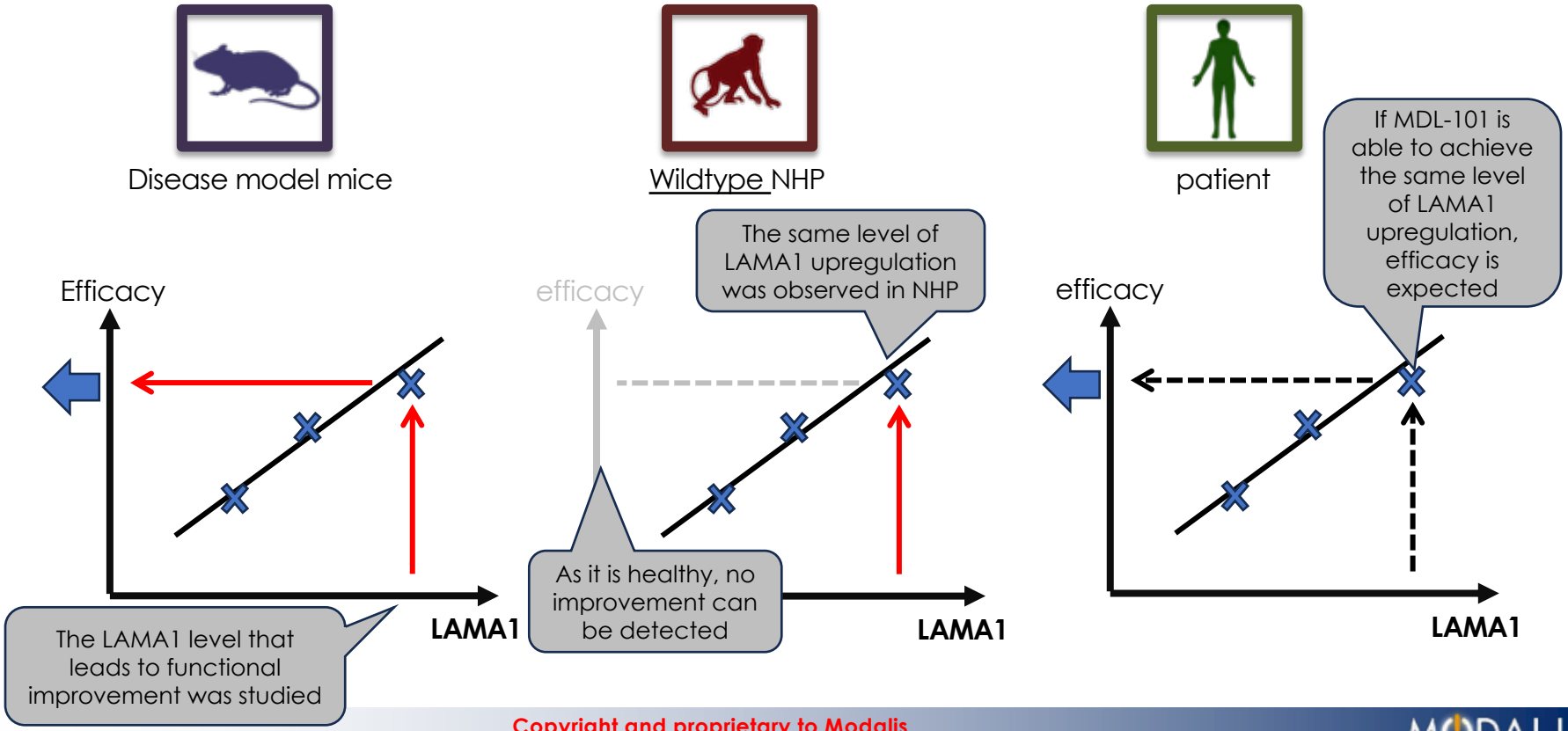
- LAMA2-Europe (Mar 29)
- ASGCT 2026

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Estimation of drug efficacy in clinical settings

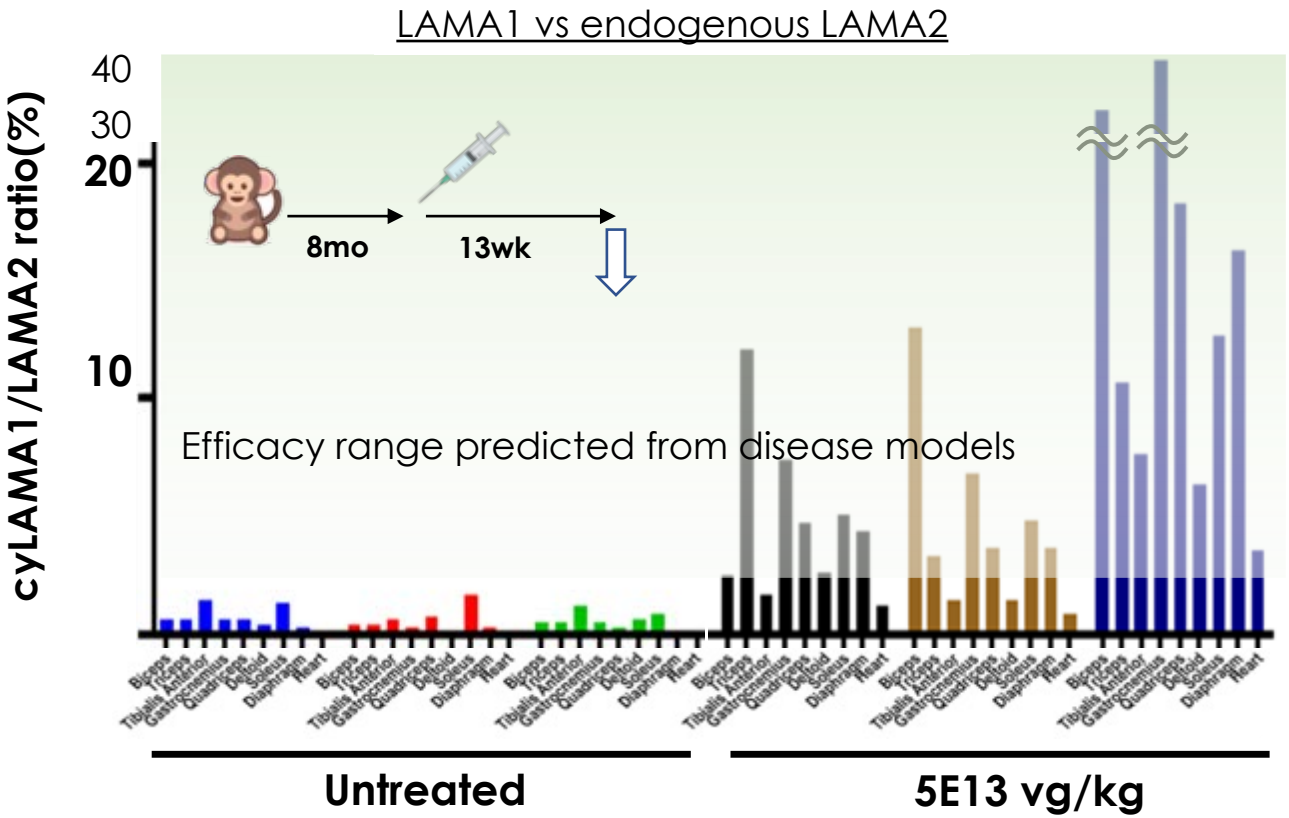
Observed LAMA1 elevation to a level at which functional improvement was observed in the disease model



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Monkey data suggesting efficacy in humans

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



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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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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

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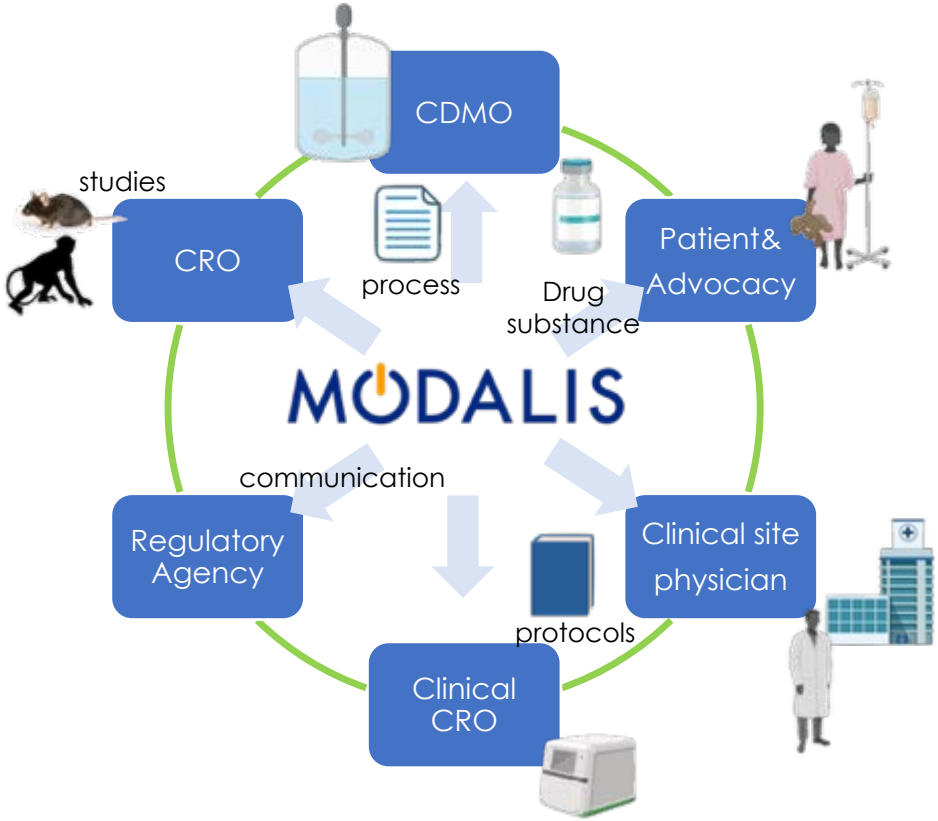
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Alignments for the clinical trial

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





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Updated

Advantages of ODD and RPDD, which MDL-101 has been granted

Various economic benefits will be generated

- **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

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

RPDD Vouchers has been revived

■ **September 2024**
Original Expiration Date
↓
■ **December 20, 2024**
Short-term extension (via Budget Act) ends
↓
■ **February 3, 2026**
Via the Consolidated Appropriations Act:
- PRV program reauthorized
- FDA grant authority extended

↓
■ **September 30, 2029 (New Expiration Date)**

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Progress towards the FIH trial

Development update of MDL-101

- GLP Tox Study
  - The in-life phase has passed the 3-month mark and is awaiting 6 months of data.
- Mouse IND Enabling
  - Study progressing smoothly. Interim analysis demonstrated significant survival and functional recovery effects compared to the control group in the disease model, with no issues expected for completion.
- Manufacturing
  - Investigational drug AAV manufacturing (GMP) is underway.
- Clinical Trial Preparation
  - Interviews with US trial candidate sites/PI completed. Selection in progress.
  - For clinical trials outside the United States, a memorandum of understanding has been signed with the pharmaceutical company in the relevant country regarding the conduct of the trial and future sales within the region.
  - Preparing for various evaluation studies.









