English translation for reference purposes only

FY2022 2Q
Financial Results



In case of any discrepancy,
the Japanese version shall prevail

MODALIS

Modalis therapeutics Corporation

(TSE : 4883)

August 5, 2022

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MODALIS

- is pioneering the first CRISPR-based gene modulation technology
- is the leading company in epigenetic modulation
- develops novel precision medicines for a genetic disorders for which there have been no cure











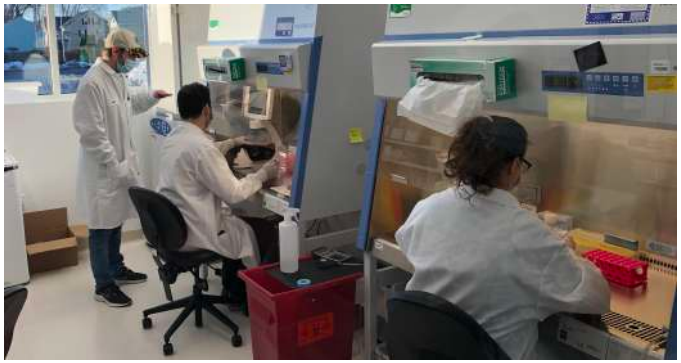

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Corporate Philosophy

Every life deserves attention

The company group, through drug discovery using the core platform technology "non-cutting CRISPR technology" (CRISPR-GNDM ® technology) to invent therapeutics targeting rare genetic disorders. True to our corporate philosophy of "every life deserves attention," we hope to contribute to society by giving patients hope to overcome their illness.

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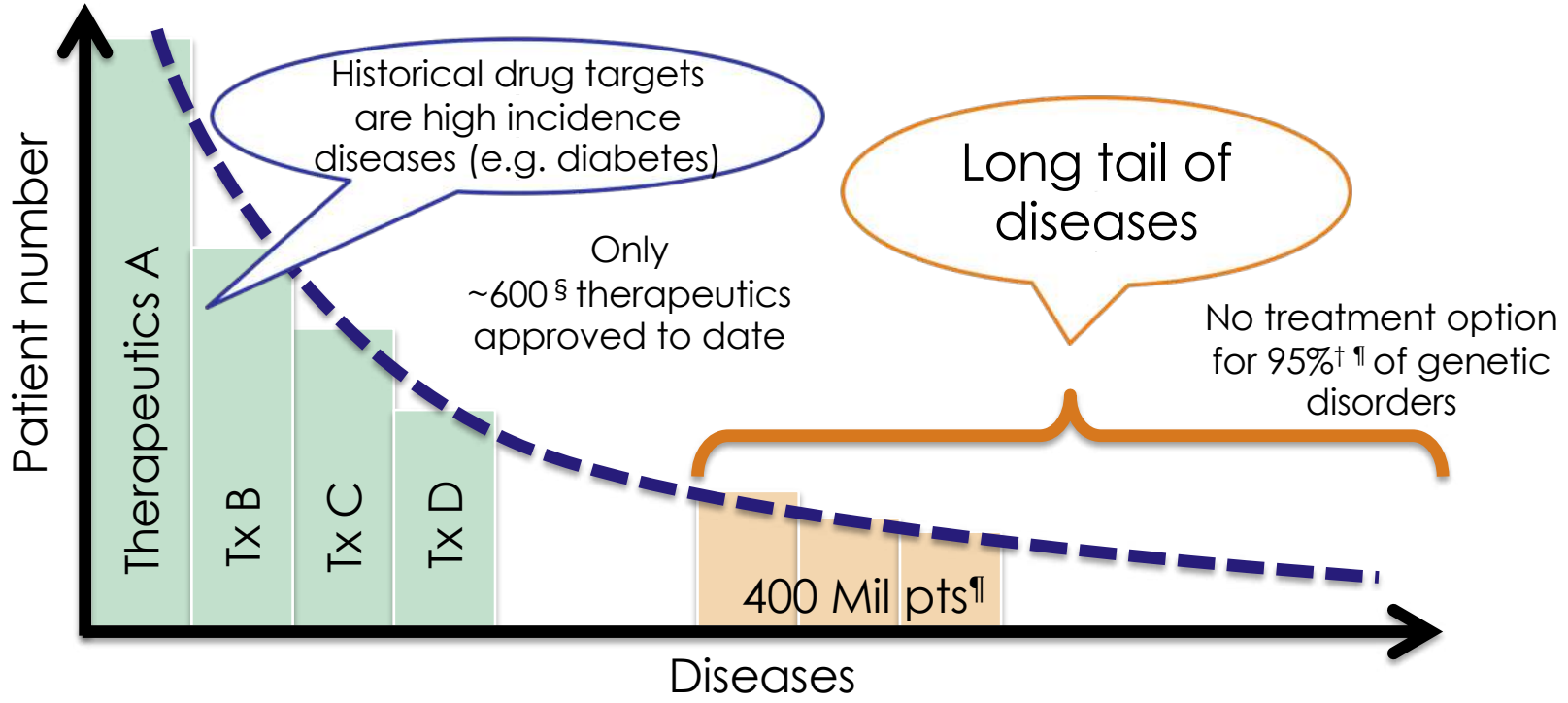
Provides solution for the long tail of disease

