English translation for reference purposes only

FY2023 1Q
Financial Results



In case of any discrepancy,
the Japanese version shall prevail

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Modalis therapeutics Corporation
(TSE：4883)
May 9, 2023

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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

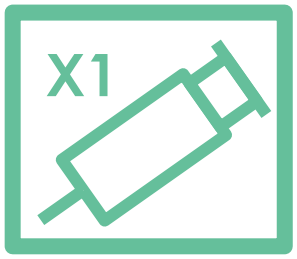
Every life deserves attention

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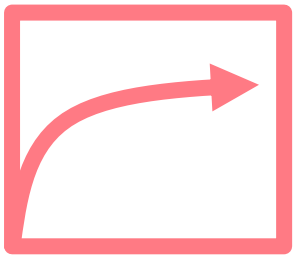
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CRISPR-GNDM® is a promising new therapeutic modality

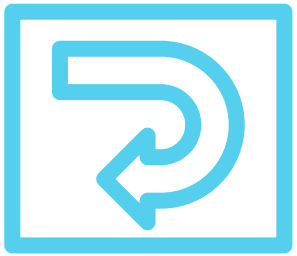
Potential benefits of CRISPR-GNDM® Technology



Single dose
Doesn't require
Repeated dosing



Long-lasting
Sustained effect
for years or decades



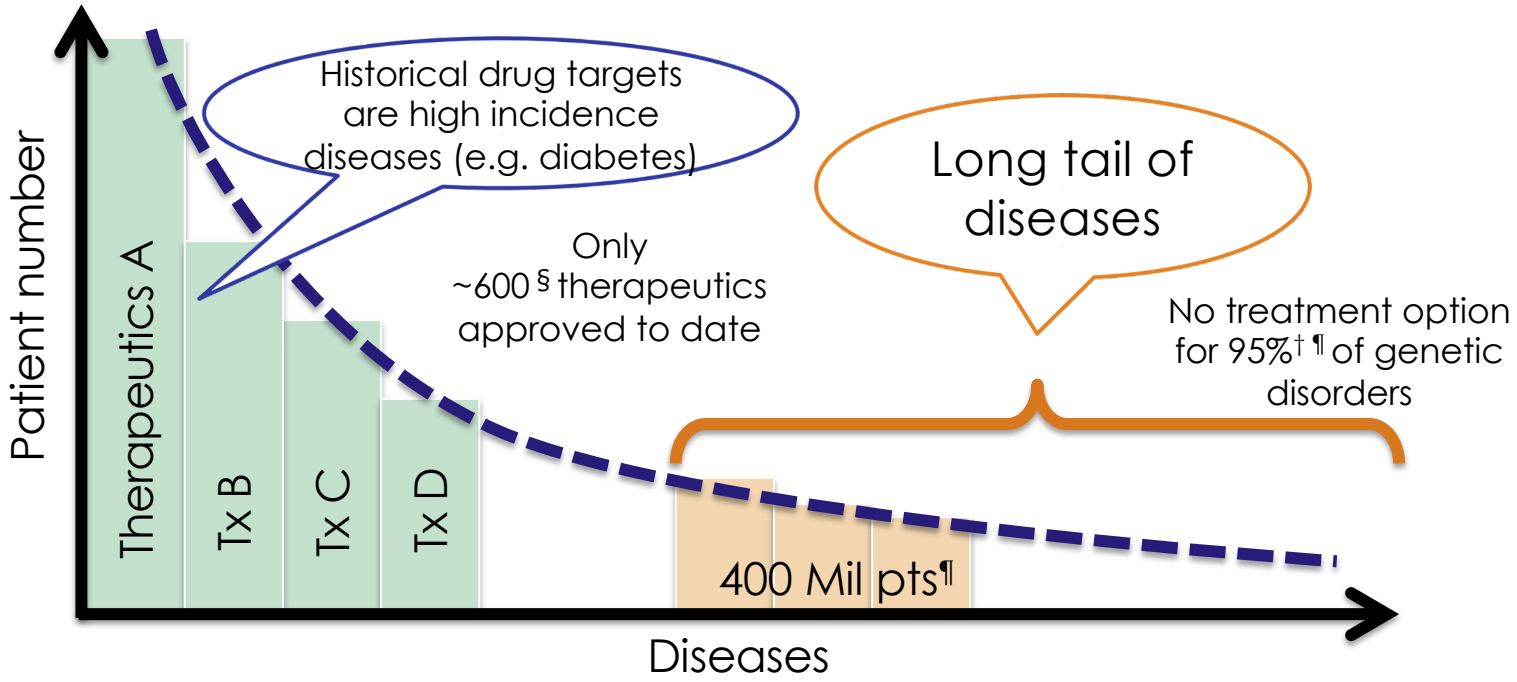
Disease Modifying
Not just to reduces
symptoms but
gives cure

