English translation for reference purposes only

FY2023 2Q
Financial Results

In case of any discrepancy,
the Japanese version shall prevail

MODALIS

Modalis therapeutics Corporation
(TSE : 4883)
August 7, 2023

Disclaimer

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

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

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

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

The first CRISPR based gene modulation Therapeutic technology

Leading company in epigenetic Modulation/ editing

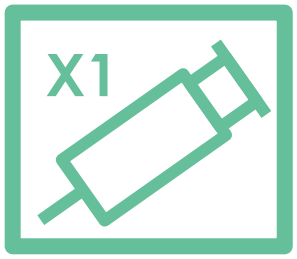
Novel precision medicines for genetic disorders for which there have been no cure

Every life deserves attention

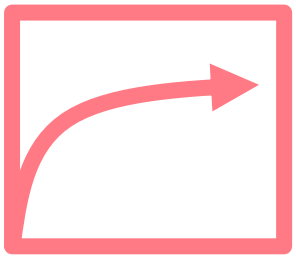
MODALIS

CRISPR-GNDM® is a promising new therapeutic modality

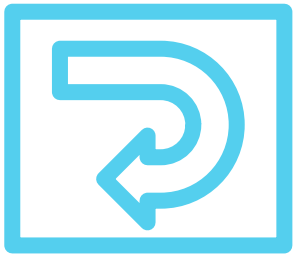
Potential benefits of CRISPR-GNDM® Technology



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

MODALIS

Table of contents

MODALIS

1. Key Topics

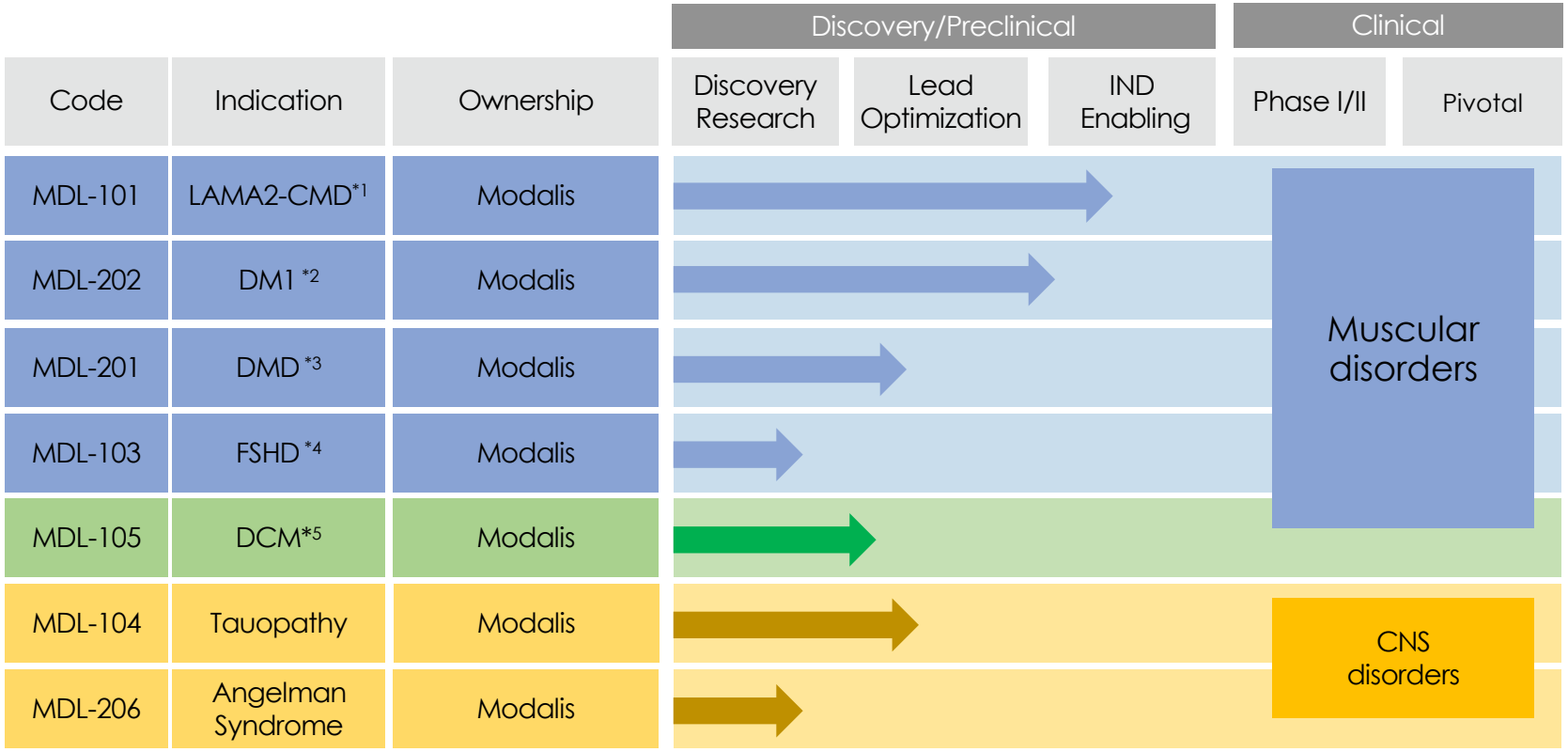
Modalis regains right of MDL-201 and 202 from Astellas

- Modalis regained the rights of MDL-201 and 202 from Astellas
- The target indications of the programs are DMD and DM1, respectively
- The market size of the indications is relatively large and Modalis will gain new revenue opportunities including new partnership
- Applying the know-how accumulated in the development of MDL-101 including the muscle tropic capsid, Modalis will strengthen the products
- As target engagement is confirmed in the NHP study of MDL-101, the company has confidence that the new version of the molecules that share the same vector system shall have extrapolated efficacy and safety.
- As new assets have been added, the company sharpened its strategy to put focus on 101 and 202.
- With this reacquisition, the company reorganize the pipeline to shift to muscular diseases where delivery and our know-how are well established
- The development of CNS programs will be resumed, subject to resource allowances while research continues.