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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Table of contents

1. Financial Highlights

2. Key Topics

3. Growth Strategy

4. Q&A

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1. Financial Highlights

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PL & Business Result

(Million Yen)

	FY2021 2Q (A)	FY2022 2Q (B)	(B)－(A)
Operating revenue	1	40	39
Operating expenses	478	908	430
R&D	349	778	429
SGA	129	130	1
Operating income	(477)	(868)	(391)
Ordinary income	(464)	(780)	(316)
Profit	17	(775)	(792)

Operating revenue

・Earning collaborative R&D milestone income

Operating expenses

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

SGA: Selling and Generally Administrative Expenses

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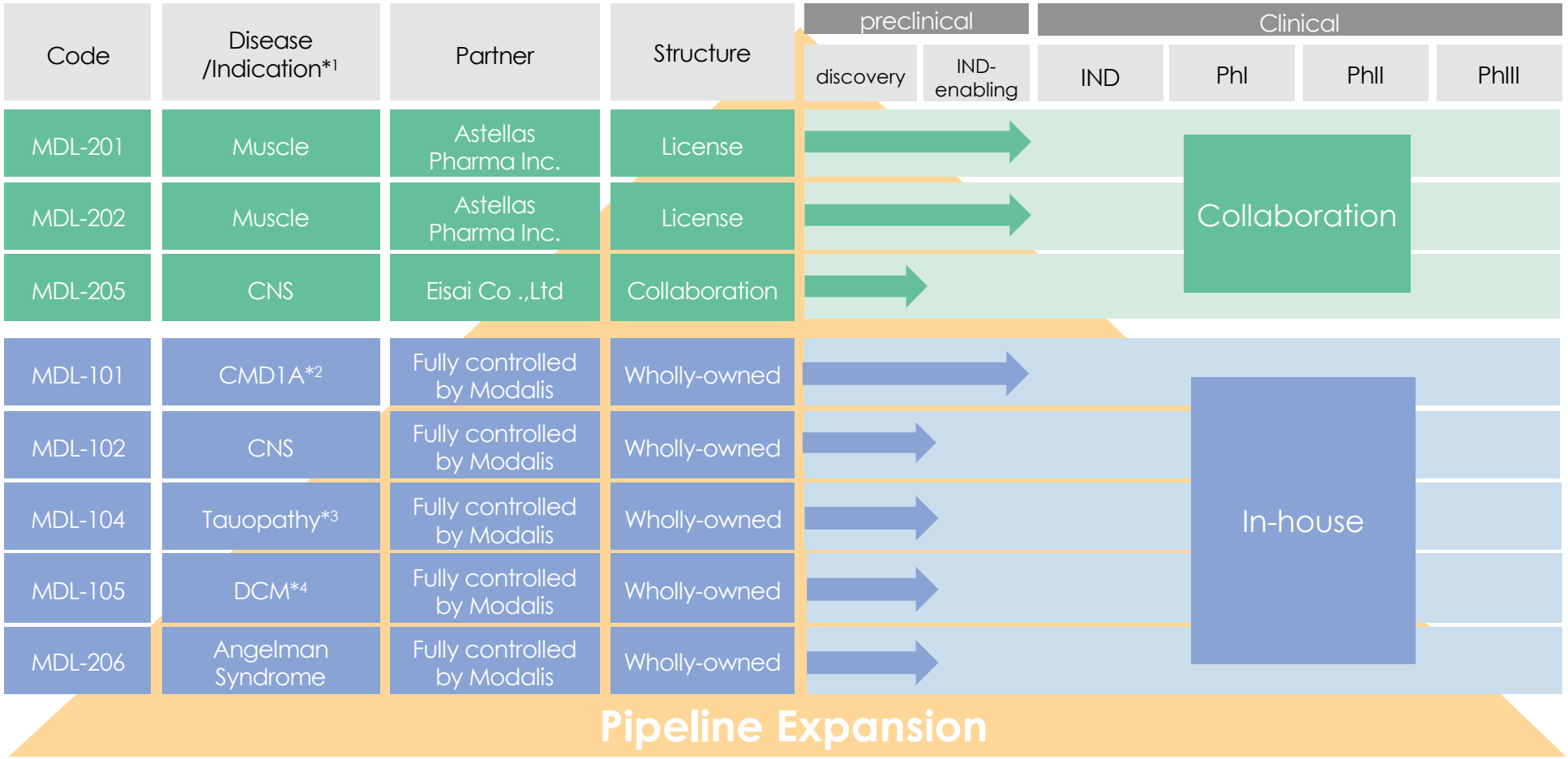
Pipeline