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Provides solution for the long tail of disease

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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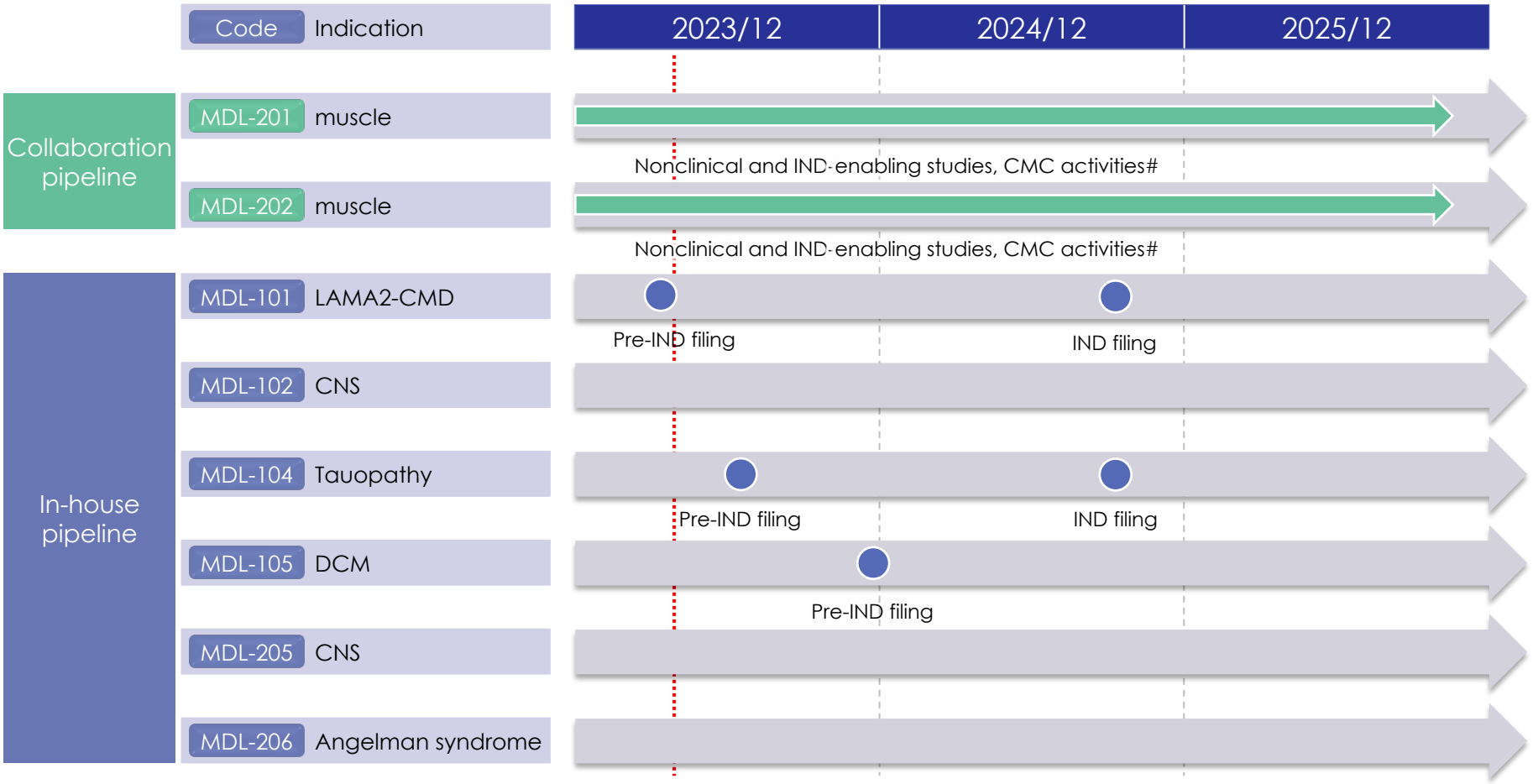
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1. Key Topics