MODALIS

Pipeline Status

As Modalis regains the rights of MDL-201 and 202, the pipeline was reorganized



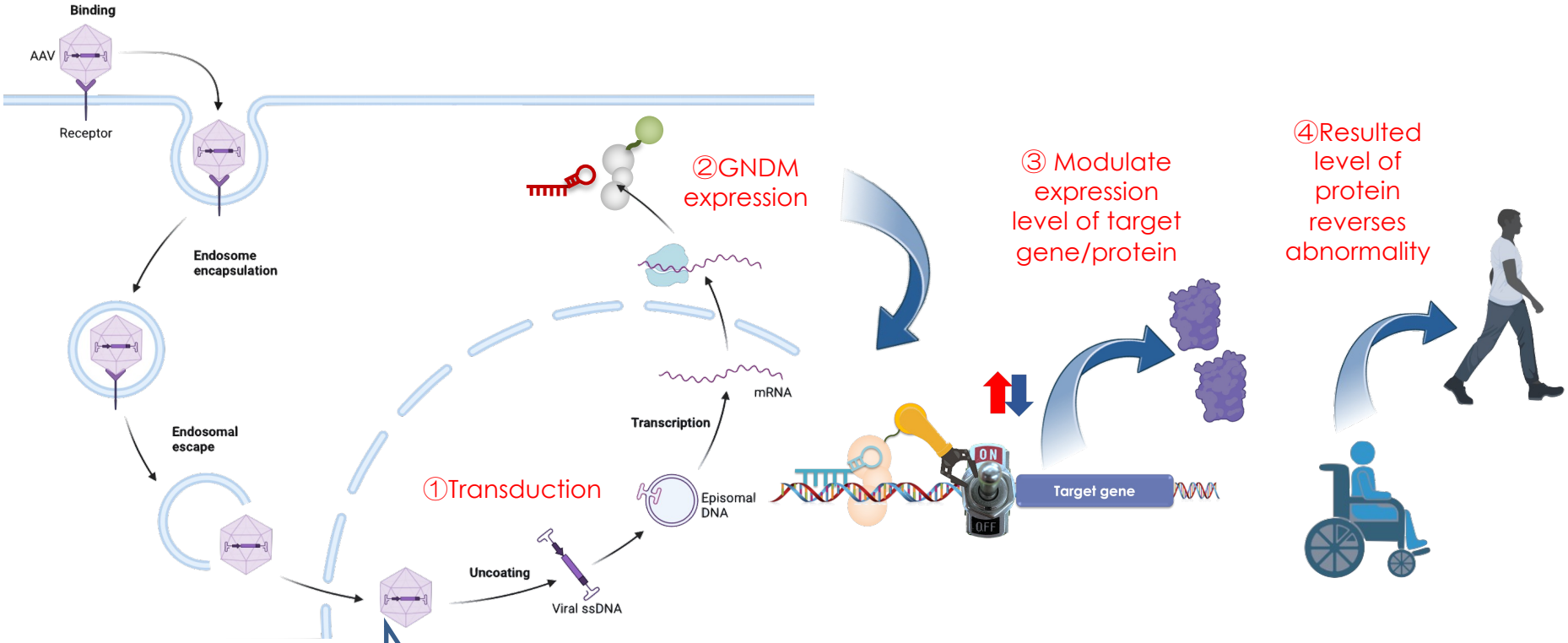
*1: LAMA2-related congenital muscular dystrophy
*2: Myotonic Dystrophy Type 1
*3: Duchene Muscular Dystrophy
*4: facioscapulohumeral muscular dystrophy
*5: Dilated Cardiomyopathy

MODALIS

The other topics in pipeline reorganization

- Modalis adds MDL-103 which targets FSHD by silencing Dux4 gene and the company has incubated for years.
- CNS programs including MDL-104 have been deprioritized but continue to put in research effort.
- MDL-102 and MDL-205 was removed from the pipeline.

Among the 4 steps to demonstrate efficacy, 2 steps are common to the muscle programs and confirmed to function in NHP



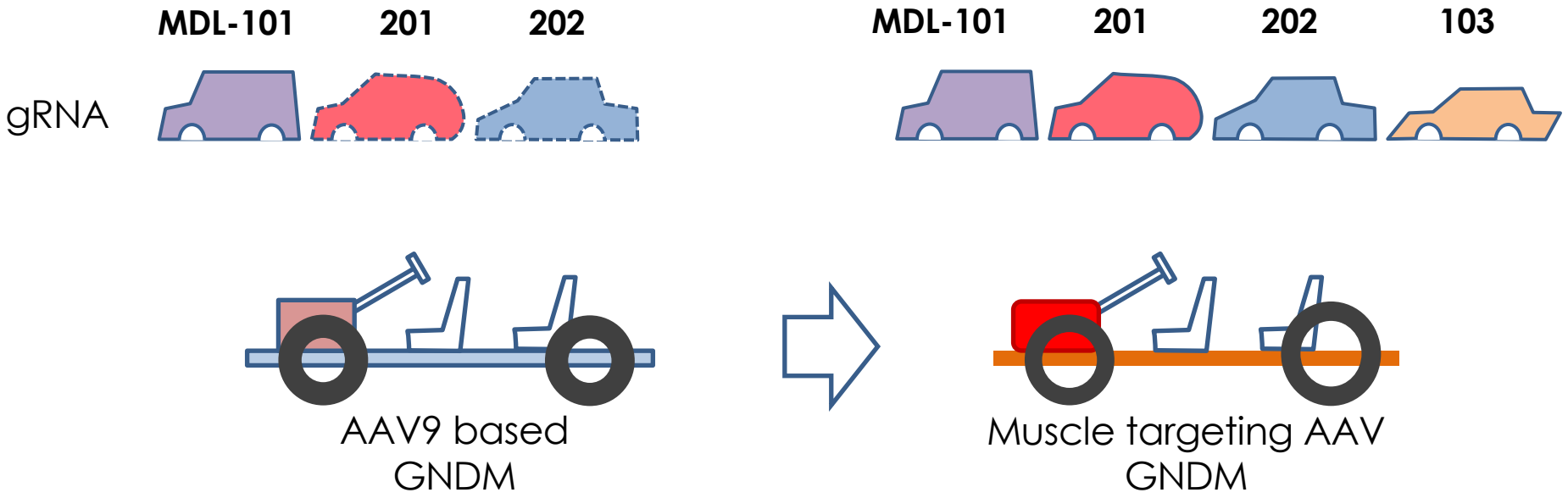
①AAV Transduction → ②GNDM expression → ③Modulation of target → ④Efficacy

Vector system (platform)

gRNA

MODALIS

Like MDL-101 which has already been transplanted to the new system, 201and 202 will be transferred together with 103 to increase their potency



MODALIS

LAMA2-CMD (aka CMD1a)

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

MDL-101

Potential to be the first-in-class and the first LAMA2-CMD treatment

Prevalence	**1 in 30,000*** 10,000 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: *Ophanet #*Modalis assumption based on prevalence and potential*