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Key Points for Plan Revision

Confirm biological validity and promote optimization for clinical transition

1. Biological foundation maintained and strengthened

- Clear survival time extension compared to control group confirmed in IND enabling studies using disease model mice
- Mechanism of action and pharmacological efficacy consistently supported
- No new safety concerns identified at this time
- No change to the treatment concept itself

2. Refinement of Development for Clinical Transition

- Conduct additional analyses to enhance certainty of transition to clinical phase
- Strengthen translational reproducibility through refinement of development parameters
- Maximize success probability through data-driven decision-making

3. Clear Next Steps

- Complete additional analysis and optimize development plan
- Ensure alignment with regulatory authorities
- Reviewing IND filing timing to ensure optimal clinical readiness
- Conduct site preparation in parallel

By prioritizing the optimization of biological and clinical readiness, we aim to maximize the probability of long-term clinical success

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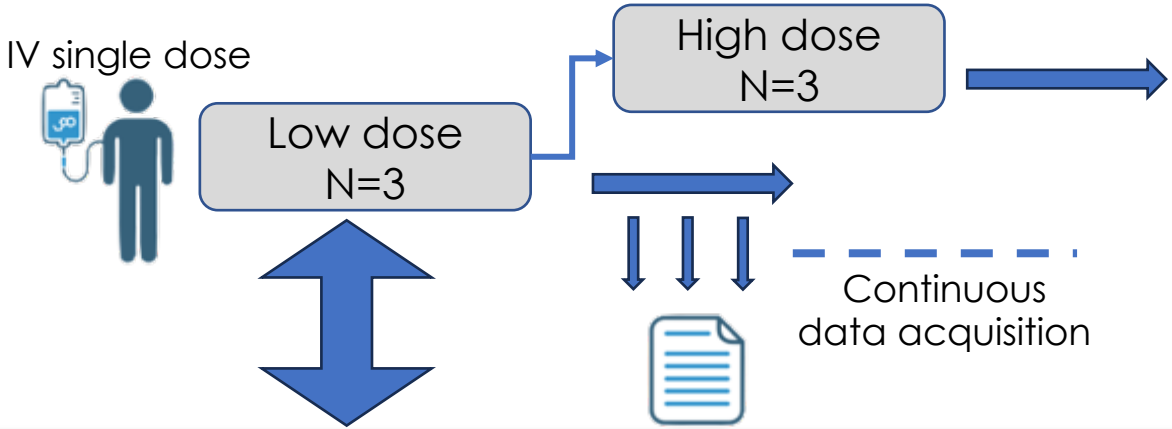
Updated

MDL-101-001 Trial design

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

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

Phase1/2 Open-label dose escalating trial



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

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Updated

MDL-101 is potentially the first upregulating 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 PROLONGED SURVIVAL AND 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

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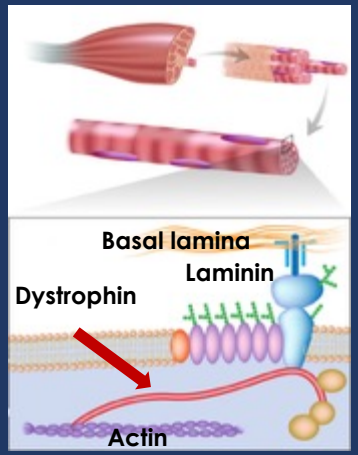
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Duchenne Muscular Dystrophy (DMD)

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

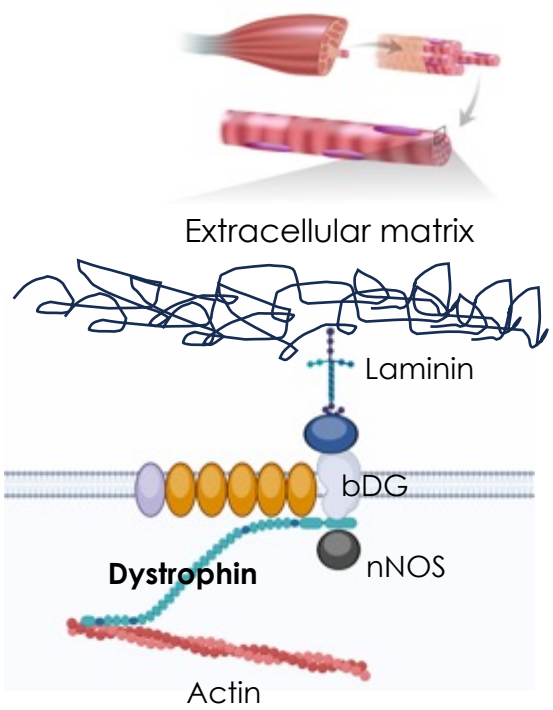
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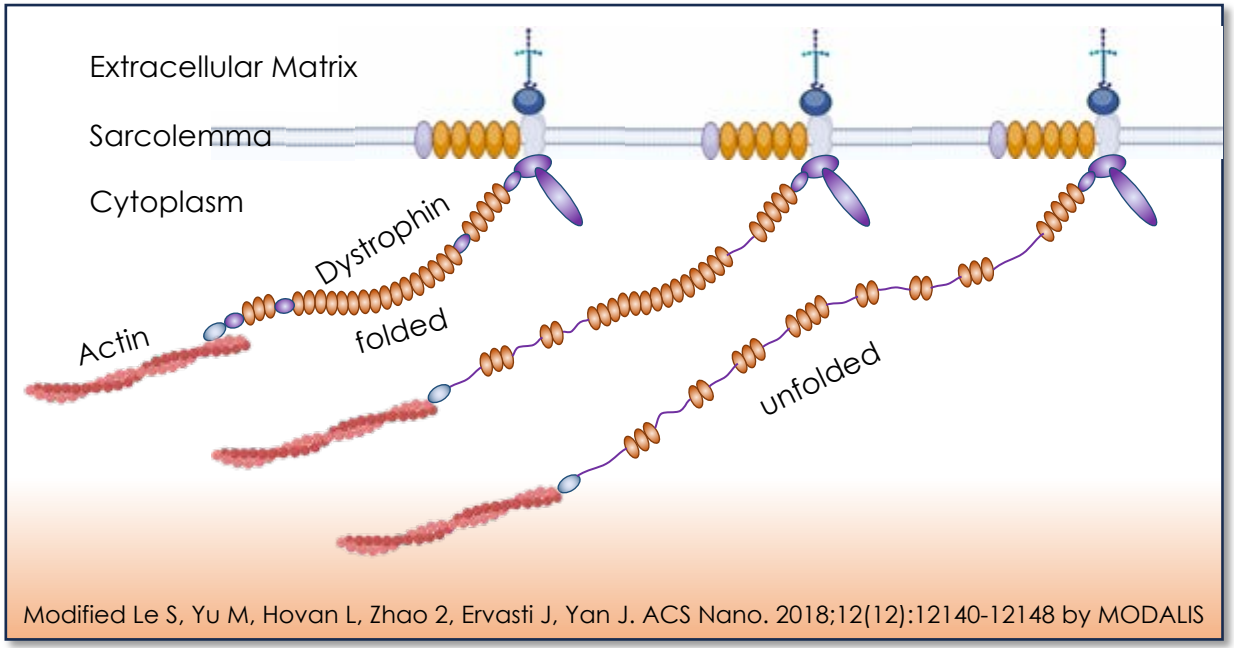
Dystrophin's function

Functions as a shock absorber and signal transmitting molecule in muscles

Dystrophin location



Dystrophin stretches and contracts to connect the cell membrane and actin

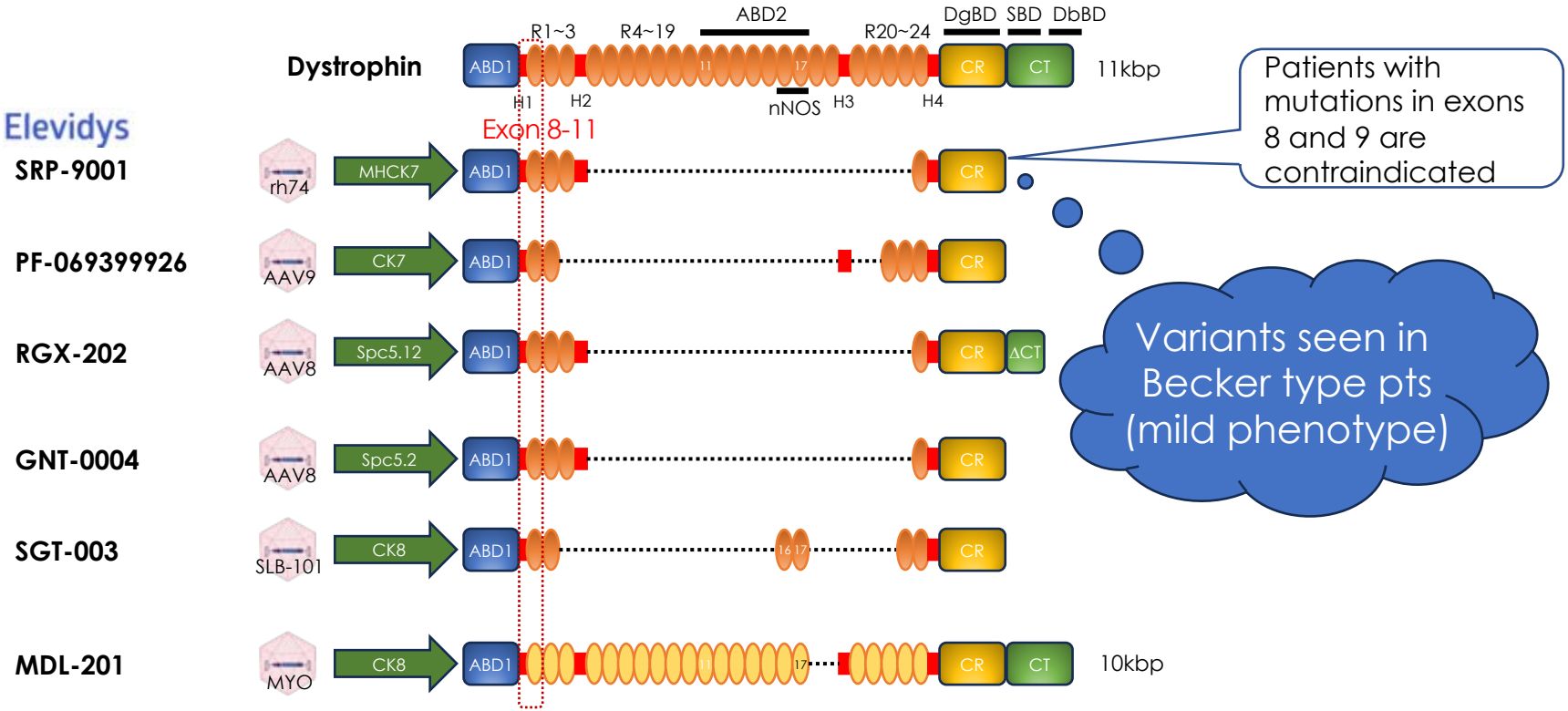


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micro-Dystrophins payload comparison

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

Dystrophin/Utrophin and mini-Dystrophin structure

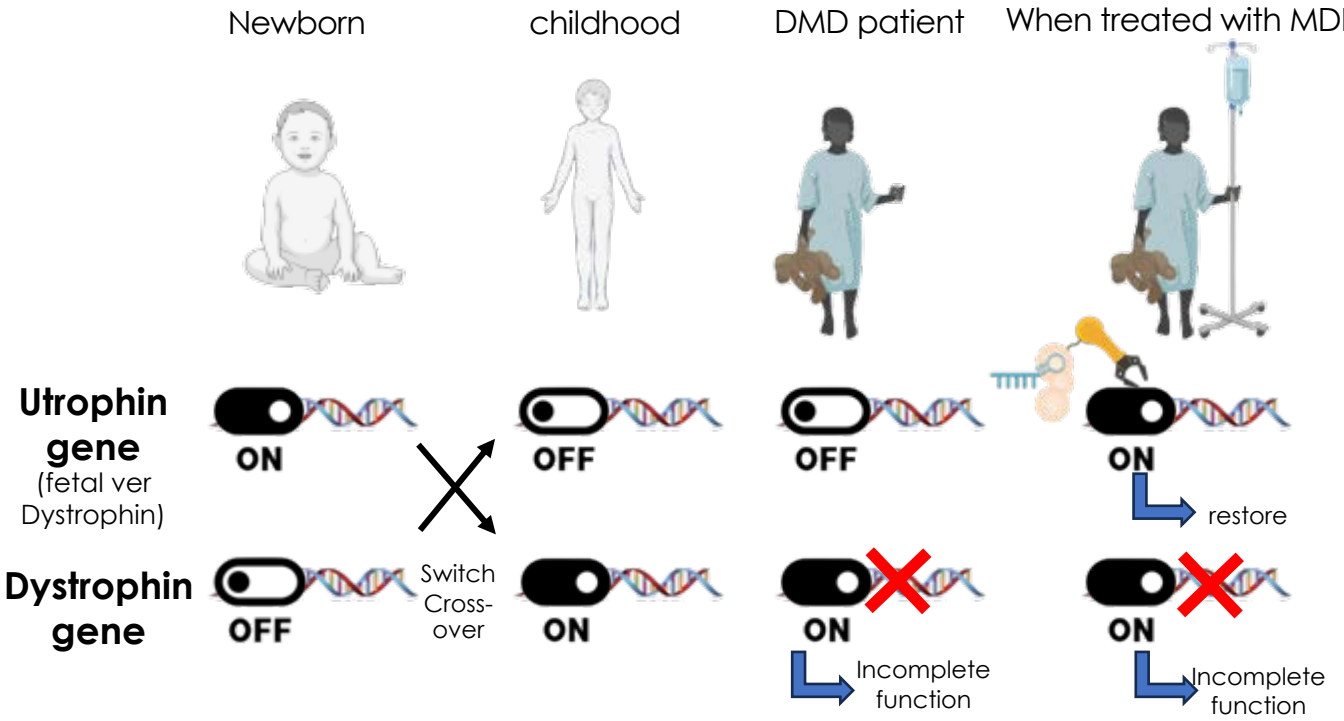


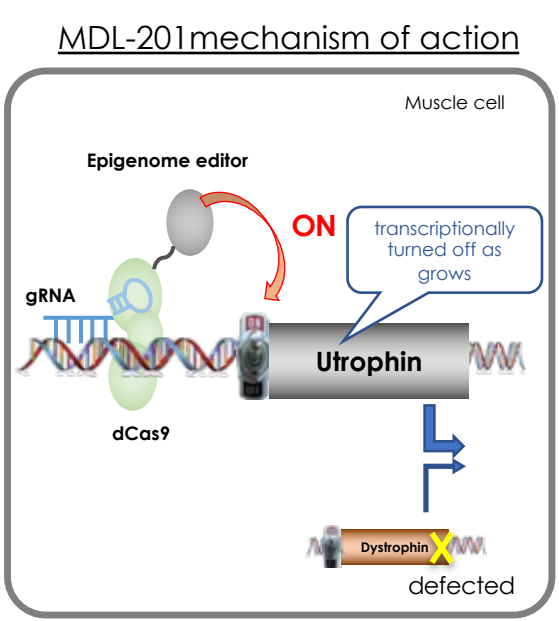
Modified from Crudele &Chamberlain, 2019