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Pipeline Status

MDL-101 on track to file PreIND in 1H 2023, and Portfolio under review



*Scheduled milestone events are informational in the future and subject to change
#The partner is taking a policy of not disclosing status of projects in preclinical or earlier

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Summary of MDL-101 for LAMA2-CMD

- Reported by 4Q/2022
  - 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
  - pilot NHP study to explore dose and to assess immune reaction against GNDM
  - 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

KOL: Key Opinion Leader

- Progress thereafter
  - **PreIND meeting request filing**
  - **Accepted as a late-breaking abstract of ASGCT meeting**
- Next steps:
  - **ASGCT presentation (May 19th US time)**
  - **PreIND meeting (July)**
  - Continue IND enabling GLP tox and PK/PD
  - Continue process development and pilot productions for GMP campaign

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NHP study summary

- Cynomolgus Monkeys were treated with a monkey surrogate version of MDL-101 (cyMDL-101)
- Confirmation of AAV gene transduction → GNDM expression → increased expression of LAMA1 within the range of doses generally considered safe
- Based on the above results, estimate the dose range at which the human version of MDL-101 (hMDL-101) is likely to be safe and effective in the clinic. Incorporated into clinical trial design

- Going further, extrapolation of the vector transduction and GNDM expression to other muscular disease pipelines suggests that they may also be effective.

- Details to be reported after our ASGCT presentation on 5/19

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Summary of other R&D activity

- MDL-104（Tau）
  - biodistribution study in NHP ongoing
- MDL-105（TTN）
  - evaluation of animal PoC study ongoing
- MDL-205
  - Coordinating reacquisition of rights related to joint research.
  - As soon as we agree on the terms, Modalis will share the target, development status as well as plan for the development.

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Other updates on business

- Progress on intellectual property
  - A patent that Modalis co-filed with Univ. Tokyo, JP2019-217432 (PAM Flex Cas9 patent), was granted in Japan(Apr)

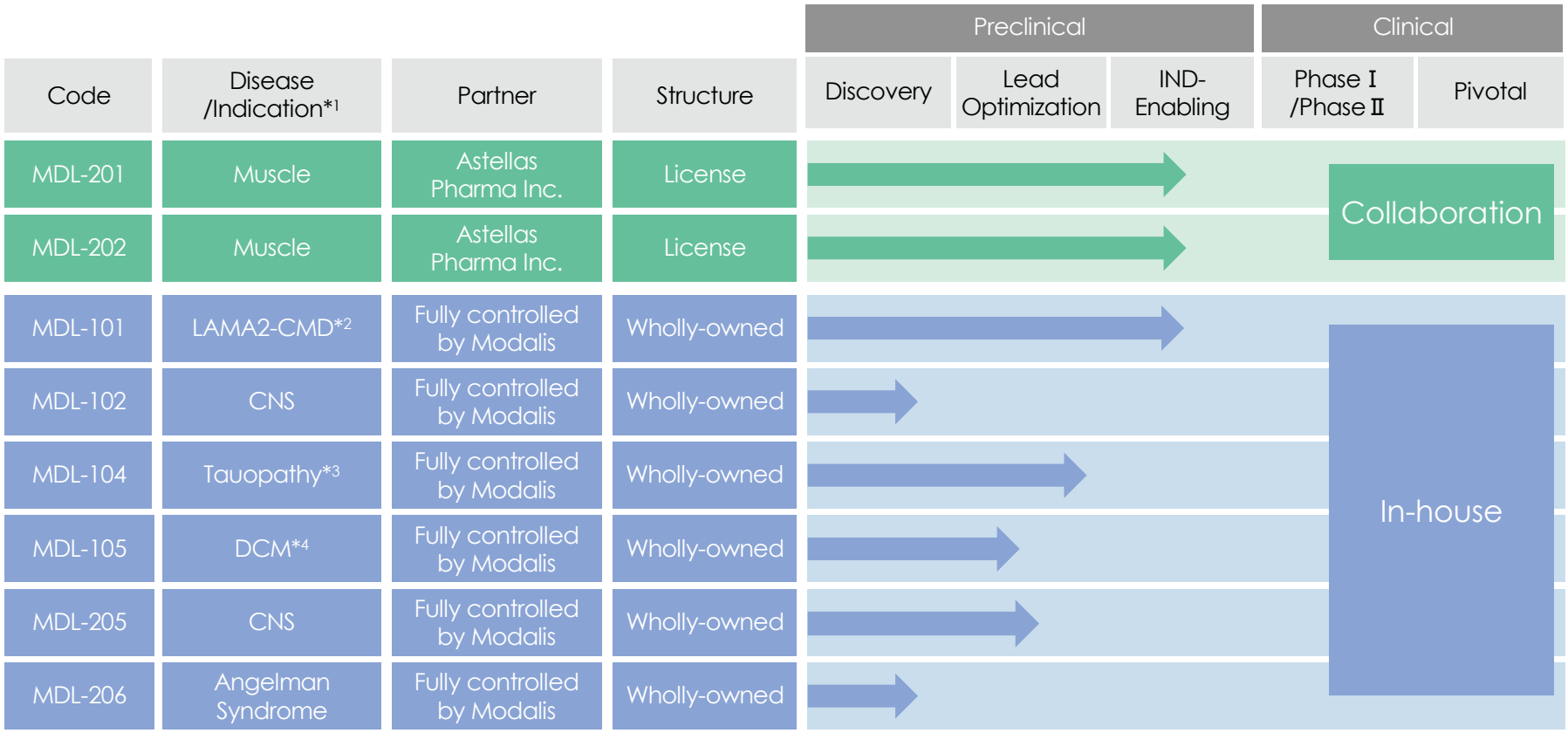
- Progress on partnering
  - Partnering discussion ongoing with pharma/biotech companies with the new MDL-101 data
  - Research collaboration: In discussion with pharma/biotech companies on new targets