MODALIS

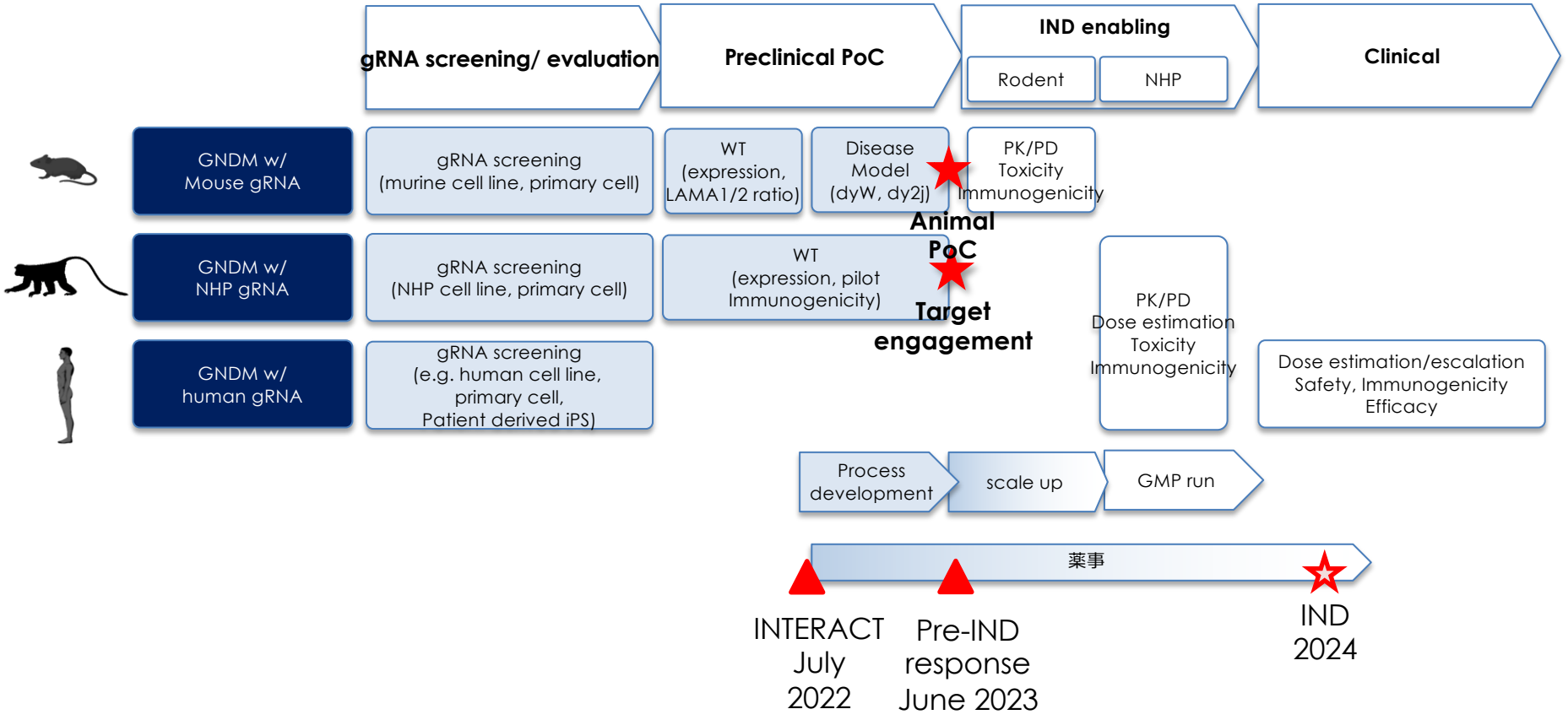
Summary of MDL-101 for LAMA2-CMD

- Reported by 1Q/2023
  - Mouse model data in two disease strains (dy2j and dyW) and wildtype
    - Upregulation of LAMA–1 gene and protein along with GNDM expression
    - Improvement in biochemical and physiological readouts as well as prolonged survival
    - Sustained expression of GNDM in WT mice for 2 years
  - INTERACT meeting with FDA (Jul 2022)
  - Capsid change (Sep 2022)
  - Evaluation of new constructs with new capsids in rodents and NHPs (started in Dec 2022)
  - Redesigning the manufacturing process for the new version molecule
  - KOL meetings and drafting clinical synopsis and protocol
- Progress thereafter
  - **Received Pre-IND response from FDA (June)**
  - **Presented development updates of MDL-101 as a late-breaking abstract at ASGCT**
- Next steps:
  - Continue IND enabling GLP tox and PK/PD
  - Continue process development and pilot productions for GMP campaign

MODALIS

Conducting IND enabling studies as well as process development

Current status of MDL-101 and road map to clinic



MODALIS

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

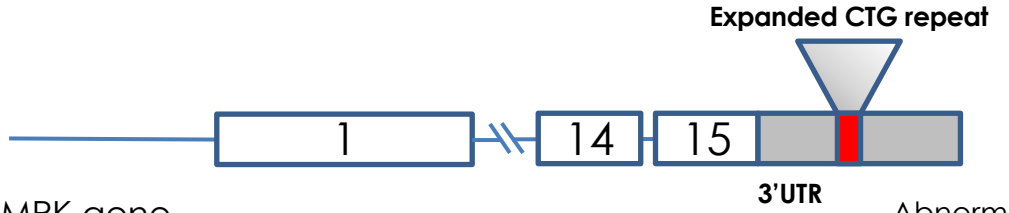
Prevalence	**1-4.8 in 10,000** (1 in 2,300*)	DM is the most common muscular dystrophy among adults of European ancestry
Disease onset	DM1 can occur from birth to old age	Age at onset is between 20 and 70 years (typically onset occurs after age 40)
Disease Burden	muscle weakness and wasting (atrophy), 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)

MODALIS

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

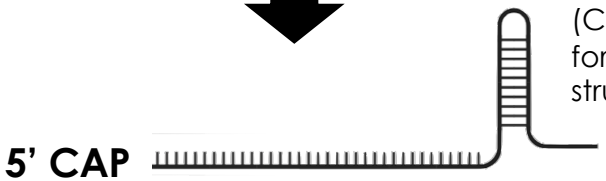
DM1disease causing mechanism



DMPK gene

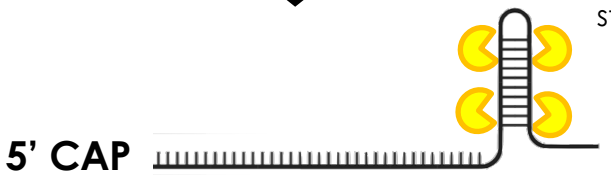
Abnormally expanded (CUG)n repeats form hairpin-like structures

DMPK mRNA With CUG repeat

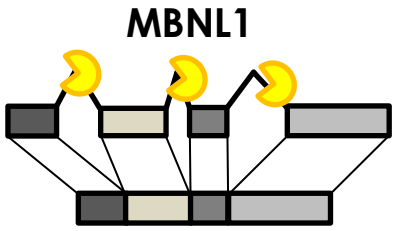


MNBL binds to hairpin-like structures

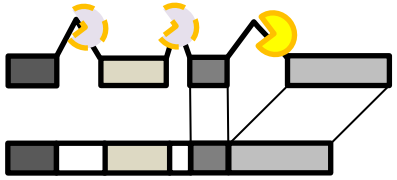
RNA to accumulate in nucleus by sequestering isoforms of the MBNL