*1: We have adopted a strategy of withholding specific indications until the patent application is published for competitive reasons.
*2: CMD1A=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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BS & Financial Position

(Million Yen)

	FY2021 (A)	FY2022 2Q (B)	(B) – (A)
Current assets	5,067	4,255	(812)
Cash & deposits	4,936	4,158	(778)
Non-current assets	1,002	1,088	86
Property, plant and equipment	223	342	119
Right to use patent	704	673	(31)
Total assets	6,069	5,343	(726)
Current liabilities	181	205	24
Non-current liabilities	339	325	(14)
Total liabilities	520	530	10
Total net assets	5,549	4,813	(736)
Total liabilities and net assets	6,069	5,343	(726)
Capital adequacy ratio	91.4%	90.0%	

- Stable financial base, High Equity ratio
- Increased property, plant and equipment such as research equipment due to the expansion of the laboratory of the US subsidiary

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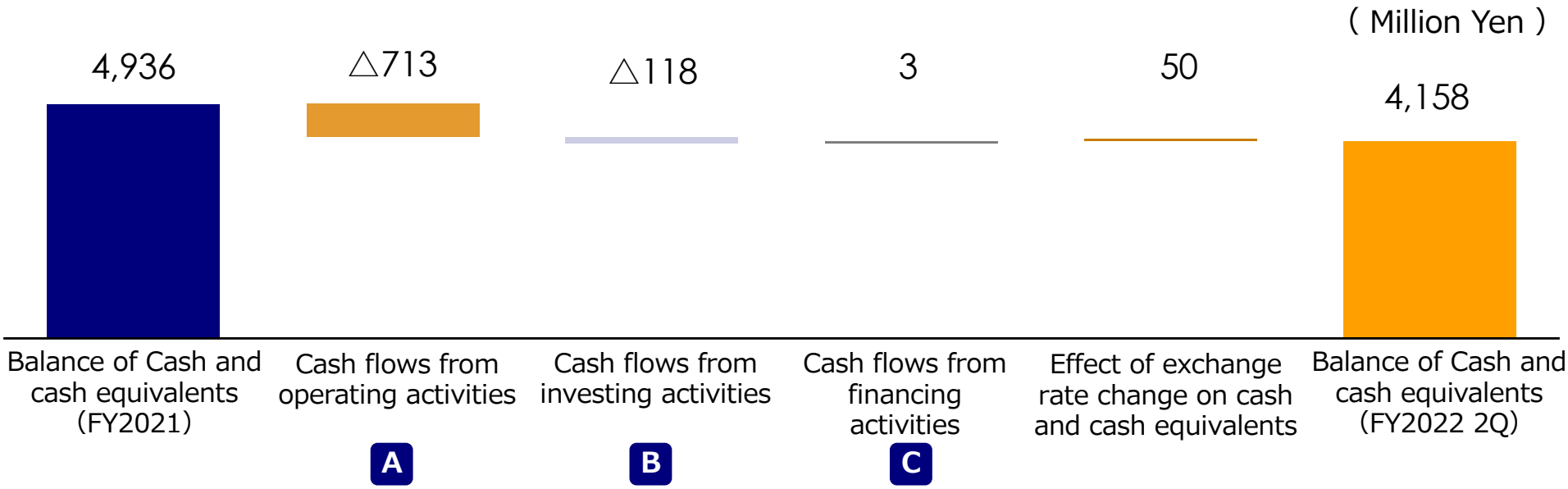
Cash Flow Status