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2. Financial Highlights

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Pipeline



*1: We have adopted a strategy of withholding specific indications until the patent application is published for competitive reasons.
*2: LAMA2-CMD = Merosin-deficient congenital muscular dystrophy type 1A
*3: Tauopathy belongs to a class of neurodegenerative diseases involving the aggregation of tau protein. Correlation with Alzheimer's disease has been suggested.
*4: DCM = Dilated cardiomyopathy

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PL & Business Result

(Million Yen)

	FY2022 1Q (A)	FY2023 1Q (B)	(B) – (A)
Operating revenue	40	-	(40)
Operating expenses	507	514	7
R&D	442	443	1
SGA	65	71	6
Operating income	(466)	(514)	(48)
Ordinary income	(443)	(509)	(66)
Current Profit	(438)	(532)	(94)

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

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BS & Financial Position

(Million Yen)

	FY2022 (A)	FY2023 1Q (B)	(B) – (A)
Current assets	3,061	2,831	(230)
Cash & deposits	2,933	2,708	(225)
Non-current assets	68	68	0
Total assets	3,129	2,899	(230)
Current liabilities	141	201	60
Non-current liabilities	47	44	(3)
Total liabilities	188	245	57
Total net assets	2,941	2,653	(288)
Total liabilities and net assets	3,129	2,899	(230)
Capital adequacy ratio	93.4%	90.9%	