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MDL-201 therapeutic concept

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





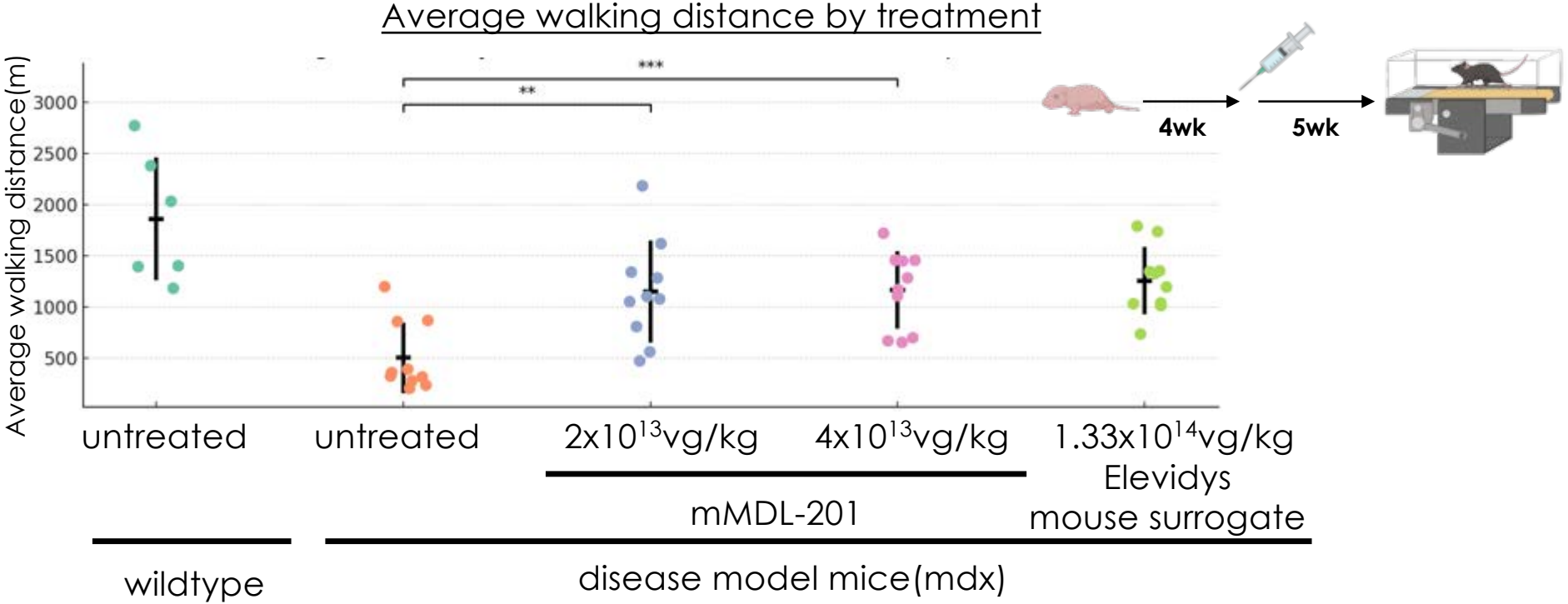
activating Utrophin using GNDM is expected to have a greater medicinal effect than mini-Dystrophin

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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 GTx 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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Myotonic dystrophy type 1(DM1)

extension of CTG repeat in 3' UTR of DMPK gene

MDL-202

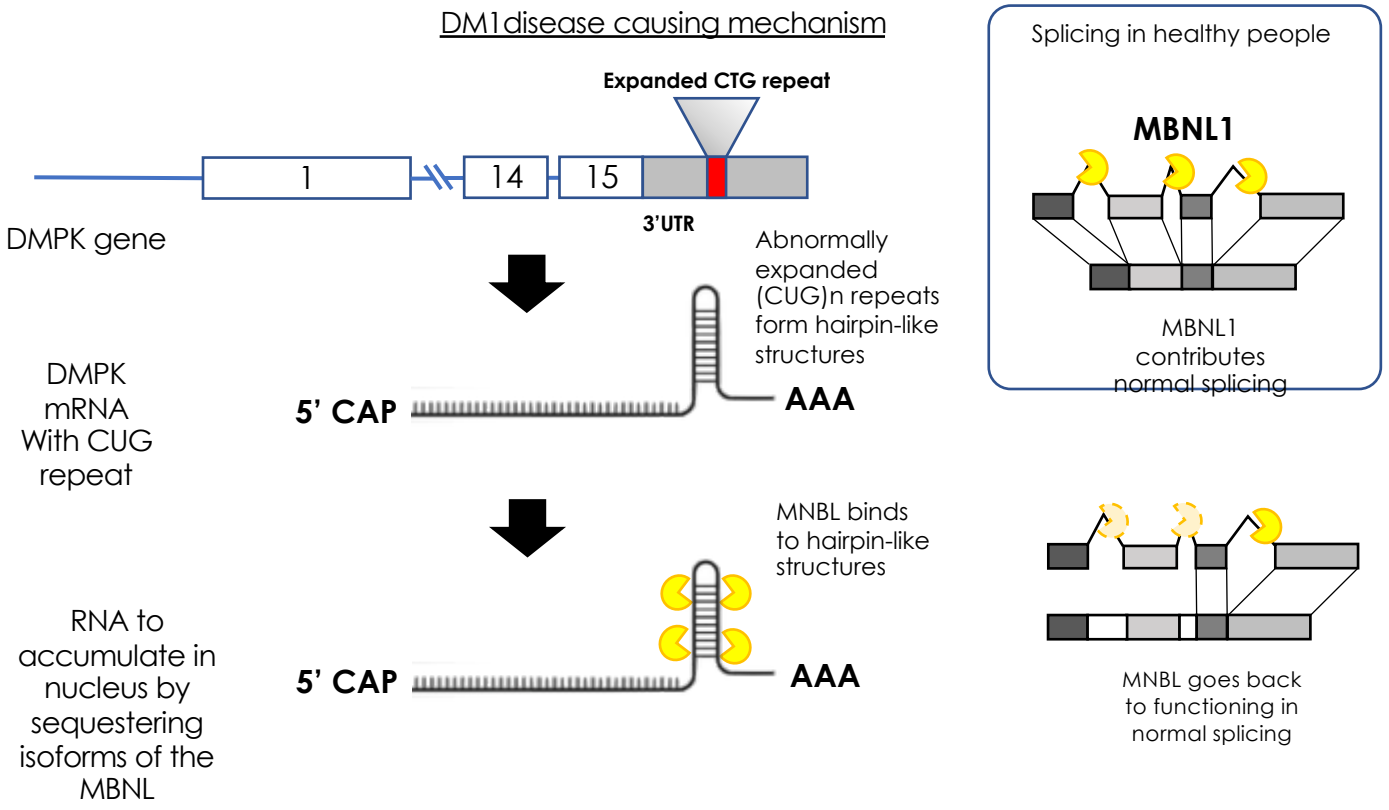
Potential to be the first-in-class and the first DM1 treatment

Prevalence	**1-4.8 in 10,000** (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 #** By 2032	$80M market as of 2022 without any treatment but is expected grow

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

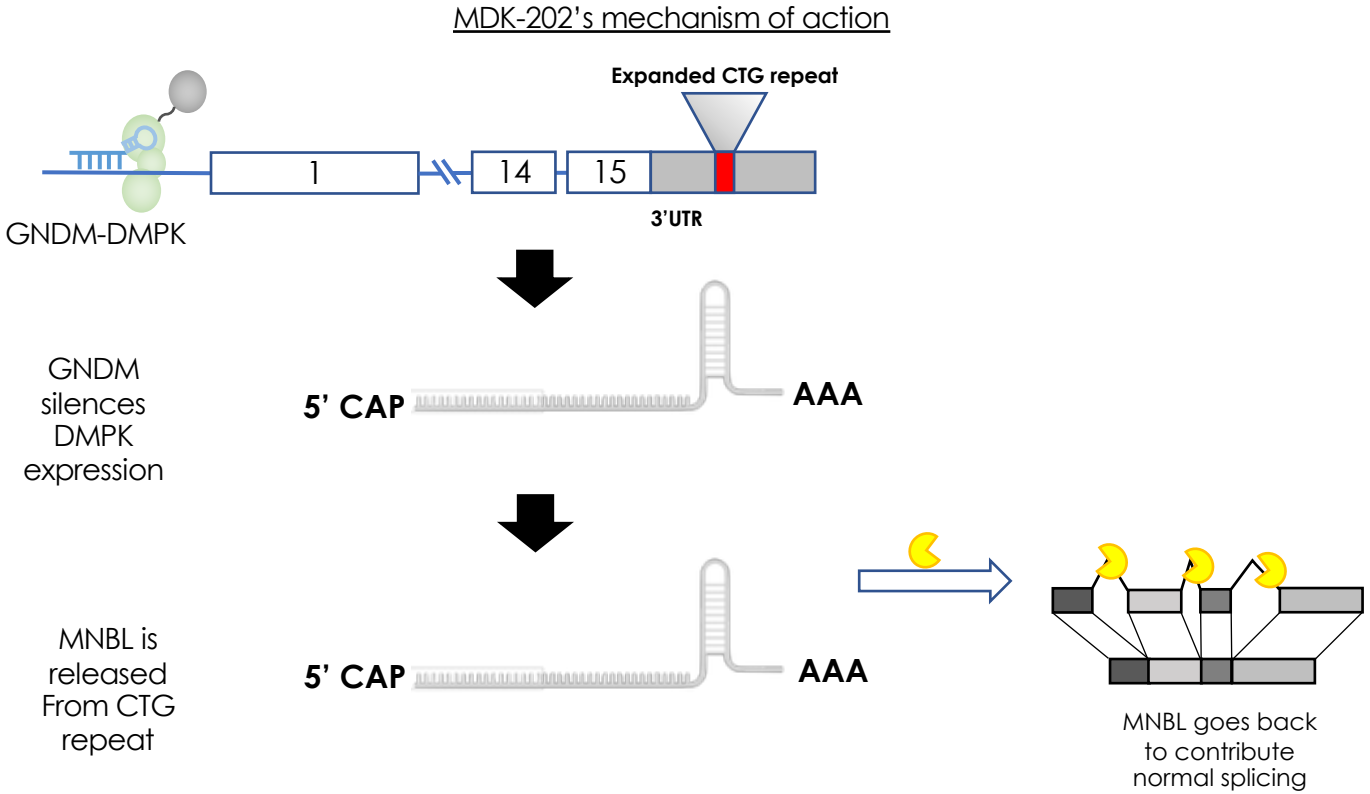
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DM1 is caused by abnormal splicing rooted from CTG extension in 3'UTR of DMPK gene