A Cash flows from operating activities	• Loss before income taxes （△780） • Depreciation （58）
B Cash flows from investing activities	• Purchase of property, plant and equipment （△129）
C Cash flows from financing activities	• Proceeds from issuance of stock acquisition rights （7）

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2. Key Topics

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Summary of MDL-101

- Reported by 1Q/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 explorer dose and to assess immune reaction against GNDM
  - Kicked off GMP targeting process development in collaboration with a CDMO.
- Progress thereafter
  - INTERACT meeting with FDA (Mid Jul) -> summarized in the next page
  - In-life* part of 2nd NHP study completed. Sample analysis ongoing.
  - Design and execution of the studies toward pre-/IND
  - Process development ongoing for GMP manufacturing
  - Engage with clinical advisors
- Next steps:
  - Filing pre-IND meeting (by end 2022)
  - Continue IND enabling GLP tox and PK/PD
  - Continue process development and pilot productions for GMP campaign

in-life*: Phase of a study following treatment in which the test system is ongoing

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INTERACT* Meeting summary

- Held in Mid July
- Non-binding
- Modalis provided development summary and questions to FDA and FDA answered to them in writing and follow them up in a web meeting.
- Primary agenda includes
  - Manufacturing process and method to assess clearance of the resulted product
  - Compatibility among samples used in animal studies and clinical trials
  - Species selection for the GLP studies
  - Using surrogate products for animal studies
- FDA responses were found to be within Modalis' expectations and under control. They did not result in significant changes to the planned studies and development strategies.

INTERACT : *INitial Targeted Engagement for Regulatory Advice on CBER Products*

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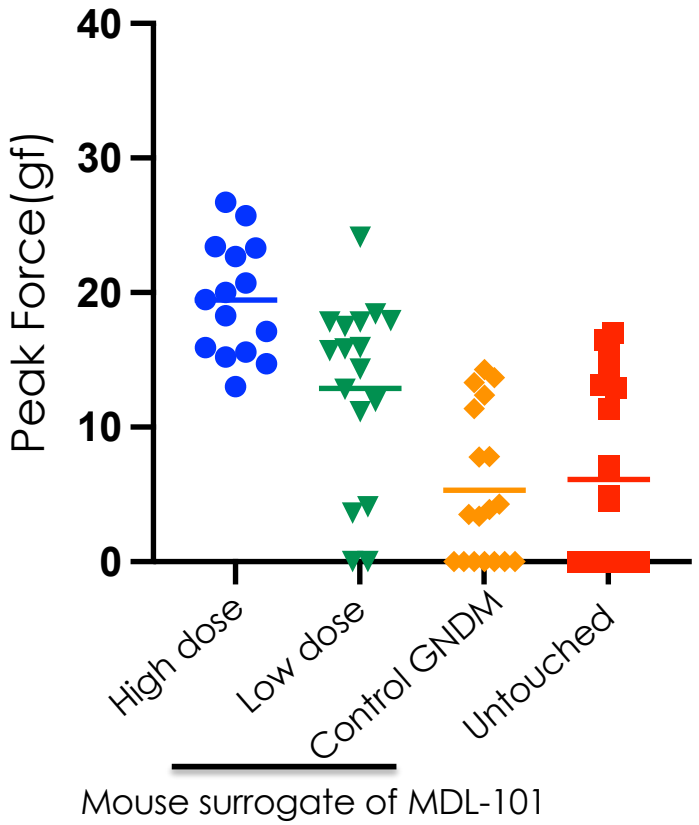
Mice study demonstrated significant improvement in muscle function



- dyW (severe MDC1a model) mice injected with GNDM (control gRNA, or active gRNA at low and high dose) compared with untouched.
- Grip strength assay on 34-day post injection.