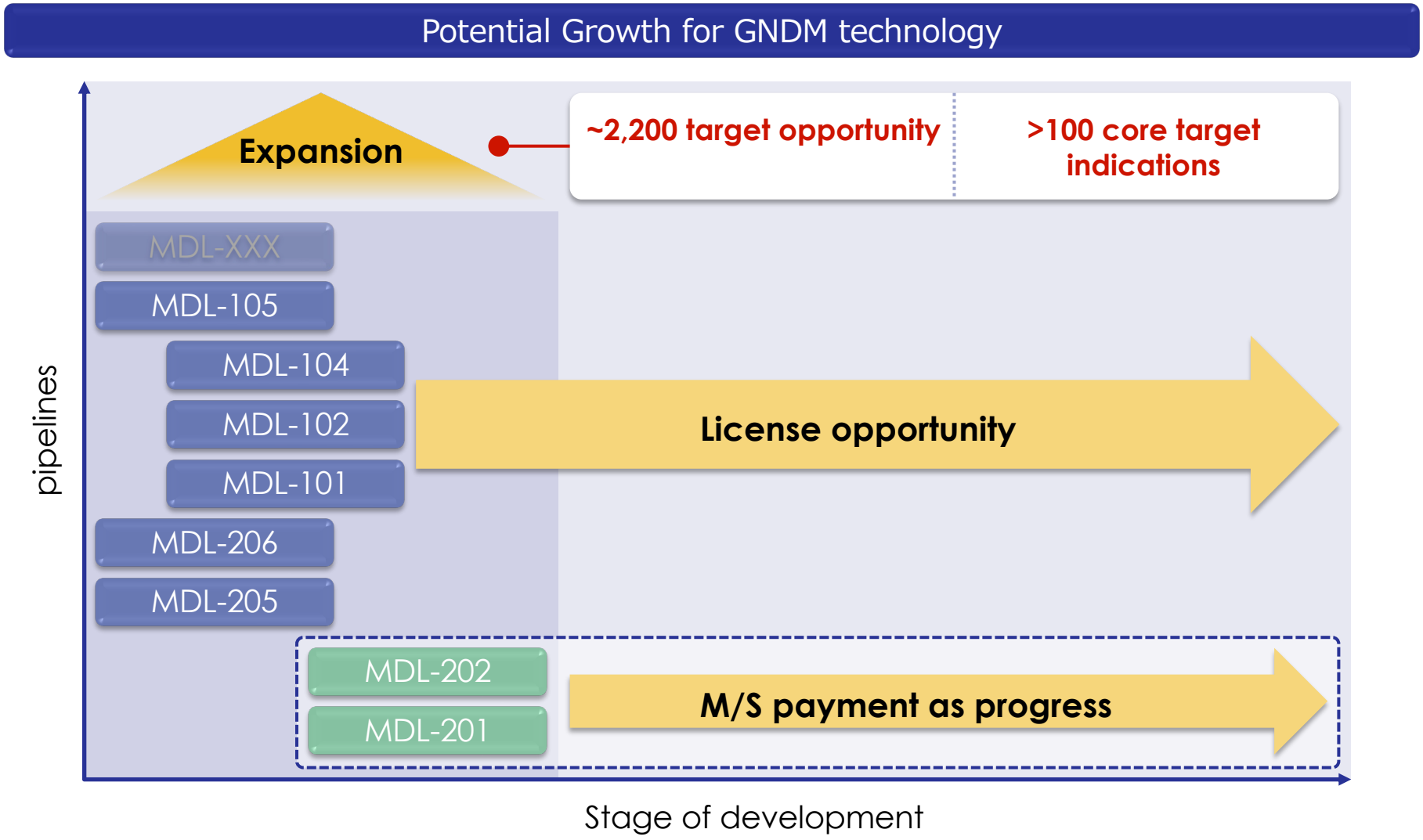
- High Equity ratio
  Under financing to secure a more stable financial base
- Decrease in property, plant and equipment and intangible assets due to impairment loss

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3. Growth Strategy

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Growth Strategy
opportunity expands two dimensionally