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

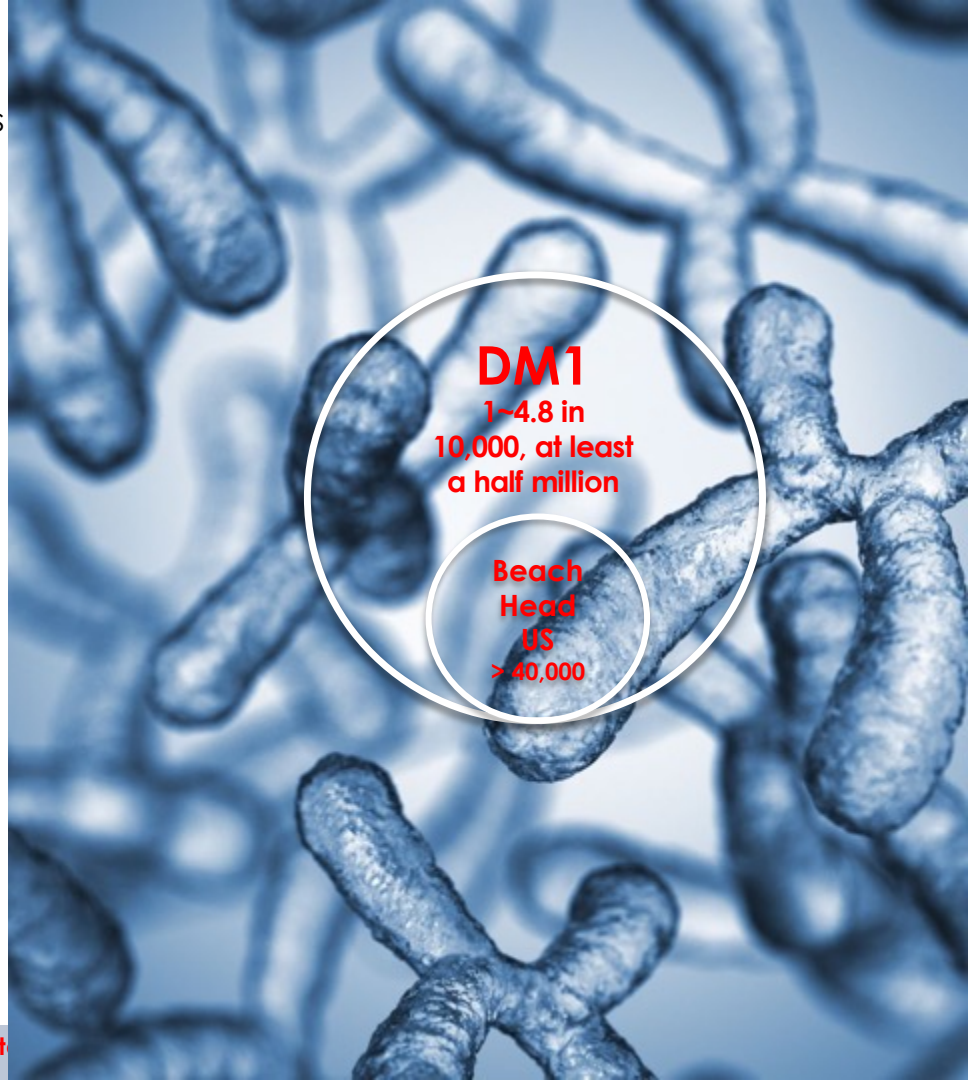


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Prevalence of DM1

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

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MDL-202 holds significant potential as a GTx for DM1, a disease affecting many patients

01

Directly acts on the DMPK gene at the DNA level, which is the mechanism of onset for DM1

02

Significant DMPK inhibition has been confirmed in the disease model

03

Access to a relatively large patient population even for muscle disorders

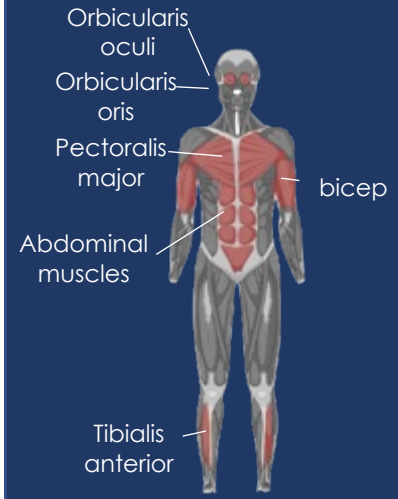
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Facioscapulohumeral Muscular Dystrophy (FSHD)

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 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+**	

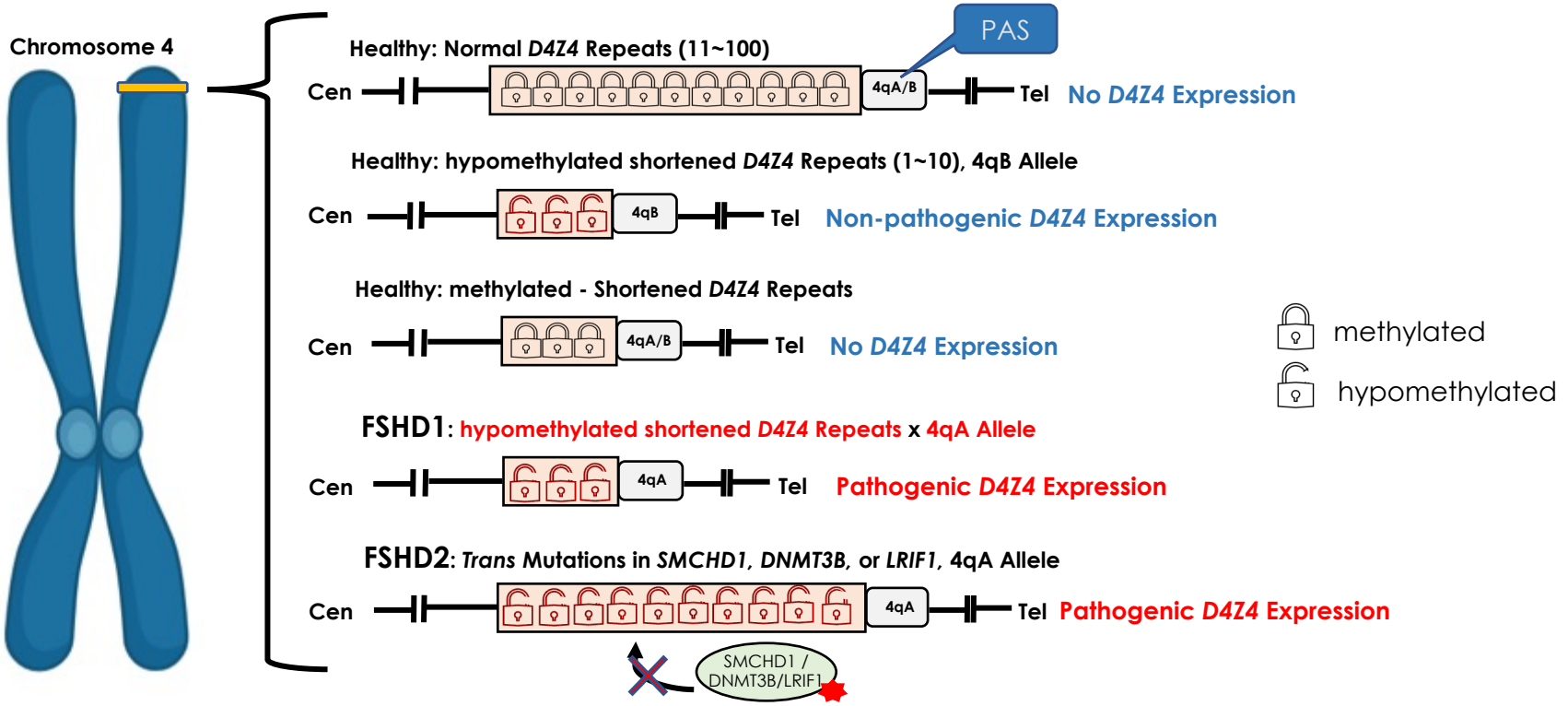
Source: https://doi.org/10.1212/WNL.0000000000011425
Orphanet, Raymond A. Huml MD A concise guide

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FSHD disease mechanism

Dux4 expression causing toxicity to skeletal muscle due to epigenetic changes leading to a state of disinhibition



DeSimone et al. 2020, *Dis Model Mech*

PAS: polyadenylation signal

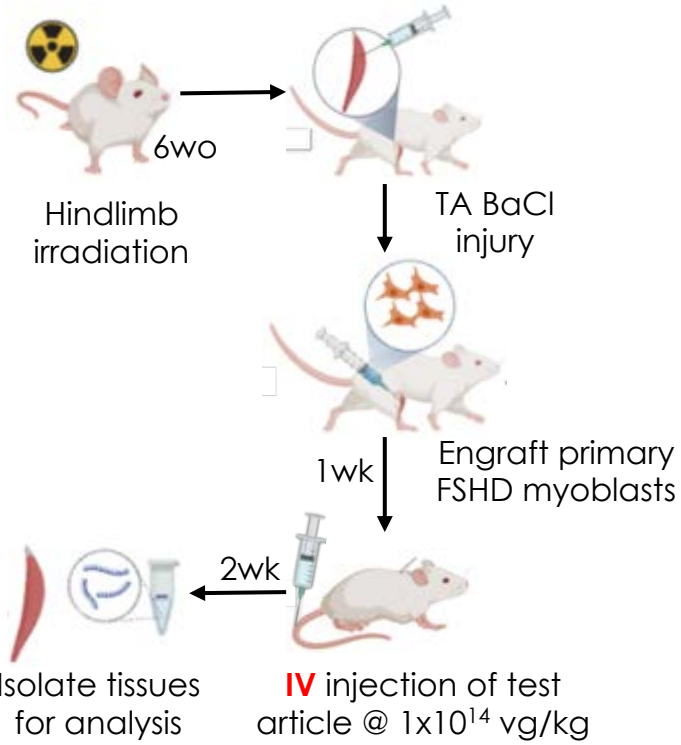
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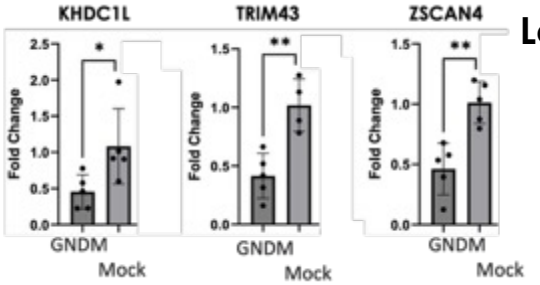
New

Clear efficacy in a FSHD disease model

The DUX4 downstream gene was even strongly suppressed by systemic administration

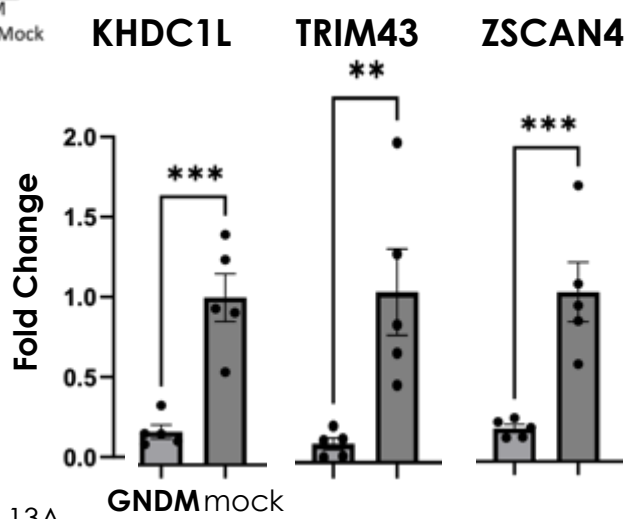
Expression of DUX4-Target Genes In Xenografted human muscle





Local(*i.m.*) injection

Systemic(i.v.) injection



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

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Research funding to MDL-103

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

Source: Solve FSHD website

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MDL-103 offers a reasonable development potential as an FSHD gene therapy

01

A target with clearly demonstrated causal relationships between disease and gene

02

Powerful suppression of the DUX4 pathway has been clearly demonstrated in animal disease models

03

Development is supported by funding from multiple external grants

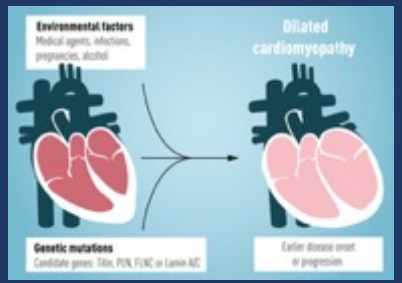
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Dilated Cardiomyopathy (DCM)