In addition to the survival benefit, the functional improvement is confirmed

average of 3 trials

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Summary of other R&D activity

- Other pipelines
  - MDL-104 (Tau)
    - Robust Tau suppression confirmed in humanized MAPT mice
  - MDL-105 (TTN)
    - Engaged and discussed with Scientific and Clinical advisors
- Other
  - Presented 6 articles including MDL-101, 104, 105, and 205 at 26th American Society of Gene and Cell Therapy (ASGCT) annual meeting (May 16-19 @Washington DC)
  - Presented LAMA-1 and Titin programs at CureCMD (curecmd.org)conference (Jun 29-Jul1 @Nashville TN)
    - https://www.scifam.info

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Other updates on business

- Progress on intellectual property
  - Received notice of allowance (NOA) from USPTO on a patent co-filed with Astellas titled 'Method for treating muscular dystrophy by targeting utrophin gene (Jun)

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

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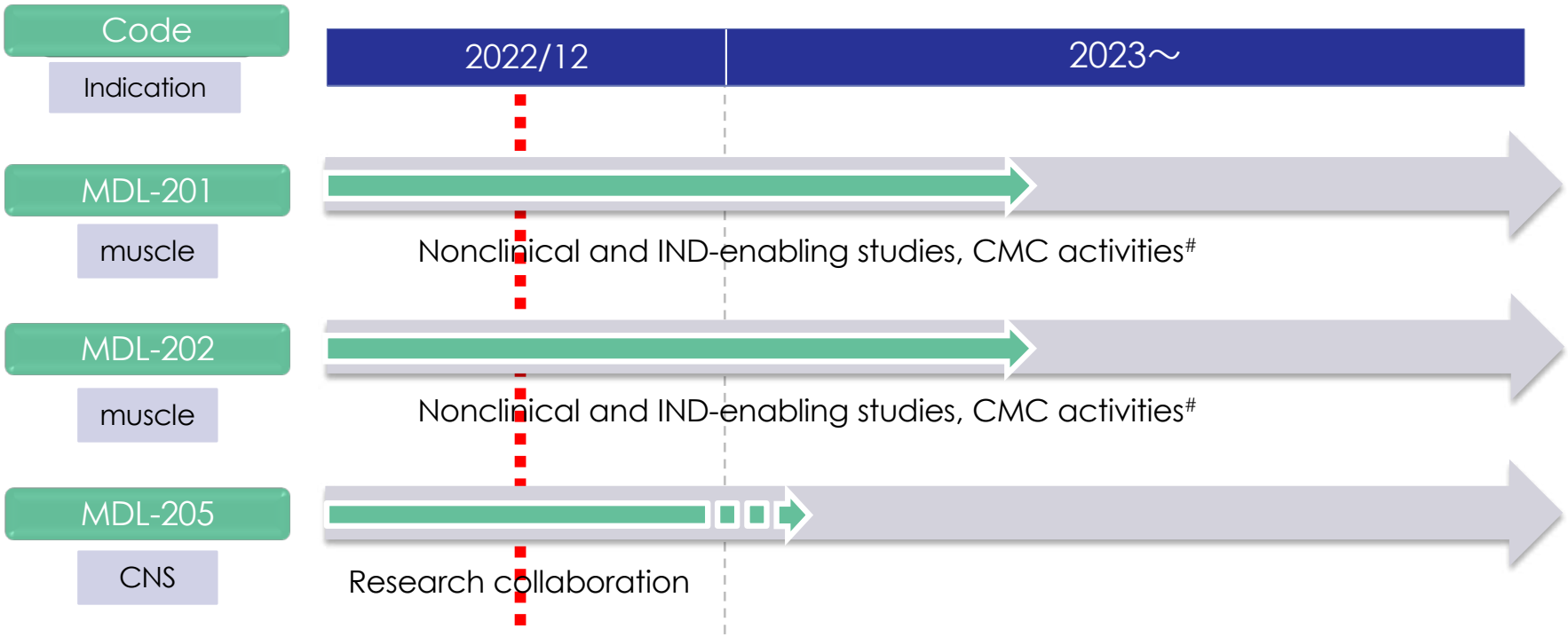
Steady progress in IND enabling of 201 and 202
MDL-205 has achieved MS and collaboration is extended