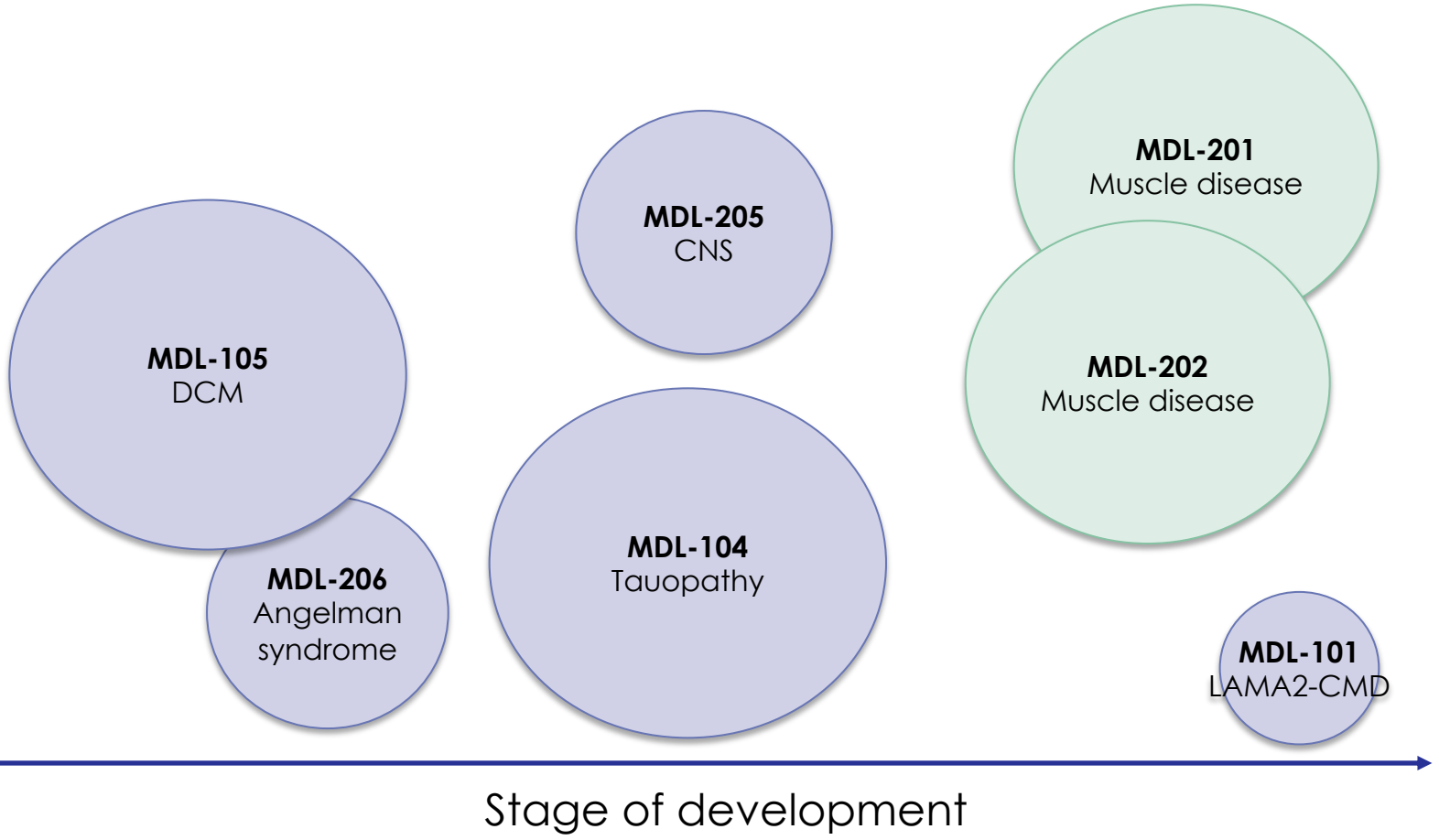
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Modalis' pipelines and market size