A condition in which the heart becomes enlarged

MDL-105

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



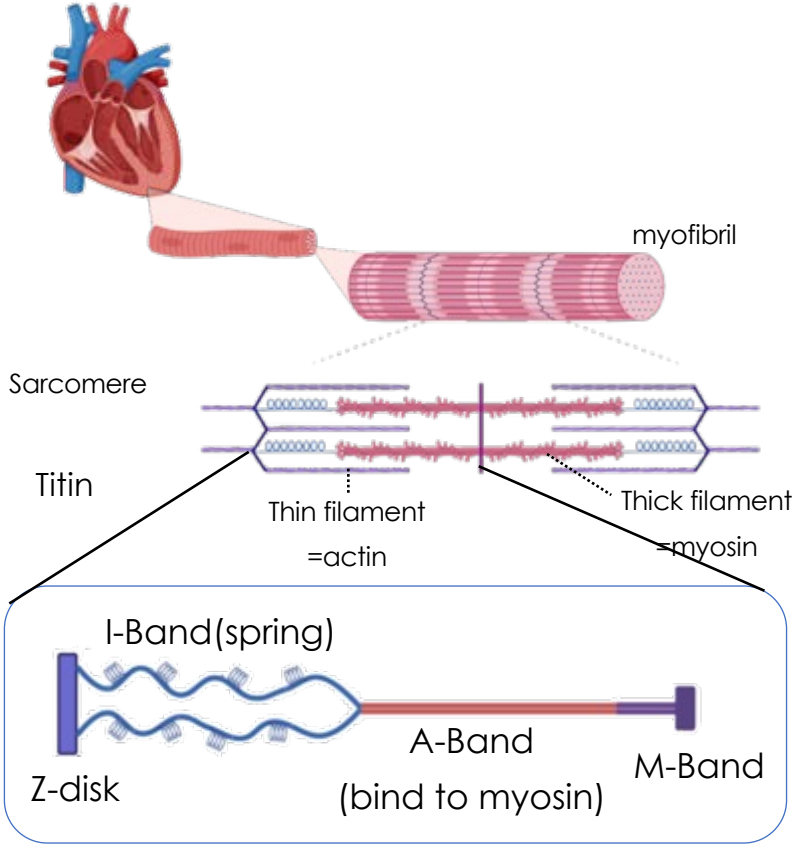
Prevalence	**1 in 250-2,500#**	• ~20% of DCM is estimated to be caused by TTN variant • Half is by truncated variant
Disease Onset	Middle age around **20-60 yo**	
Disease Burden	Five-year survival rate is about **50%***	• Without treatment, the 1-year survival is 70%–75%, with a 5-year survival of as low as 50% • 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

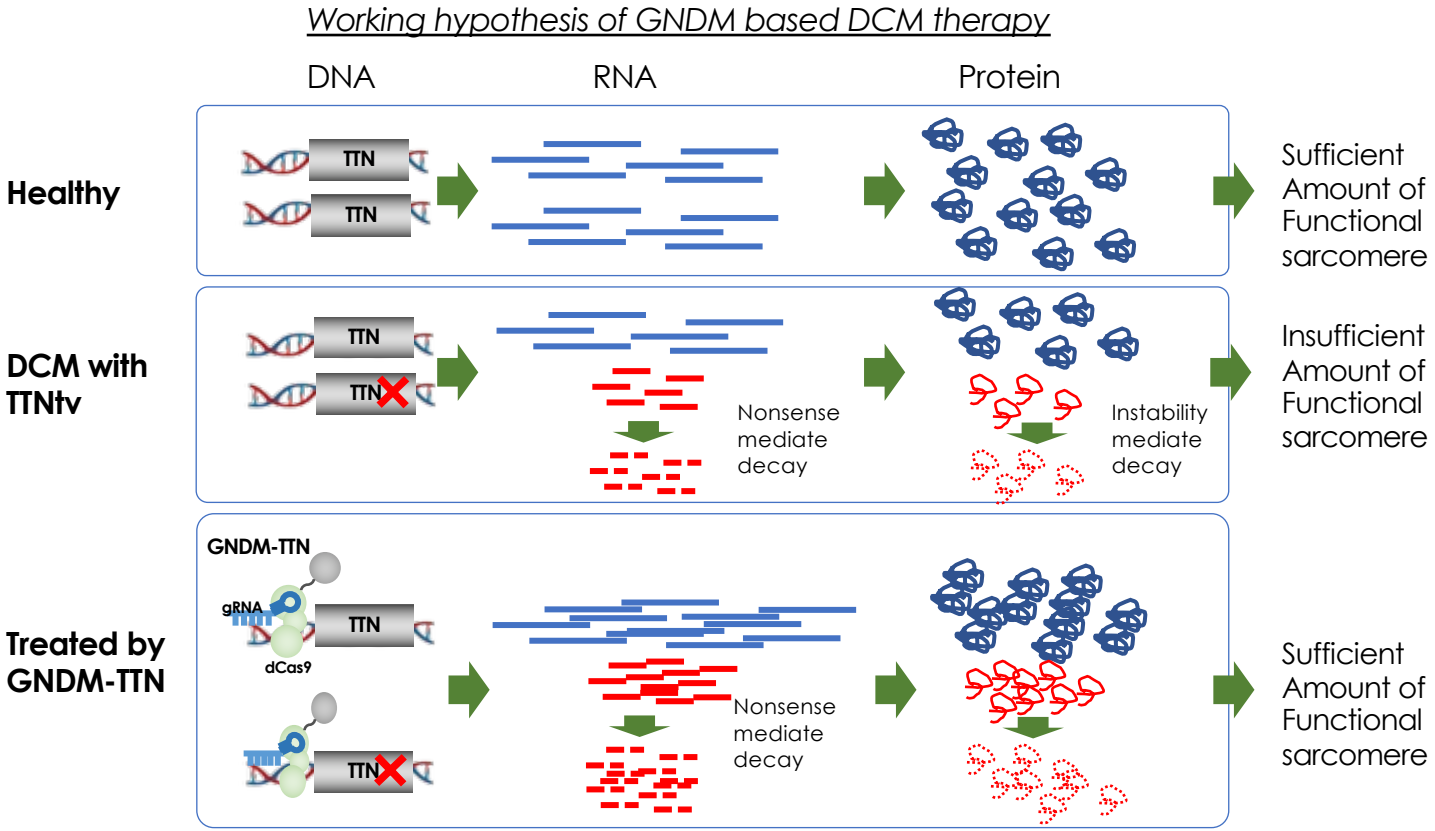


- **Largest** human protein
  - 35,000 amino acids /17kb
  - 363 exons
  - Acts as spring in sarcomere
  - Tension during relaxation
- **Abundant** in human body
  - Third most abundant protein in muscle next to myosin and actin
  - Adult human contains approximately 0.5 kg of titin
- **~90% mutations**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

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MDL-105's mechanism of action

Restore normal sarcomere levels by boosting TTN



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Why does GNDM make sense for TTN?

GNDM normalizes TTN levels, a genetic predisposition responsible for a certain percentage of DCM cases

- 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

The selection of the optimal gRNA to achieve increased expression of human TTN has been completed

- Achievements so far
  - Human gRNA screening completed
    - Filed patent
  - 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 molecules with
  - Explorer funding including partnership opportunities
  - Reconsider timing of PreIND contingent on identifying and pursuing disease model study and funding.

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MDL-105 provides a fundamental solution through a genetic approach for a significant proportion of DCM cases

01

Targets with clearly demonstrated causal relationships between disease states and genes

02

TTN is the largest human gene and cannot be targeted by conventional approaches

03

Screening for optimal gRNAs that achieve increased expression of human TTN has been completed

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Tauopathy (incl. Alzheimer's Disease)

Neurodegenerative disorders caused by misfolding of the tau protein

MDL-104

Potentially best-in-class molecule by silencing Tau expression

Prevalence	**1 in 9 above 65*** 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 All mutations are associated with Aβ hyperactivity
Commercial opportunity	**$4.2B** in 2022#	Estimated to grow to $15.6B by 2030#

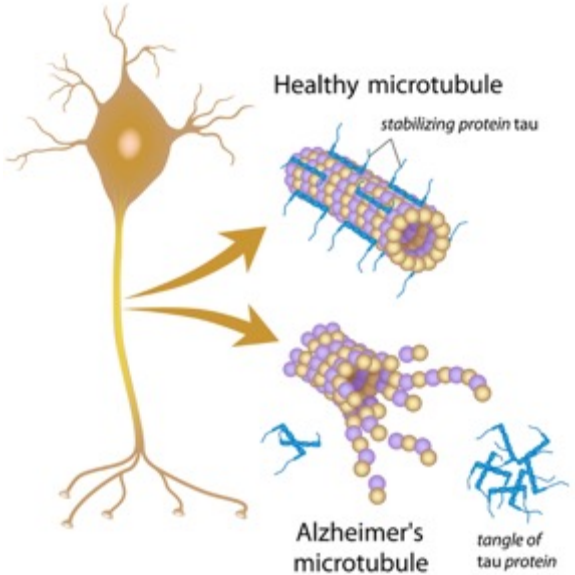
Source: * Alz.org (for Alzheimer Disorder) #Grand View Research

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Tau as a Cause of Neurodegenerative Diseases

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



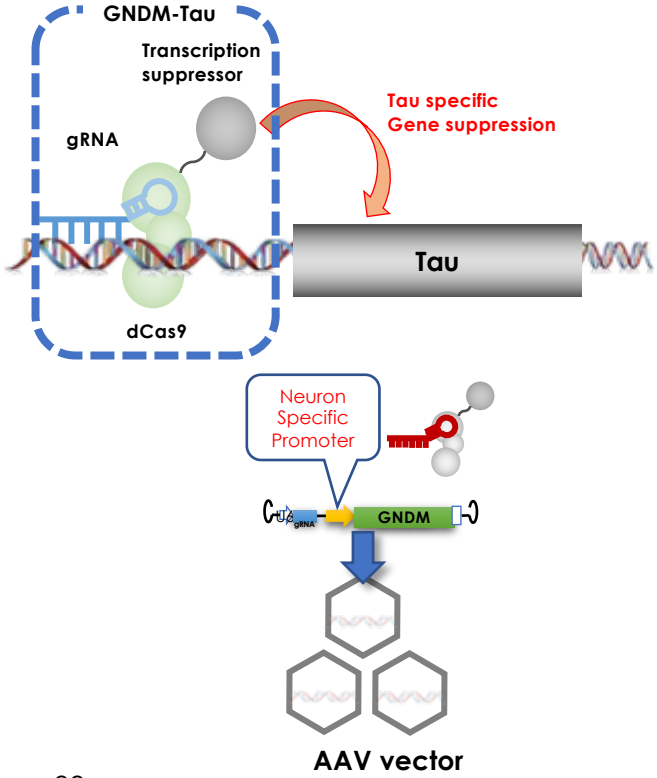
Source: Congdon EE, Nature Review Neurology 2018 "Tau-targeting therapies for Alzheimer disease"

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Mechanism of Action

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

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Potential opportunities in the tauopathy

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 1 in 3 above 85	cortex and hippocampus	memory, movement, language, judgment, behavior, and abstract thinking	6-8yrs
CBD	~5 in 100k 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 (Parkinson-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 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

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Status of Development of MDL-104

Administration of MDL-104 in the disease model has demonstrated clear tau suppression

- 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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MDL-104 is a GTx suppressing the expression of tau protein, the root cause of tauopathies including Alzheimer's disease

01

Suppressing the expression of tau, the causative gene for the disease, at the transcriptional level

02

Robust suppression of Tau has been clearly demonstrated in animal disease models.

03

Potential for non-invasive administration routes by combining with BBB-permeable capsids

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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) • 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?