Collaboration pipeline



*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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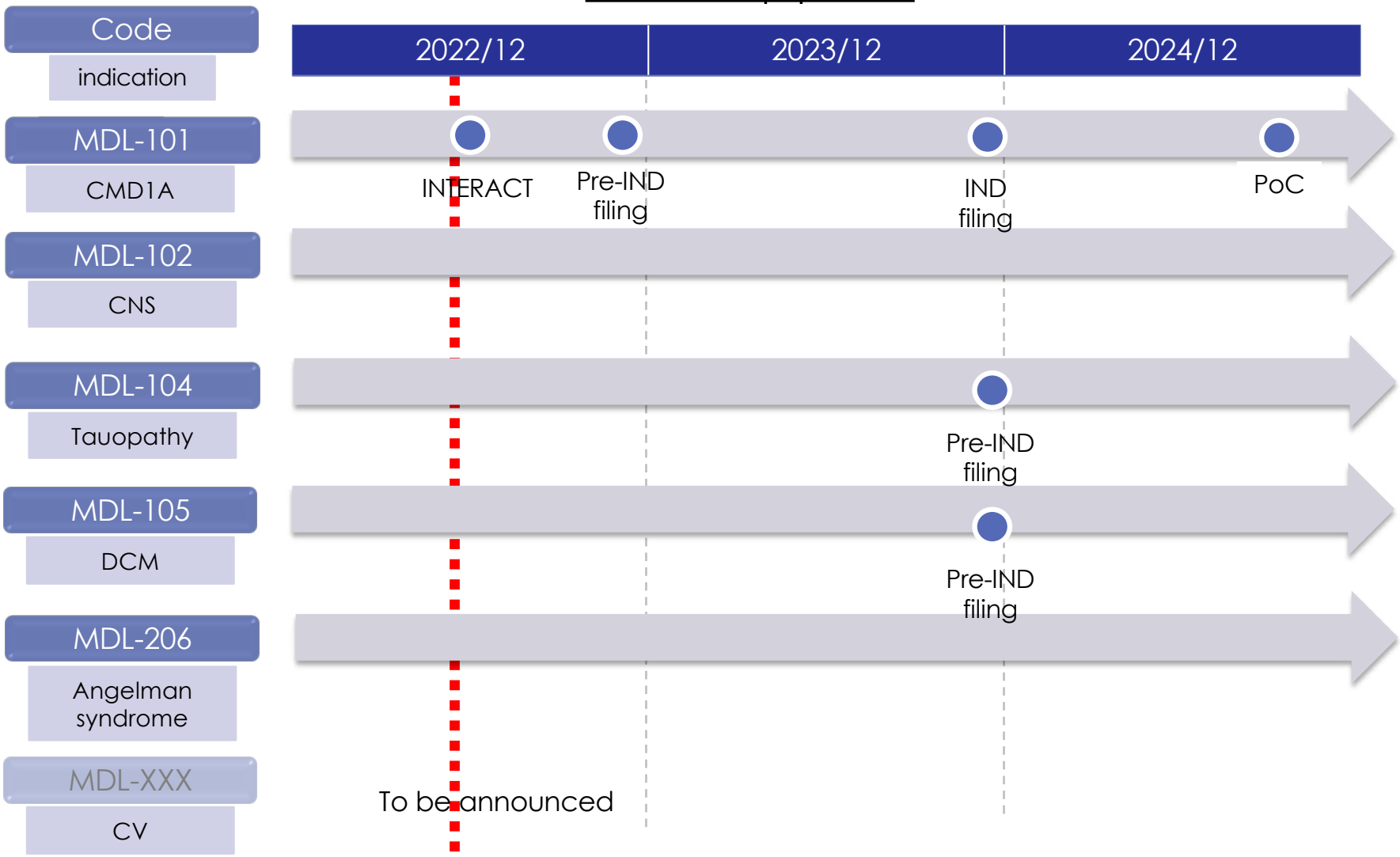
Several pipelines are coming out in this year