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

Modalis' pipelines and market size



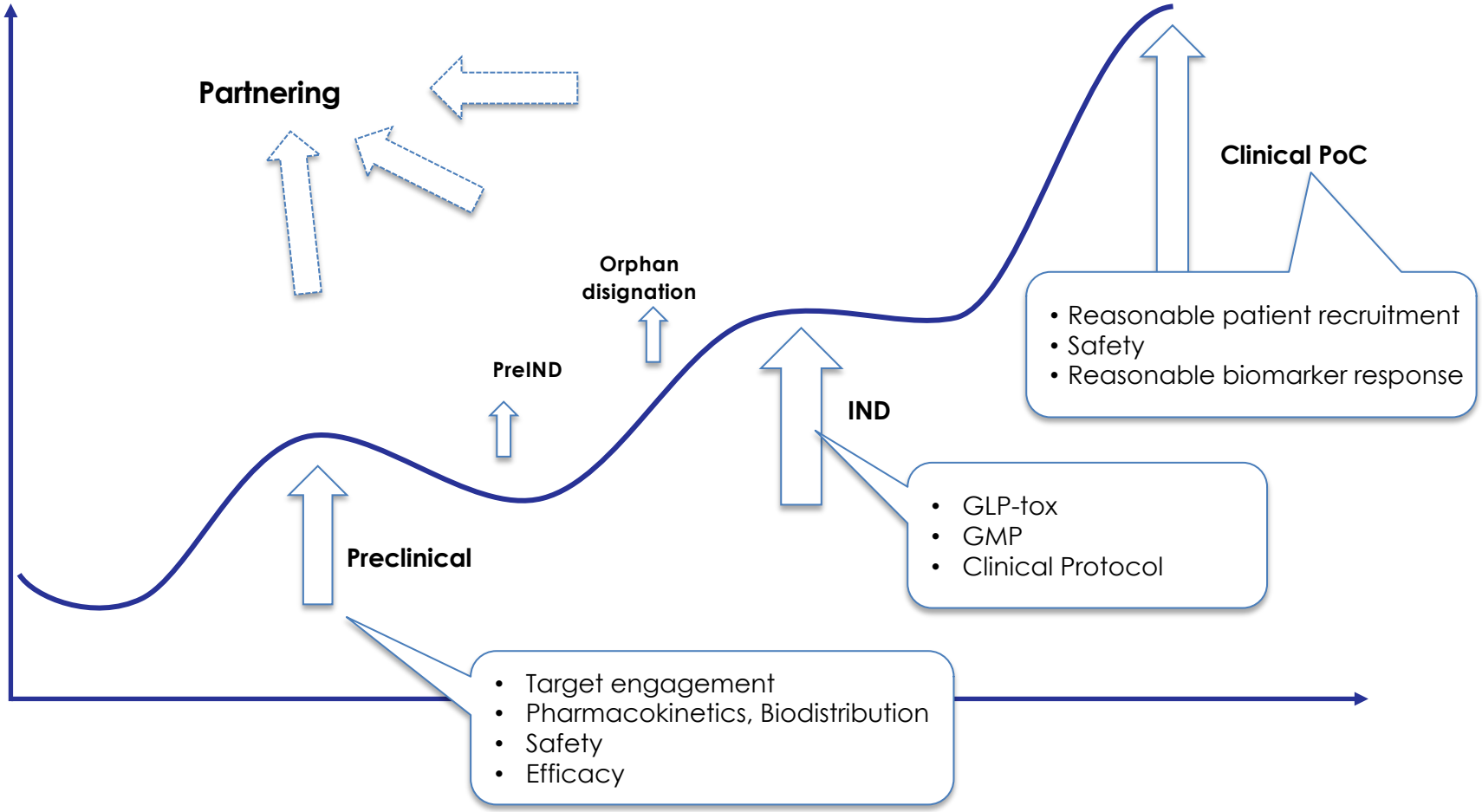
※ Size of circles represents an image of market size or patient number of each indication

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

Expected milestone events and impact on corporate value



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GNDM is efficient approach both for LoF and GoF mutation

In LoF disorders

single

Point of Mutation(s)

diversified

Limited only to ex vivo application

Base editing

Gene editing

Gene Therapy

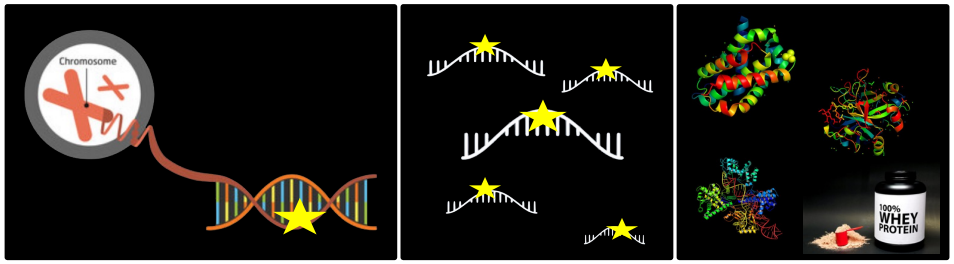
- **GNDM** (CRISPR)
- ZFP-TF (ZFN)

small — **Gene Size** — Large

In GoF disorders

Targets for suppression

DNA ⇨ RNA ⇨ Protein



1 mutant allele	Multiple copies	varied
GNDM Editing(K/D)	Si RNA ASO	Protein(Ab) peptide Small molecule