Splicing in healthy people



MBNL1 contributes normal splicing

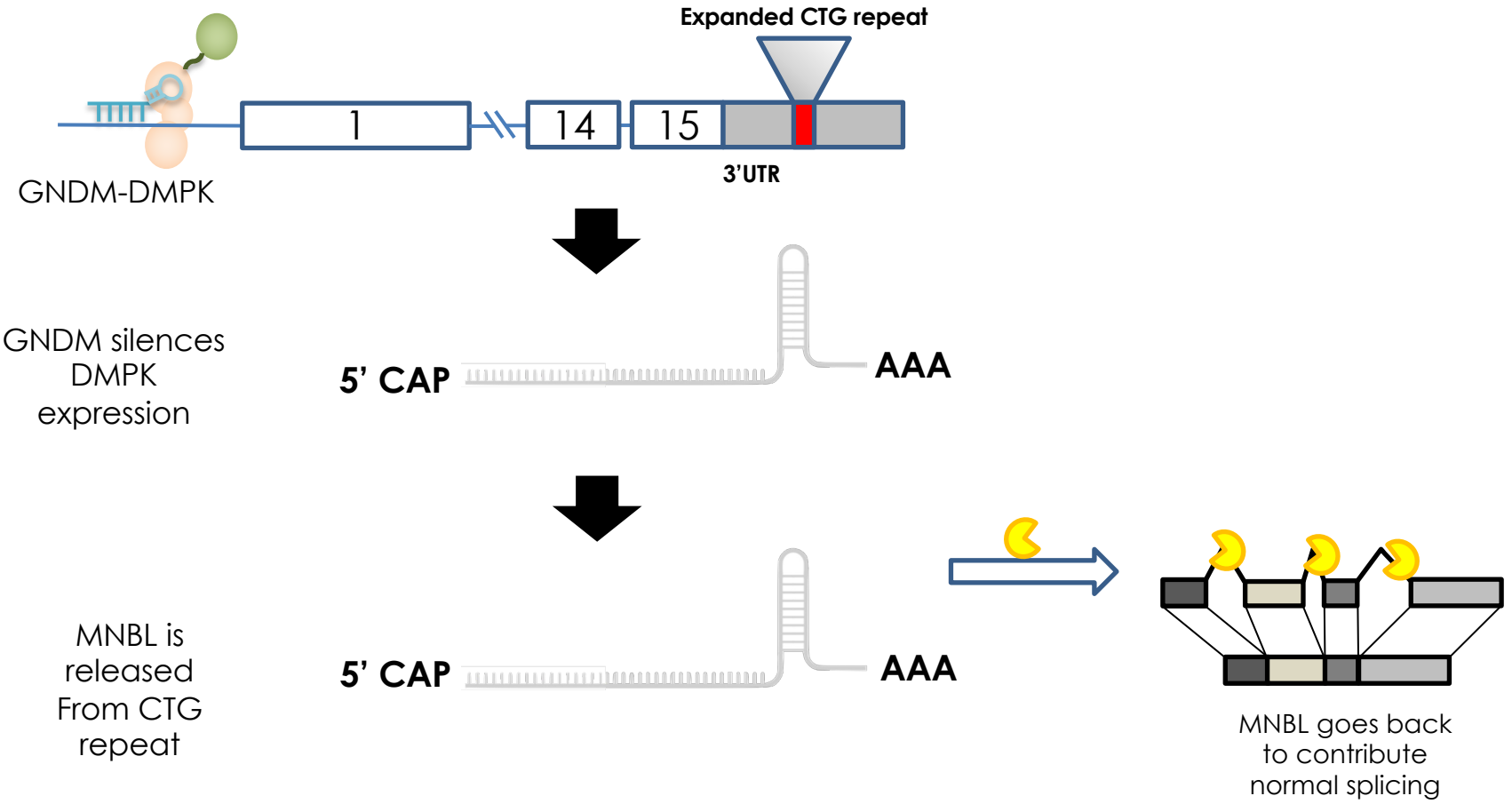


MNBL goes back to functioning in normal splicing

MODALIS

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

MDK-202's mechanism of action

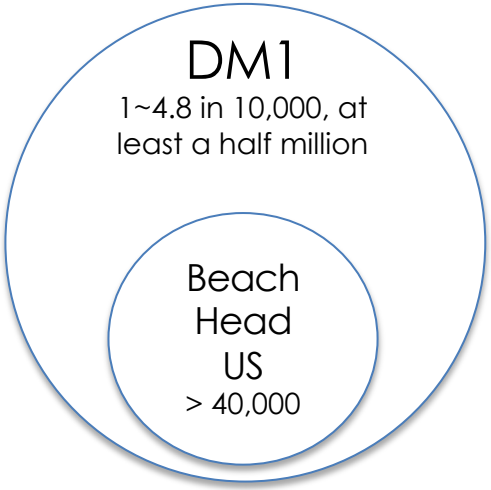


MODALIS

DM1 has relatively large prevalence in muscular disorders

Prevalence of DM1

- 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)



DM1: Myotonic Dystrophy Type 1

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

Duchenne Muscular Distrophy (DMD)

A type of muscular dystrophy caused by mutation in Dystrophin gene

MDL-201

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

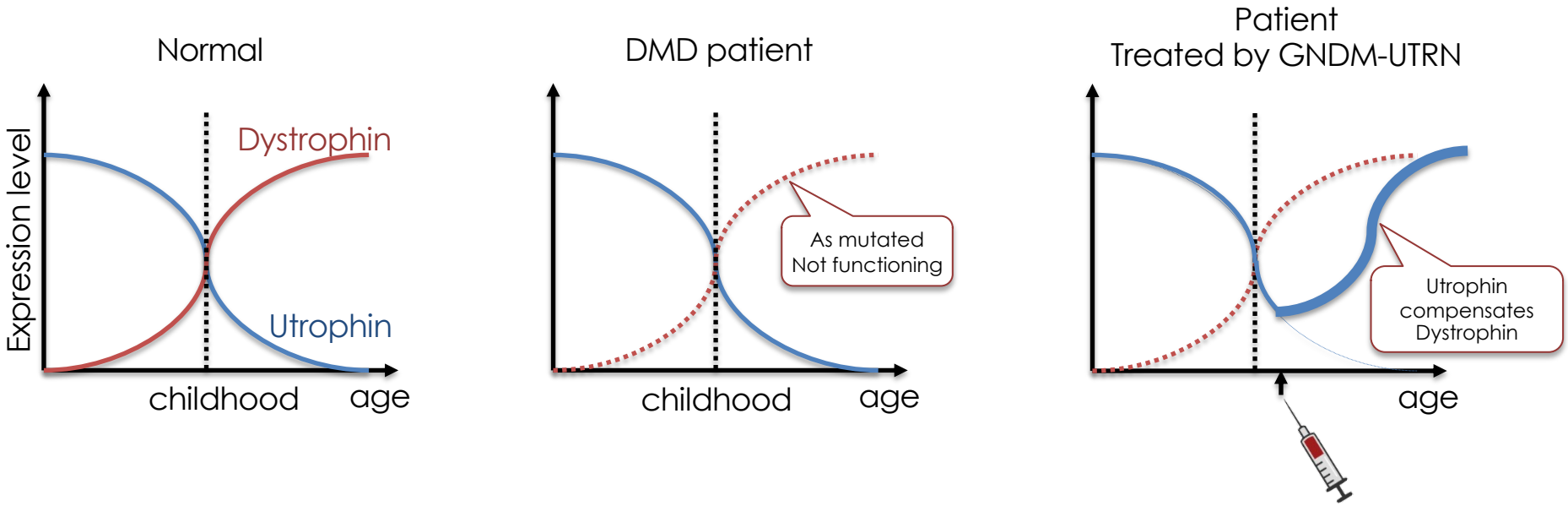
Prevalence	**1 in 3,500 to 5,000 male newborns**	Relatively high in genetic disorders
Disease onset	most commonly appears **between 3 and 6 years old**	
Disease Burden	Most severe clinical symptoms of all the muscular dystrophies including muscles weakness and atrophy	Motor development begins to slow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

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

MODALIS

UTRN-GNDM reactivate Utrophin gene to compensate non-functioning Dystrophin gene in DMD patient

Concept of GNDM-UTRN to re-activate UTRN gene



MODALIS

Facioscapulohumeral Muscular Dystrophy (FSH, FSHD)