Neurogenic genetic disorders caused by UBE3A expression or loss of function

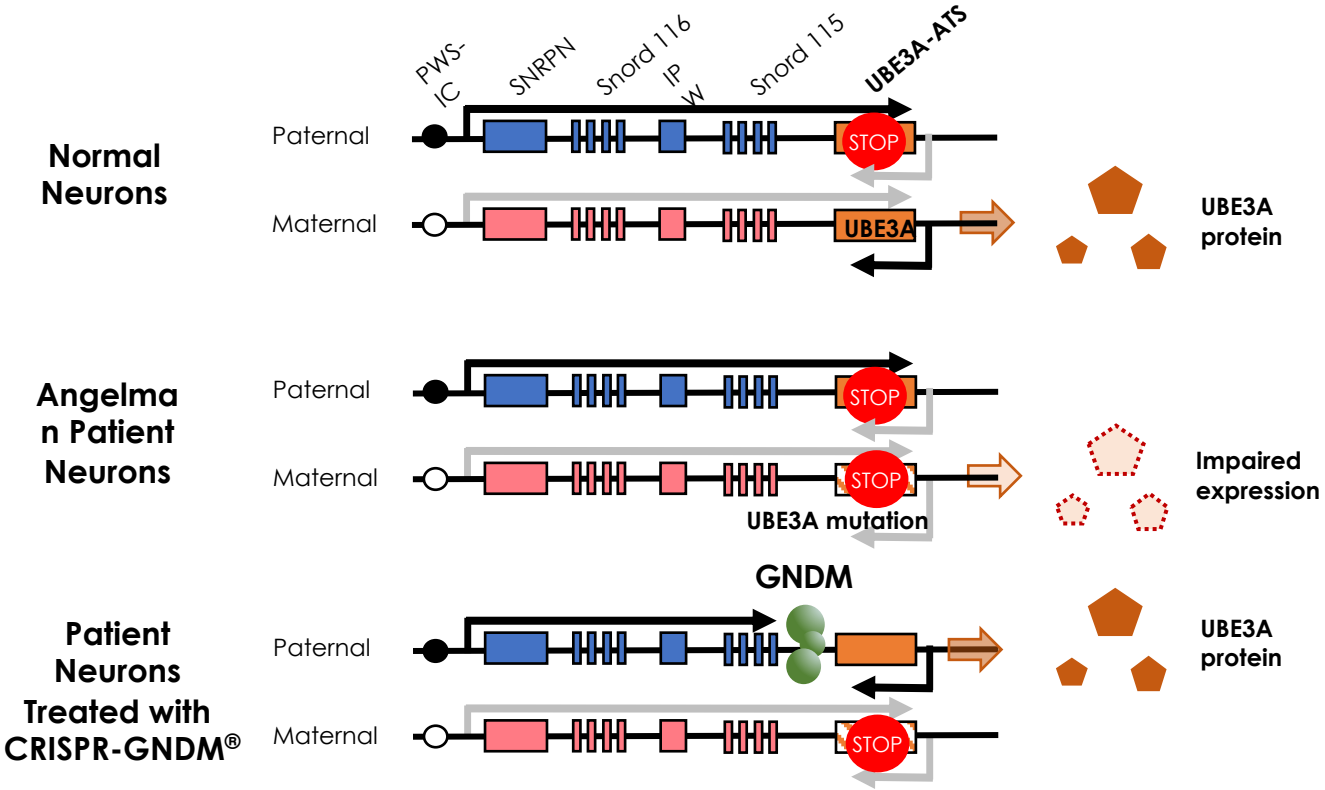
- Angelman syndrome (AS) is a rare neuro-genetic disorder that occurs in **one in 15,000 live births** or **500,000 people** worldwide.
- It is caused by a loss of function of the **UBE3A gene** in the 15th chromosome derived from the mother.
- Angelman syndrome shares symptoms and characteristics with 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

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Mechanism of Action of MDL-206

By blocking ATS transcript, GNDM un-silences UBE3A expression



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Status of Development of MDL-206

The concept of GNDM has been established in disease model mice

- 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

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MDL-206 is a treatment for Angelman syndrome based on the groundbreaking mechanism of UBE3A gene unsilencing

01

Expression of the causative gene UBE3A must not be too low, but excessive expression causes other problems

02

GNDM achieves proper levels of UBE3A expression from dormant chromosome

03

Clear unsilencing effects have been confirmed in animal models

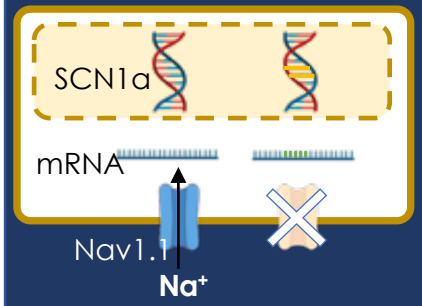
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Dravet Syndrome

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

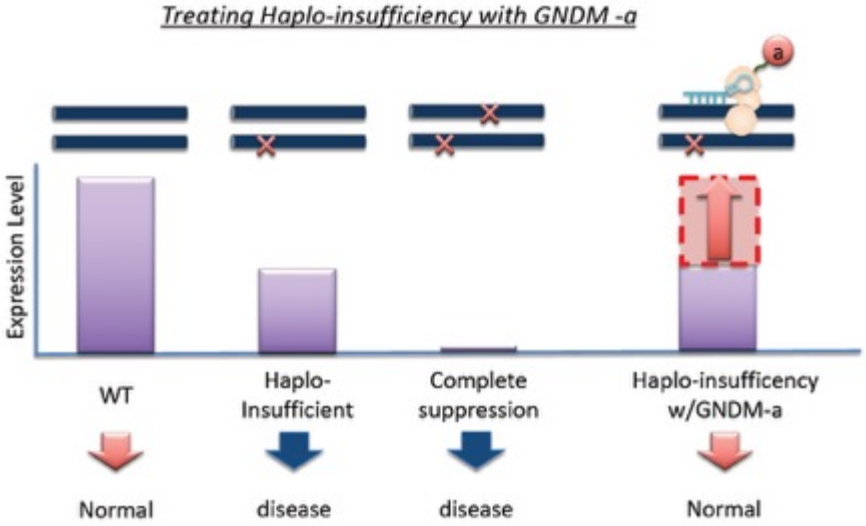


Prevalence	**1 in 20,000-40,000*** ~10,000 in US	
Disease Onset	Seizure starts between **1 and 5 yo**	
Disease Burden	**10-20%** of DS patients pass away before reaching adulthood	• SUDEP (sudden unexpected death in epilepsy patients) • status epilepticus (SE). • Autism-like spectrum (ASD) • Attention deficit hyperactivity disorder (ADHD)
Disease Causing Gene	**SCN1A**	• Haploinsufficiency of SCN1A
Commercial opportunity	**$500M+**	• Currently with no curable drugs • 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
Encoded Therapeutics	AAV-ETN (regulatory element)	• Overexpress regulatory element for Scn1a • 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 • 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 • Increase in the levels of mature mRNA and Nav1.1 protein	i.c.v.	Preclinical	2020

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Epigenome editing offers the most suitable treatment for Dravet syndrome

01

The causative gene SCN1a is too big to be contained within a single vector using conventional GTx

02

GNDM has been shown to suppress symptoms such as seizures In animal disease models

03

Potentially non-invasive route is possible by combining BBB-penetrating capsids

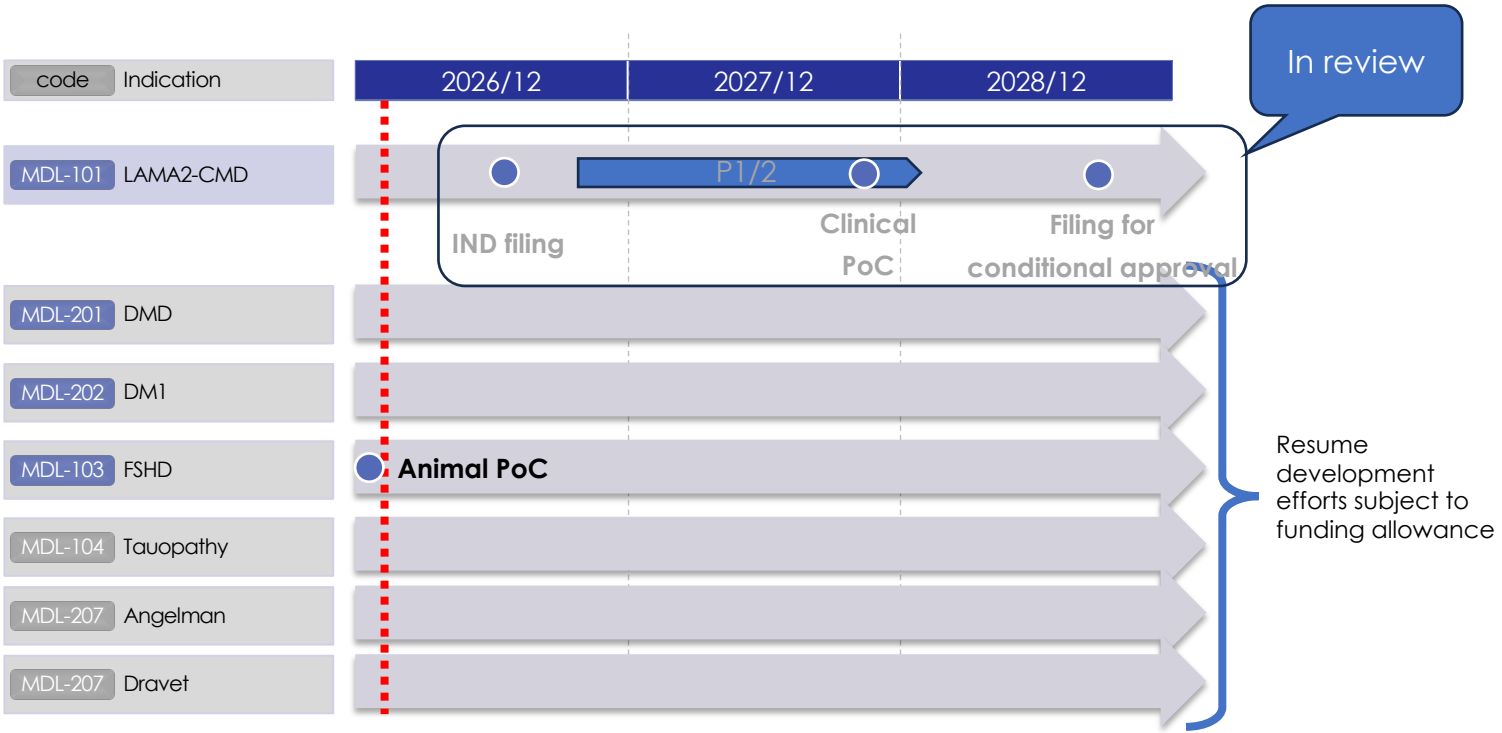
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Updated

Pipeline status and coming milestones

Target filing for conditional approval in later 2028

Pipeline status



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

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Updated

Achievements of the programs and coming milestones

	Achievement so far	Coming milestones
MDL-101 LAMA2-CMD	✓ Animal PoC ✓ Target engagement in NHP ✓ Pre-IND ✓ GMP manufacturing (Plasmid) ✓ ODD and RPDD designation ✓ **Publication on HGT (Dec)**	☐ Completion of GLP-Tox (1H) ☐ Completion of Mice IND enabling(1H) ☐ Completion GMP manufacturing(1H) ☐ **IND** } timing under strategic ☐ **FPFD** } reassessment ☐ **Clinical PoC (2027~2028)** ☐ **Filing for conditional approval(2028)**

その他	• Established animal PoC
	  • MDL-201 (DMD)
	  • MDL-202 (DM1)
	  • **MDL-103 (FSHD)**
	  • MDL-104 (Tauopathy)
	  • MDL-205 (Angelman syndrome)
	  • MDL-207 (Dravet syndrome)
	• Research collaboration with JCR in CNS
	• Collaboration with Ginkgo Bioworks, GenixCure
		• Explore optimal capsid and route of administration for CNS program
		• Allocation of development funds through partnering and grants
		• Animal PoC
		• Continuing Research and Moving to Next Steps

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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