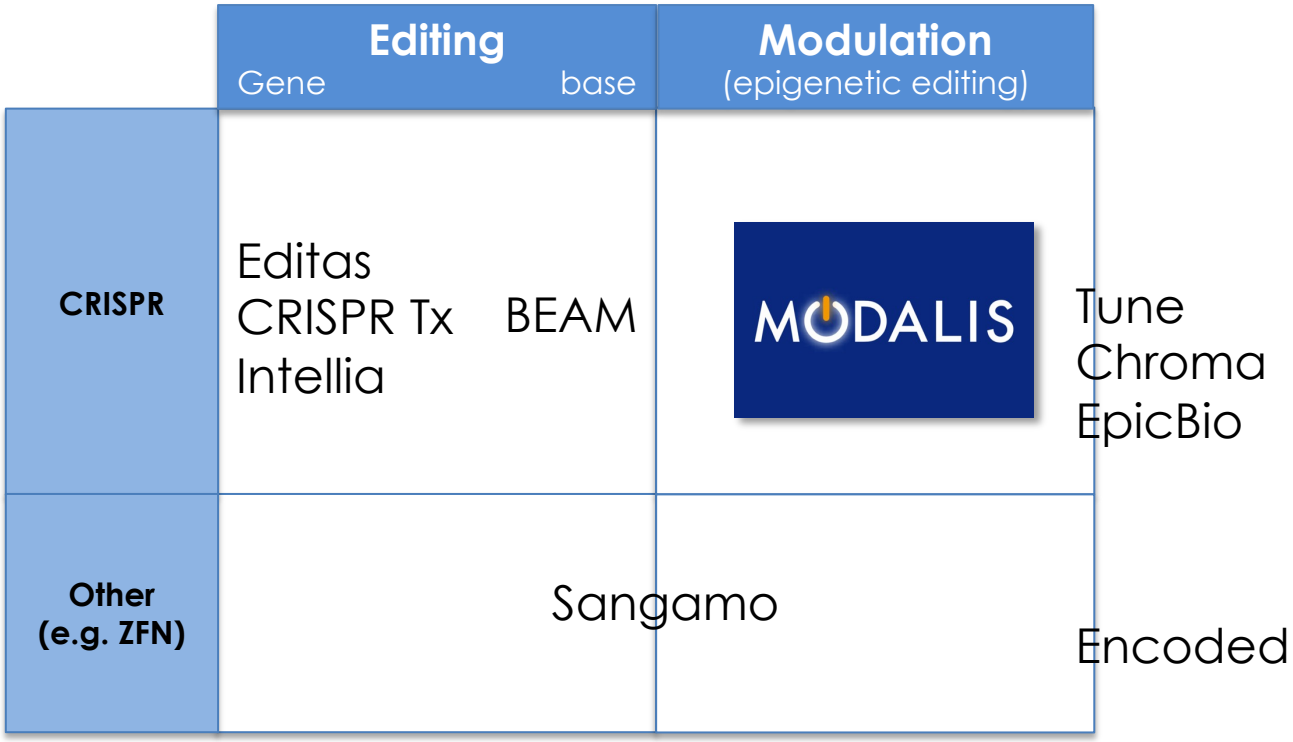
LoF: Loss of function
GoF: Gain of (mal)function

K/D: Knock-down

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Modalis is uniquely positioned within the CRISPR field



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4. Q & A

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Q1 Do you see any impact of recently reported emerging genome editing technologies?

A) Since the invention of CRISPR technology in 2012, various improvements and other genome editing technologies have been researched and developed. Even before CRISPR, genome editing by zinc finger (ZFN) and other technologies existed.

Our CRISPR-GNDM® technology is the culmination of a combination of CRISPR genome editing technology, viral capsid delivery technology, selection of guide RNA, promoters, and transcriptional activators and repressors. We believe that this is something that cannot be overcome overnight by improving only a few elemental technologies.

In addition, pharmaceuticals require not only technology but also the licensing of intellectual property necessary to manufacture and sell them, and it is also necessary for businesses to develop such things.

We have been focusing on the advantages of this technology for more than 7 years and have been developing our technology and business in this field, and we are proud to be a world leader in this field. We will continue to promote our business in order to protect our leading position.

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Q2　Does the presentation at ASGCT mean to Modalis?

A）The American Society for Cellular Gene Therapy (ASGCT) is the largest and most advanced gathering of information in the field of gene therapy in the world, and we consider it an honor to be accepted as a Late-Breaking Abstract and to give an oral presentation at this conference, where the bar for acceptance is considered relatively high. We believe it is an honor to be accepted as a Late-Breaking Abstract and to give an oral presentation at such a conference.
We believe that being able to present data on MDL-101, the world's first CRISPR-based epigenetic editing drug, in pathological model mice and monkeys is an important opportunity for us to contribute to the advancement of science and technology.
In addition, since the conference is attended by pharmaceutical and biotech companies from all over the world that are engaged in this field, we believe that attracting attention at the conference will contribute to the expansion and promotion of partnership opportunities.

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