A type of muscular dystrophy caused by impaired Dux4 gene expression

MDL-103

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

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

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

MODALIS

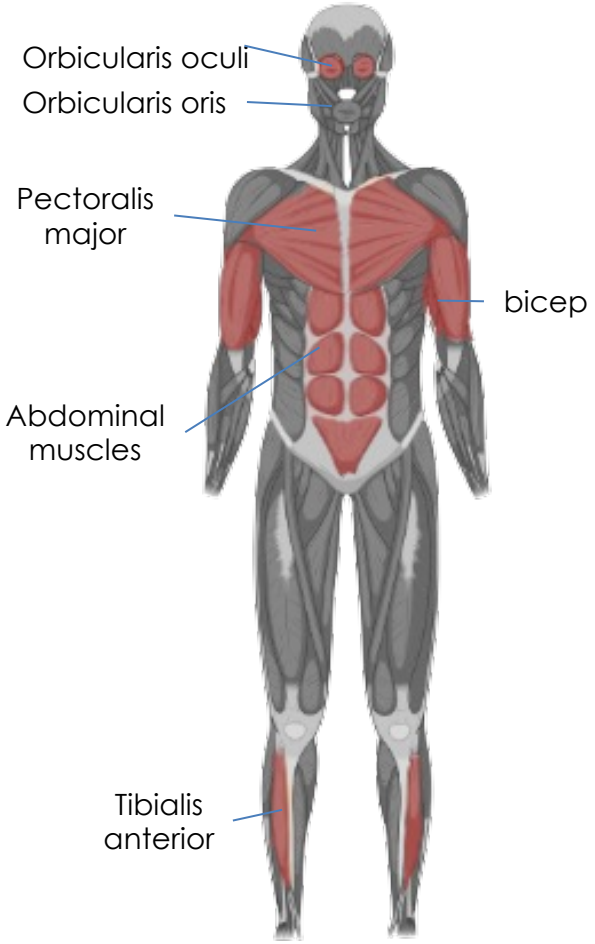
FSHD is a genetic muscle disorder in which the muscles of the face, shoulder blades and upper arms are most affected

Facioscapulohumeral muscular dystrophy (FSHD) is the **most common** autosomal dominant form of muscular dystrophy, affecting approximately **1 in 8000** individuals worldwide.

FSHD usually begins before age 20, with weakness and atrophy of the muscles around the eyes and mouth, shoulders, upper arms and lower legs. Later, weakness can spread to abdominal muscles and sometimes hip muscles.

Some experts divide FSHD into **adult-onset** and **infantile-onset** forms. The adult-onset is far more common.

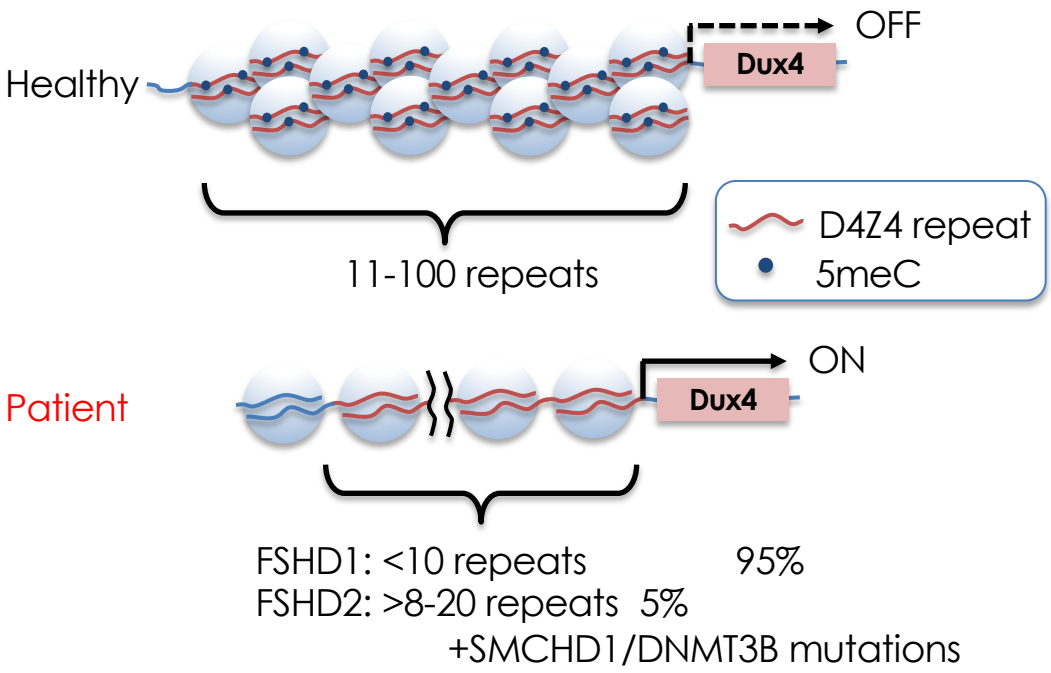
Currently no curative treatment option exists



MODALIS

FSHD disease mechanism

Inappropriate expression of Dux4 in skeletal muscles



- The D4Z4 repeat region at location 4q35 on chr4
- Healthy has numerous highly **methylated** D4Z4 repeats
- FSHD-1 and -2 affected has **hypomethylated** D4Z4 repeats.
- FSHD-1 non-manifesting, or unaffected has few repeats, but these have **higher methylation**

MODALIS

What has been achieved and coming next

	What has been achieved	What's coming next
MDL-101 LAMA2-CMD	• Animal PoC in disease model mice • Target engagement in NHP • Pre-IND with FDA (June 2023) • Presentation at ASGCT 2023	• GLP-Tox • GMP manufacturing • IND (2H 2024)
MDL-202 DM1	• Animal PoC in disease model mice • Regain rights from Astellas	• Transplantation to muscle tropic capsid • Target engagement in NHP with new version molecule • Partnering
Other	• MDL-201 (DMD) • MDL-103 (FSHD) • MDL-105 (DCM) • CNS programs	• Transplantation to muscle tropic capsid • Animal PoC (FSHD, DCM)0 • Target engagement in NHP with new version molecule • Partnering • Continuing research • Explorer neurology capsids and LNPs • Partnering

MODALIS

Other updates on business

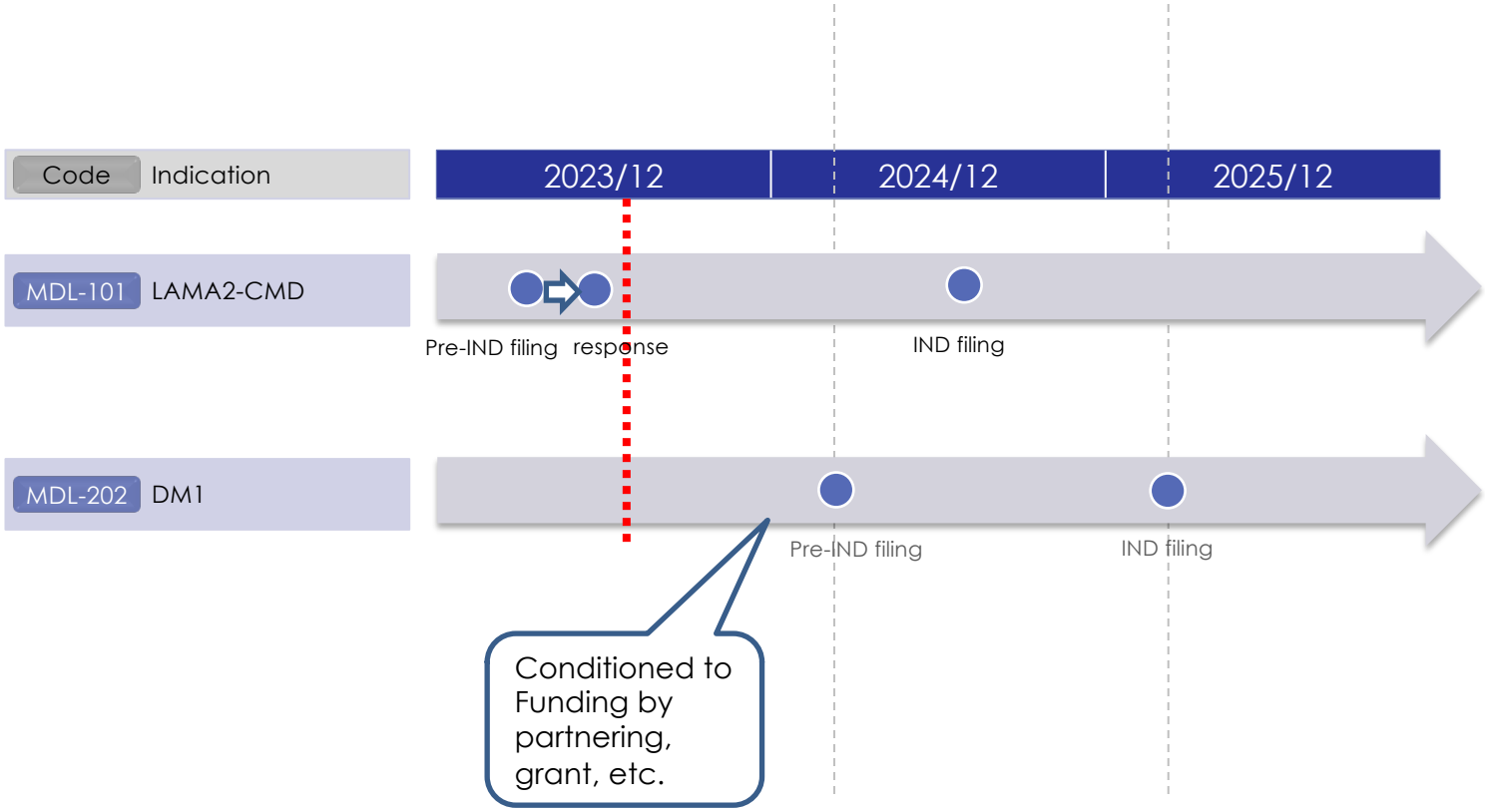
- Progress on intellectual property
  - Regained rights of MDL-201 and MDL-202 from Astellas Pharma Inc by Asset Purchase Agreement