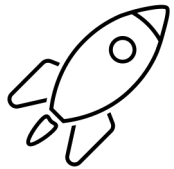
MDL-201, 202

Further approach to challenging applications

Other programs





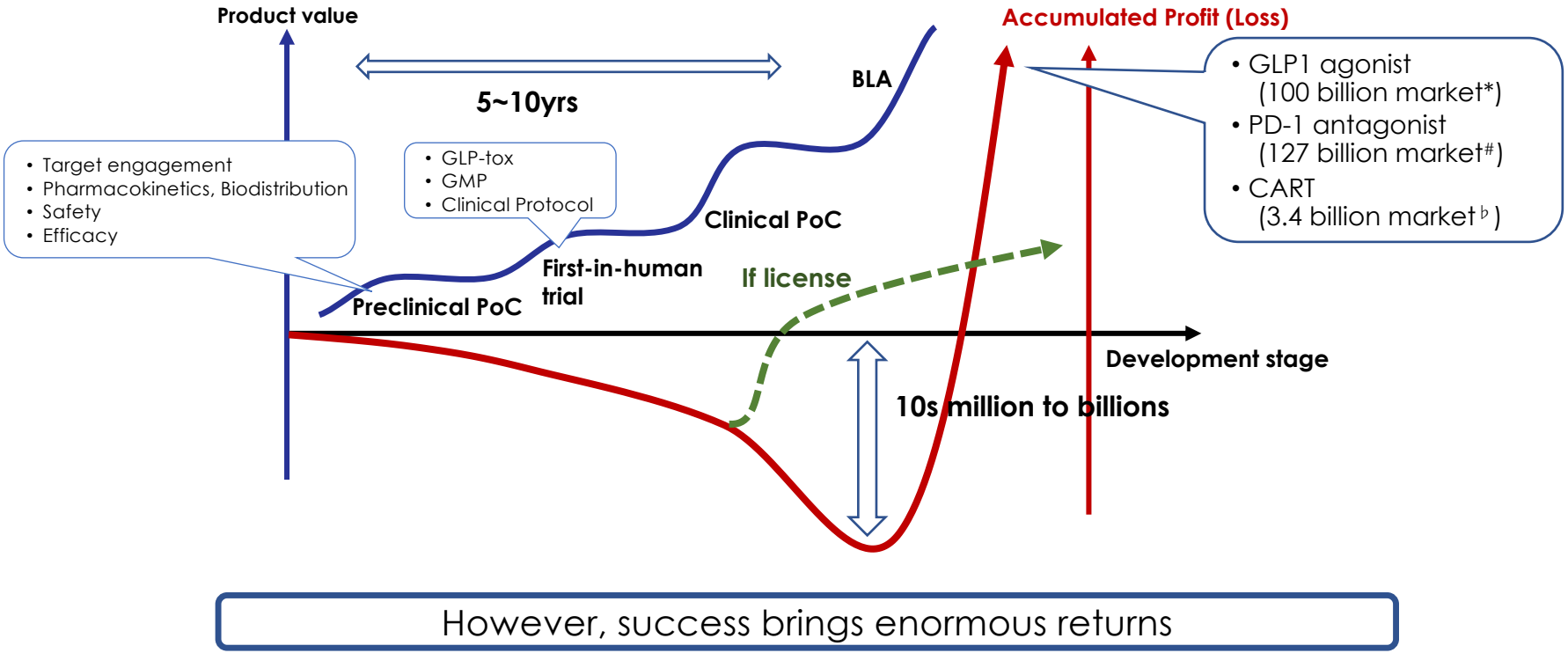


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Trend of Enterprise Value and Cumulative Costs for Biotech Companies

The higher the stage, the more money it costs in development

Product Value and Cumulative Development Costs



However, success brings enormous returns

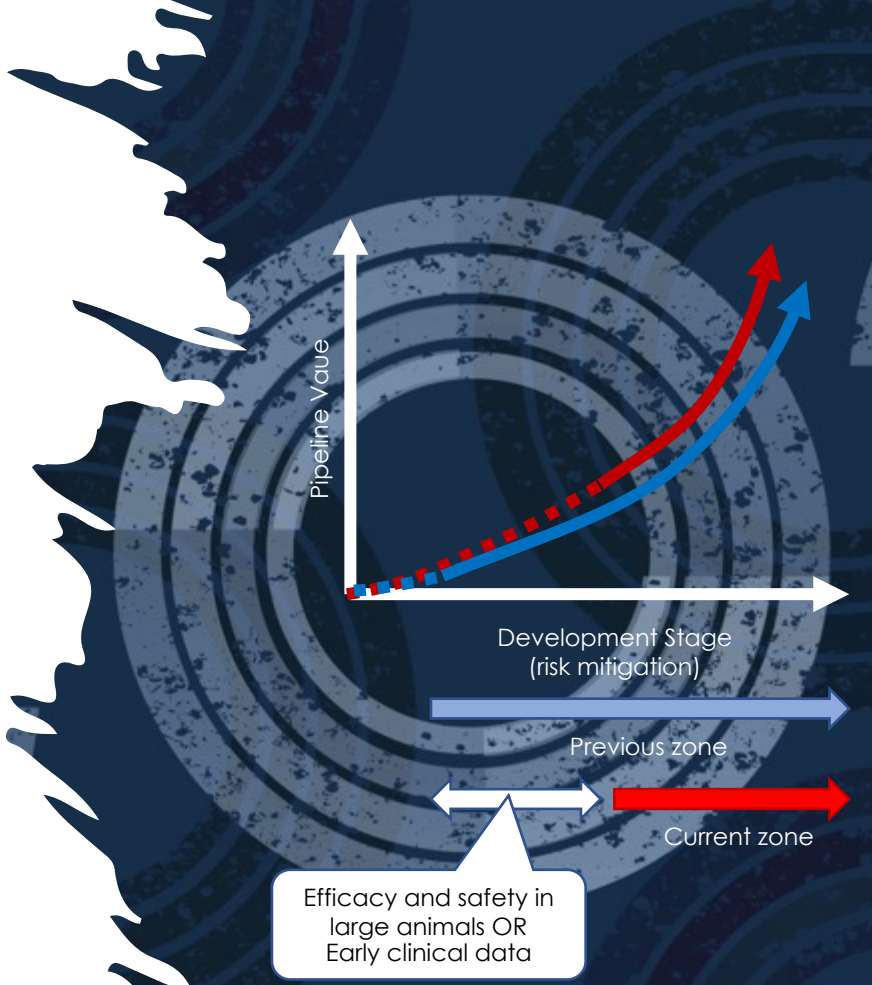
Source: *Okasan securities "The Obesity Drug That Has the World in a Frenzy" *SkyQuest Industry forecast2023-2030 ♭ Report Ocean "CAR T-CELL THERAPY MARKET BY DRUG TYPE"

BLA: Biologics License Application(Manufacturing and Marketing Approval for biologics)

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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.



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Updated

Fundraising Policy

While considering partnerships, secure funding for independent development

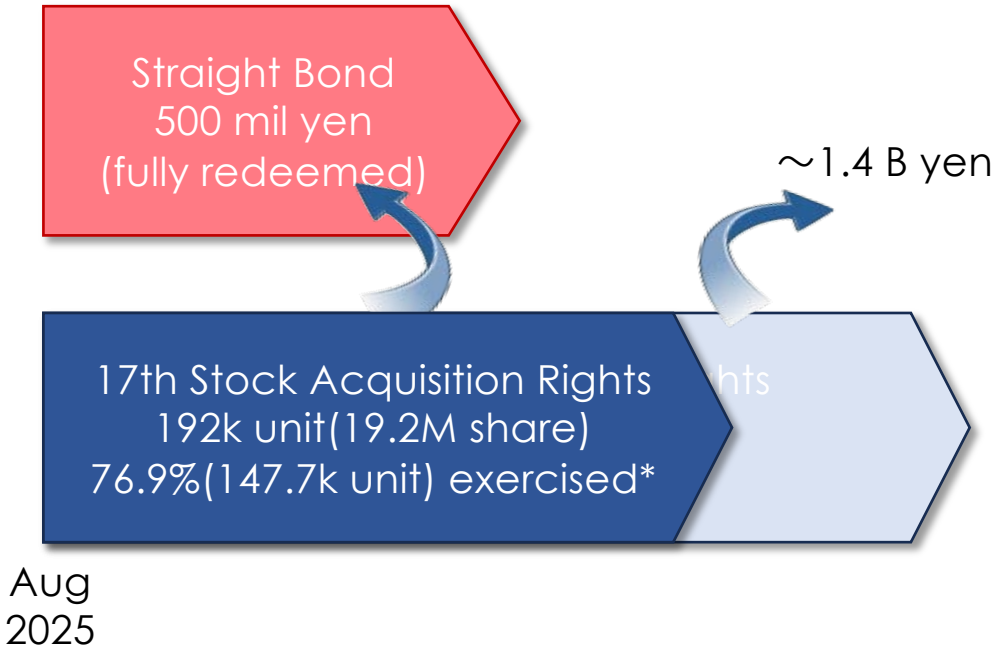
- As a result of the increased partnering hurdles in the biotech industry, P2 or PoC and beyond is a prerequisite*. Forced partnerships may lead to worsening conditions.
- Securing funds to reach PoC is key to winterizing through the biotech ice age.
- Conversely, if you can achieve PoC on your own, direct sales (which offer the potential for higher profit margins) also come within reach.
- Progress on MDL-201 and 103 is creating new growth opportunities.

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

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The status of the 17th series of MS warrant with 1st series SB

About 3/4 of the 17th series of warrant has been exercised



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

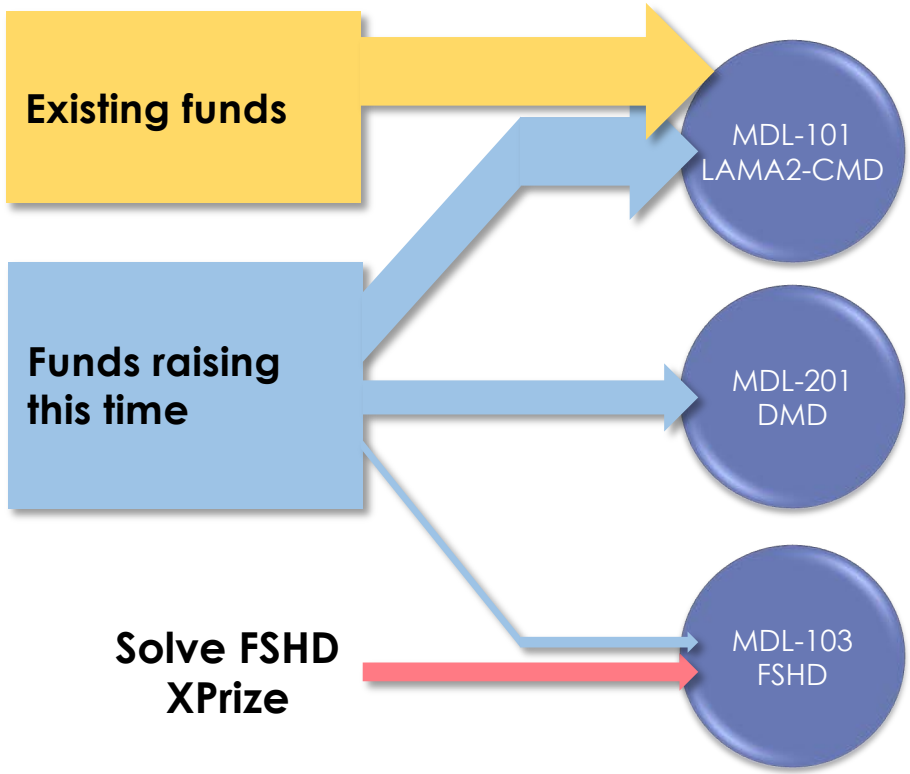
*As of press release on Mar 17, 2026

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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.