In-house pipeline



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

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3. Growth Strategy

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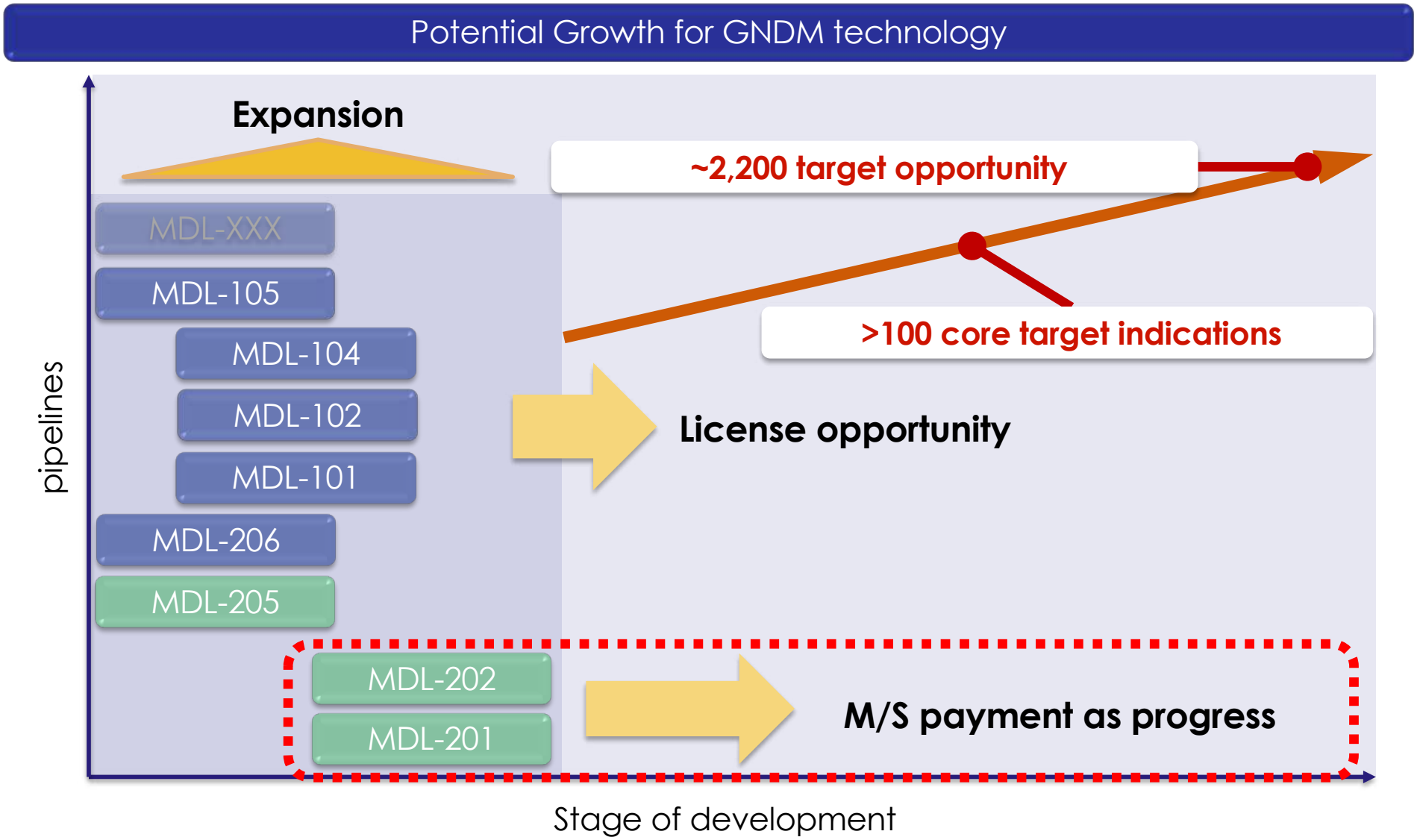
Growth Strategy