- Progress on partnering
  - Partnering discussion ongoing with pharma/biotech companies with the new MDL-101 data
  - Concurrent with the development activity of MDL-202 with the newer version of construct, the company started to explore new partner for the molecules
  - Research collaboration: In discussion with pharma/biotech companies on new targets

2. Financial Highlights

Status of the focused pipeline

As regained rights of MDL-201 and 202, reorganized pipelines and put higher priority on muscle disorder programs



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

MODALIS

PL & Business Result

(Million Yen)

	FY2022 2Q (A)	FY2023 2Q (B)	(B) – (A)
Operating revenue	40	-	(40)
Operating expenses	908	1,044	136
R&D	778	906	128
SGA	130	138	8
Operating income	(868)	(1,044)	(176)
Ordinary income	(780)	(995)	(215)
Current Profit	(775)	(1,033)	(258)

Operating expenses

- R&D increased year on year as business progressed(primarily in personnel expenses, research material expenses, rent fee, expenses for conducting clinical trials of MDL-101 and yen depreciation against US dollar)

Extraordinary loss

- Impairment loss on fixed assets

SGA: Selling and Generally Administrative Expenses

BS & Financial Position

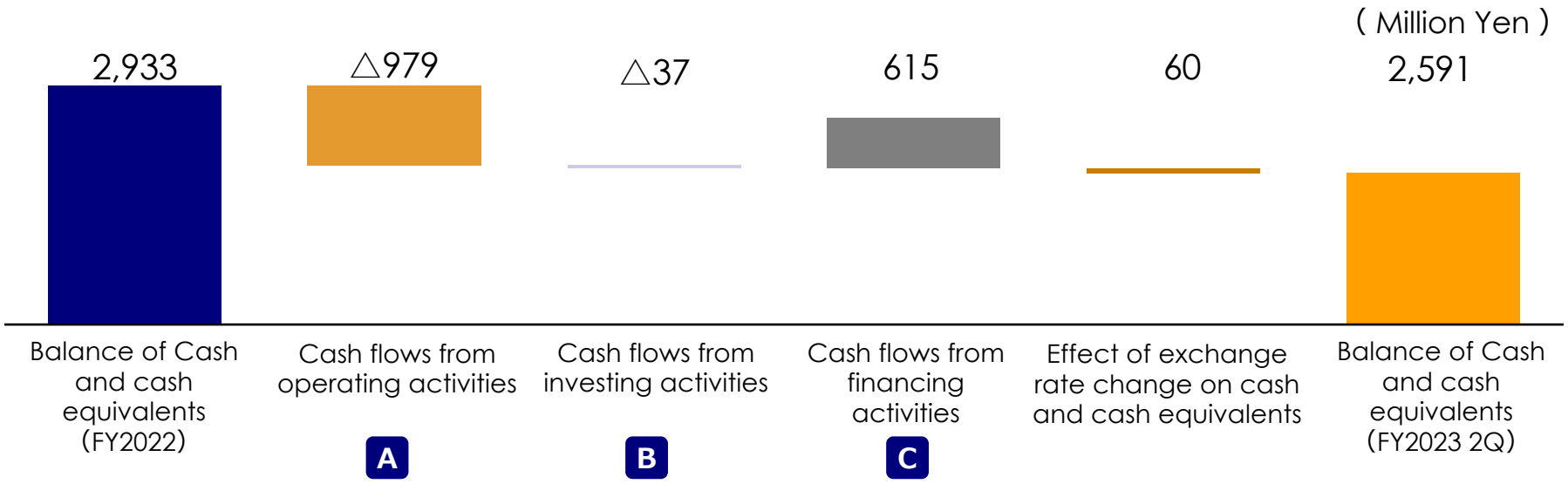
(Million Yen)

	FY2022 (A)	FY2023 2Q (B)	(B) – (A)
Current assets	3,061	2,782	(279)
Cash & deposits	2,933	2,591	(342)
Non-current assets	68	72	4
Total assets	3,129	2,855	(274)
Current liabilities	141	278	137
Non-current liabilities	47	45	(2)
Total liabilities	188	323	135
Total net assets	2,941	2,532	(409)
Total liabilities and net assets	3,129	2,855	(274)
Capital adequacy ratio	93.4%	88.0%	

- High Equity ratio
  Under financing to secure a more stable financial base
- Decrease in property, plant and equipment and intangible assets due to impairment loss