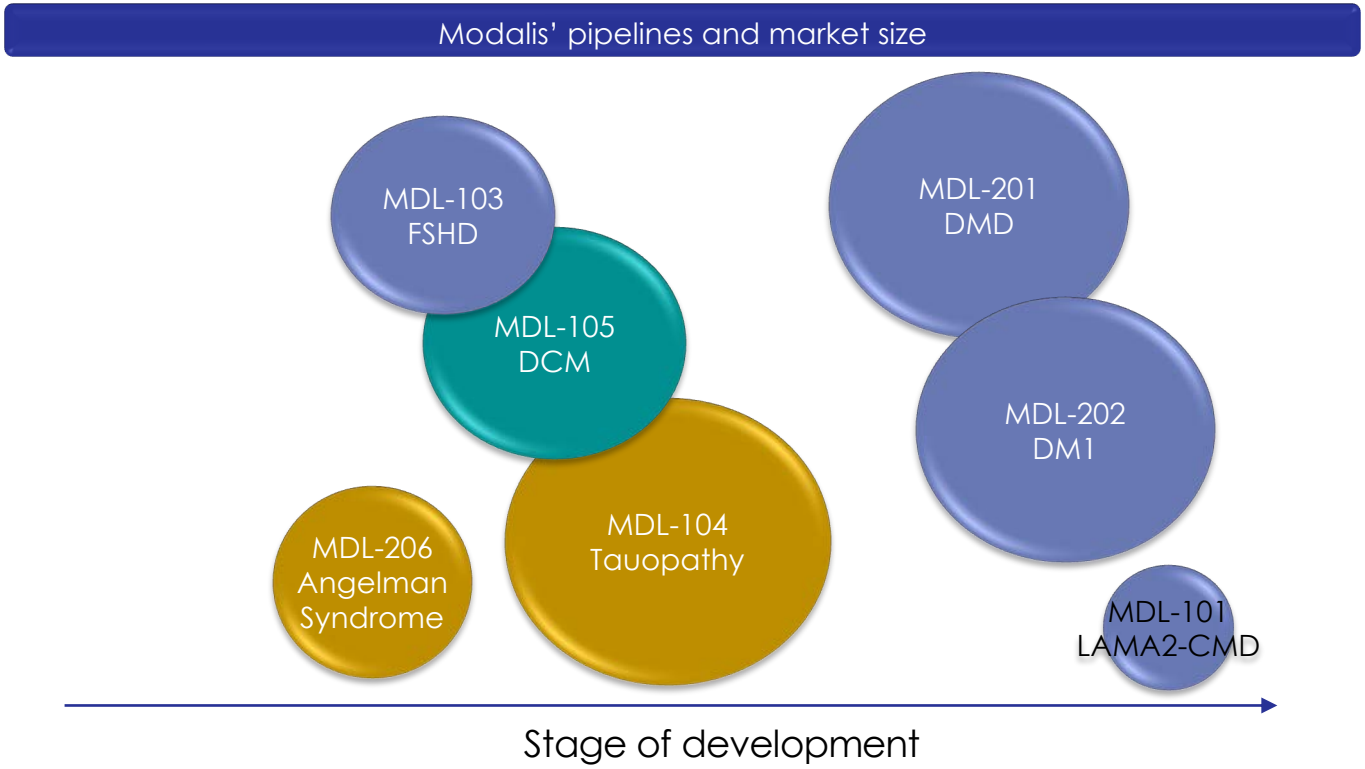


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Updated

Modalis' pipelines and market size

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



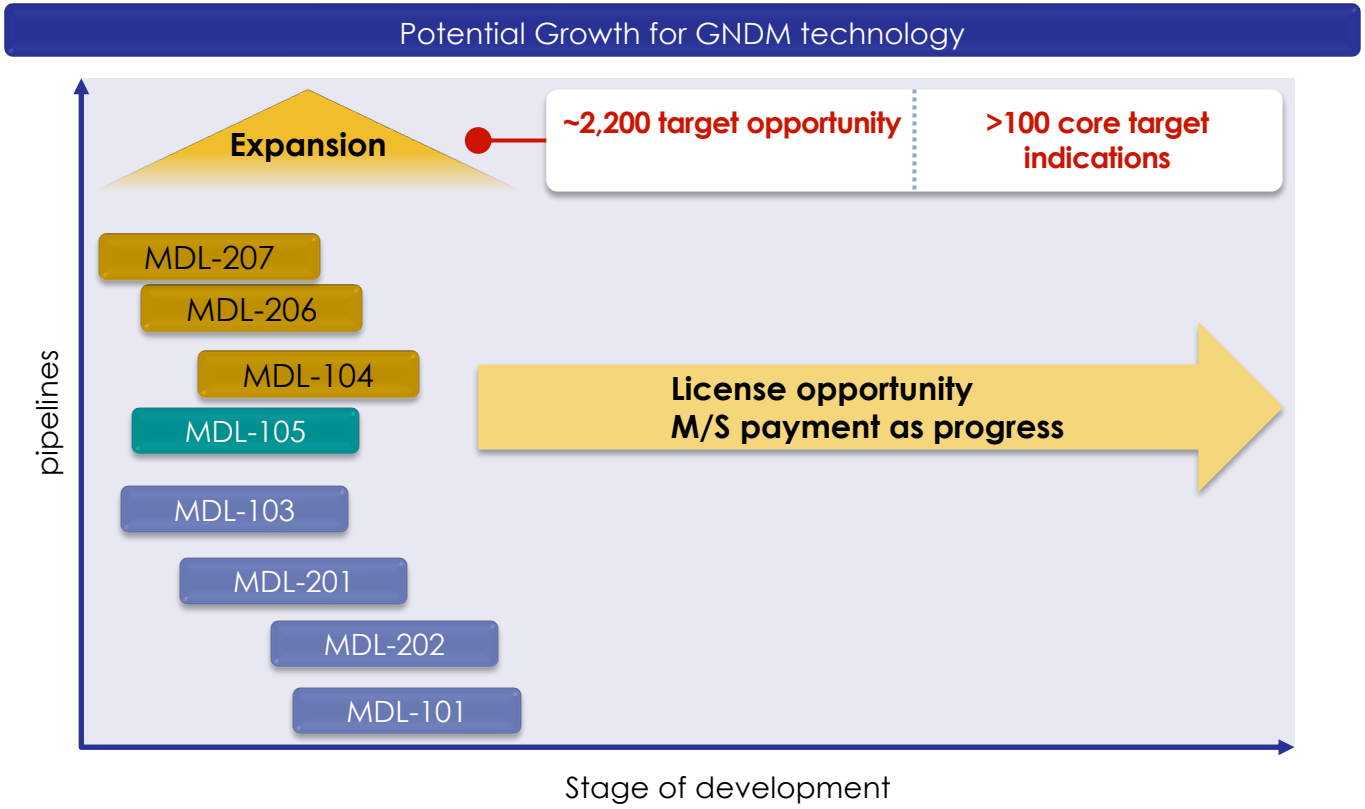
※ Size of circles represents an image of market size or patient number of each indication

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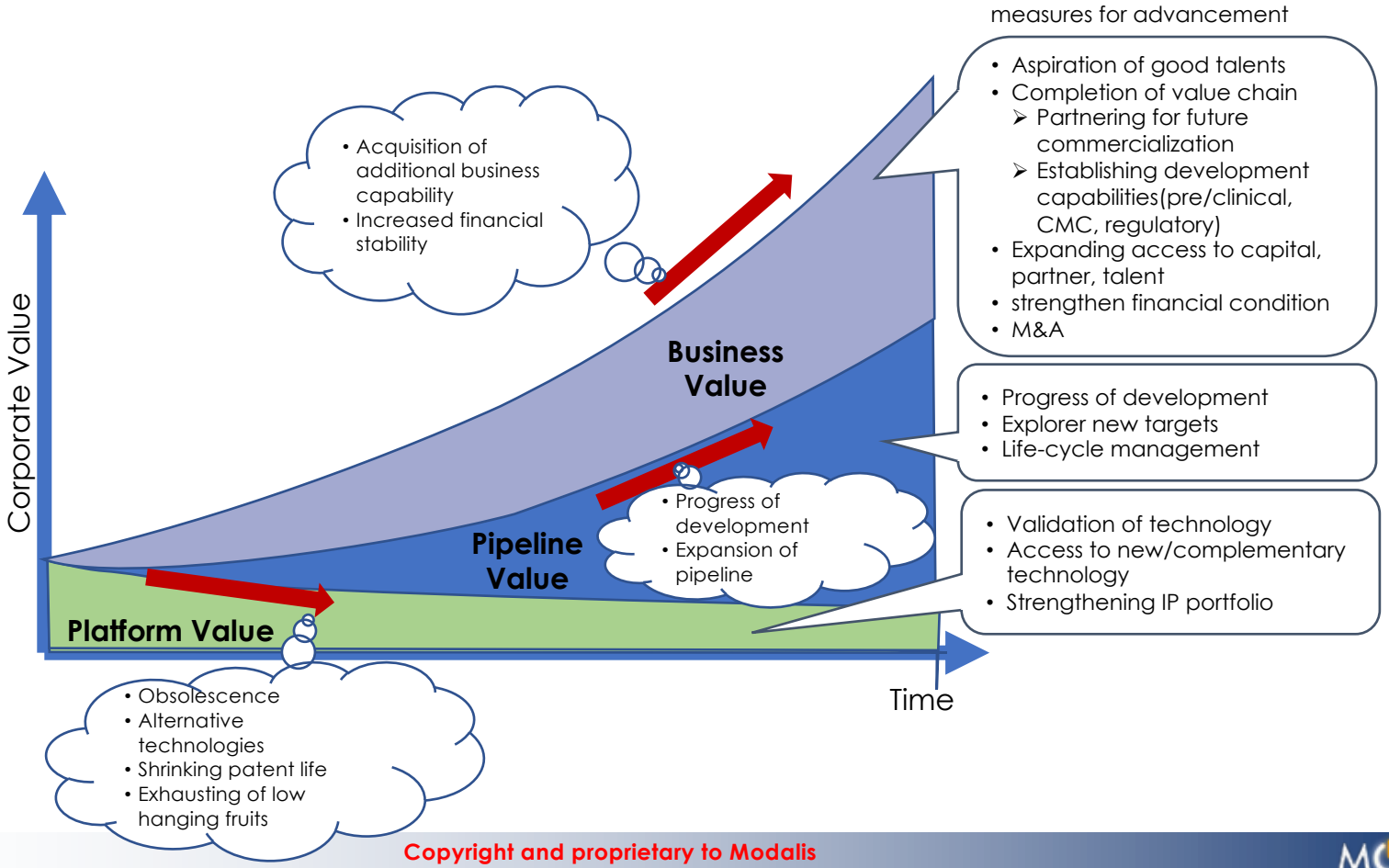
Growth Strategy

opportunity expands two dimensionally



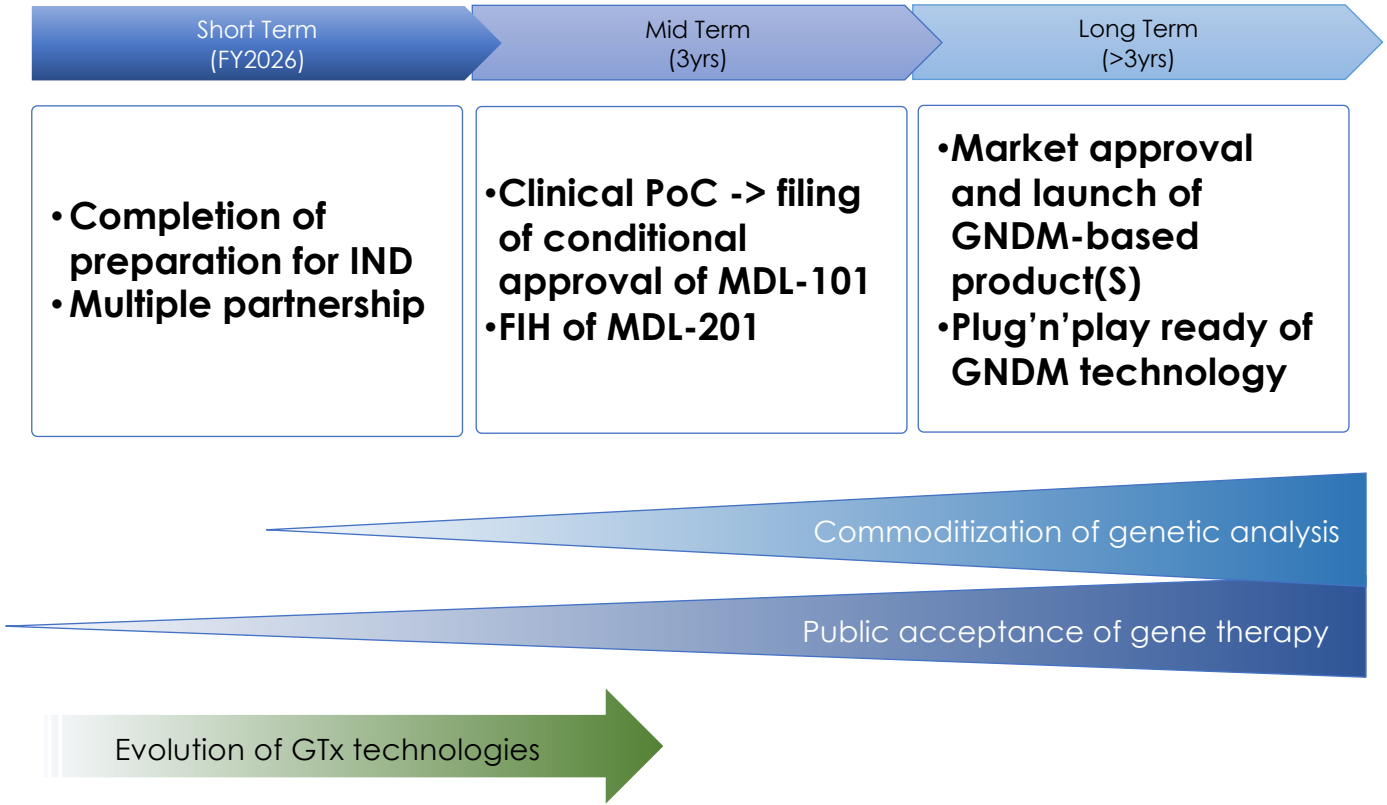
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Composition of Modalis' value and measures for advance



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The future Modalis envisioned



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6. Risk information



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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 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

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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

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Updated

MDL-101は最初の活性化型エピゲノム編集治療薬として臨床入りできる可能性を有したプログラム

01

CRISPR-GNDM は**LAMA1遺伝子を選択的に上**昇されることができる

02

生存延長と機能改善を含む強力な動物における**コンセプト実証データ**

03

筋特異的キャプシドを用いた世界で最先端の**製造プロセス**を実用的なレベルの生産性、収率、品質で確立

04

マウスおよびサルの試験で**安全性上障害のあるような問題は確認されなかった**

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