MODALIS

Cash Flow Status



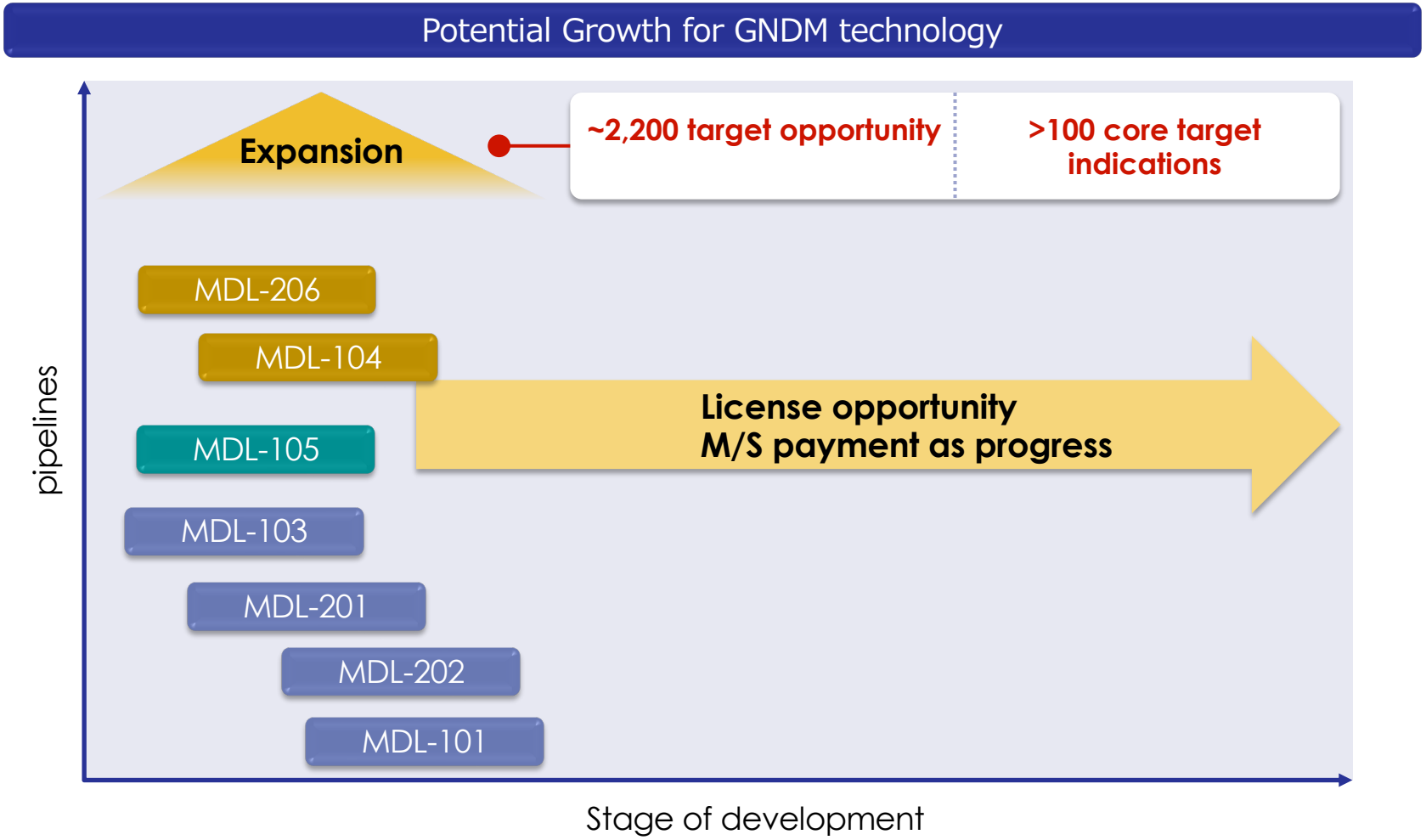
A Cash flows from operating activities	• Loss before income taxes （△1,032） • Impairment loss （37）
B Cash flows from investing activities	• Purchase of property, plant and equipment （△37）
C Cash flows from financing activities	• Proceeds from issuance of stock acquisition rights （618）

MODALIS

3. Growth Strategy

Growth Strategy

opportunity expands two dimensionally

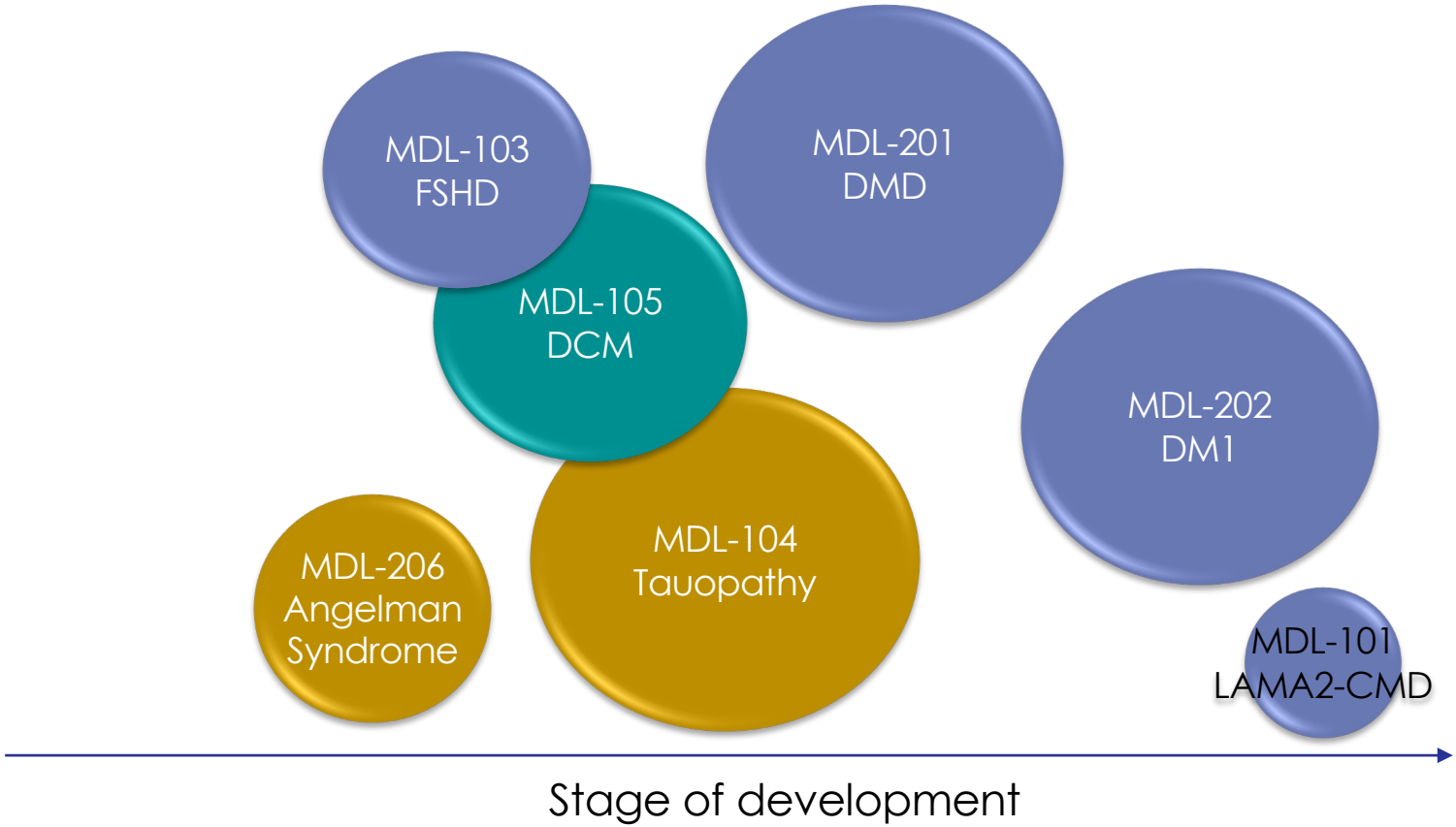


MODALIS

Modalis' pipelines and market size

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

Modalis' pipelines and market size

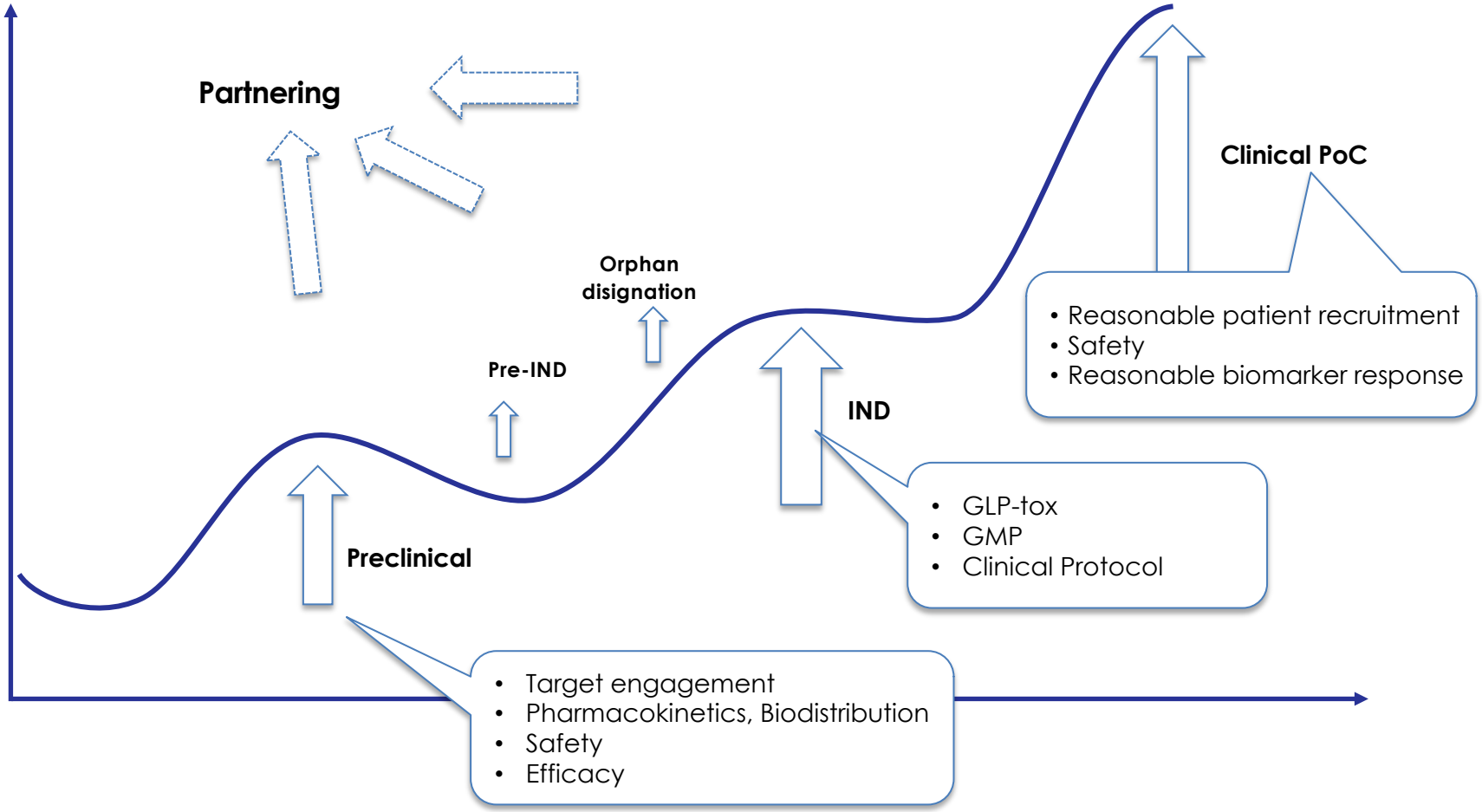


※ Size of circles represents an image of market size or patient number of each indication

MODALIS

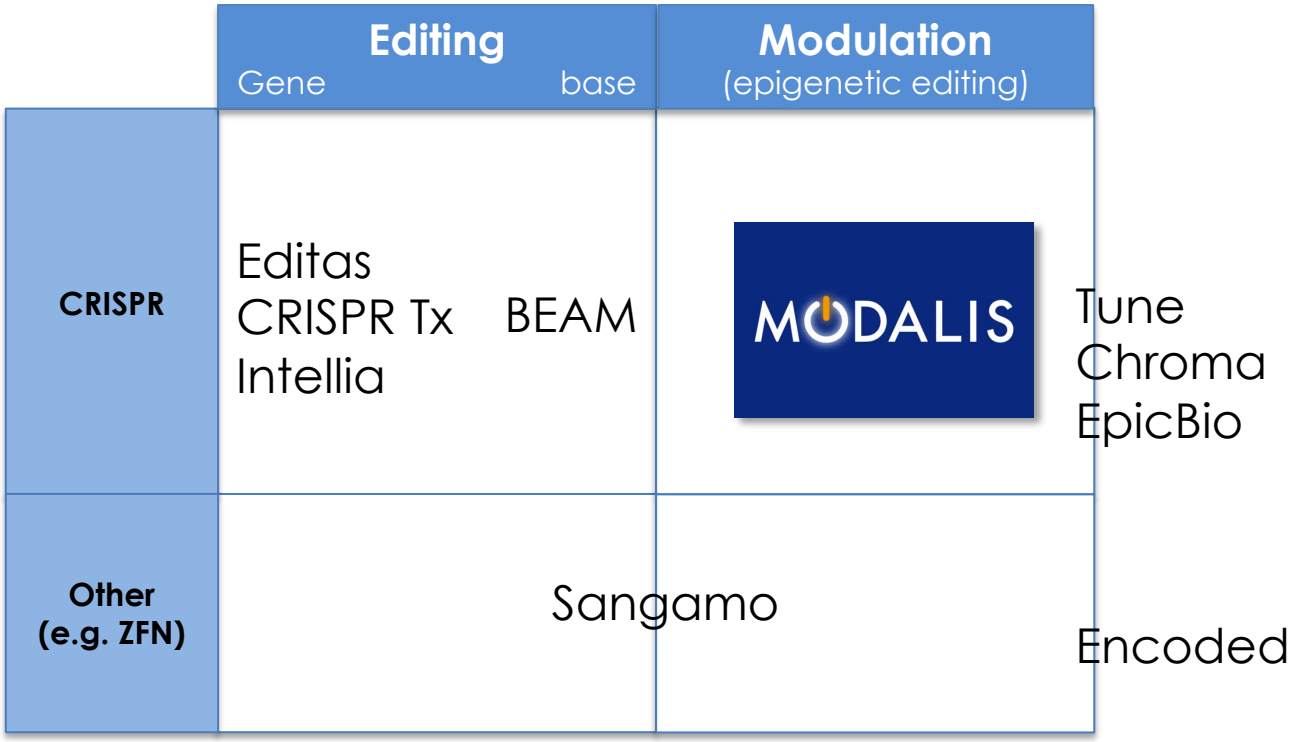
Future pre-clinical and clinical trials are expected to increase the value of the company.

Expected milestone events and impact on corporate value



MODALIS

Modalis is uniquely positioned within the CRISPR field



MODALIS

Our disclosure policy

In light of fair disclosure, Modalis thinks that it is appropriate to respond to inquiries regarding IR, etc. by enriching information disclosure on our website and making it widely and equally known to the public, rather than responding to individual inquiries by direct contact.

Inquiries are accepted on the "Contact Us" page of the Company's website.

https://www.modalistx.com/en/contact/

We will be answering questions that we think it's appropriate on FAQ page of our website or in future disclosures.

Please be advised that we will not be able to accept inquiries by phone or connect them to a person in charge.

We will continue to make every effort to disclose information fairly to our shareholders and investors, and we appreciate your understanding.