opportunity expands two dimensionally



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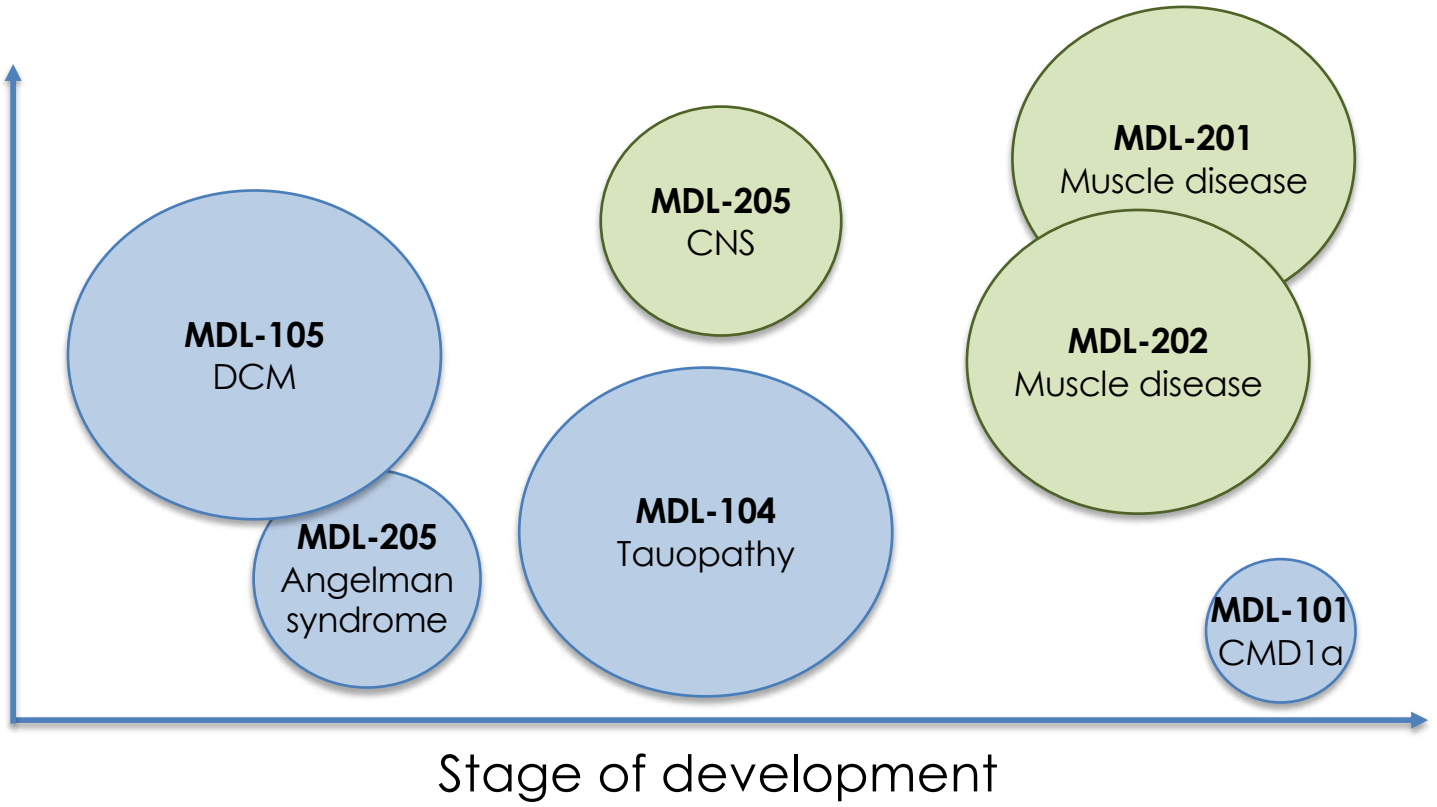
Large indication programs follow MDL-101 which paves the clinical path

Modalis' pipelines and market size



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

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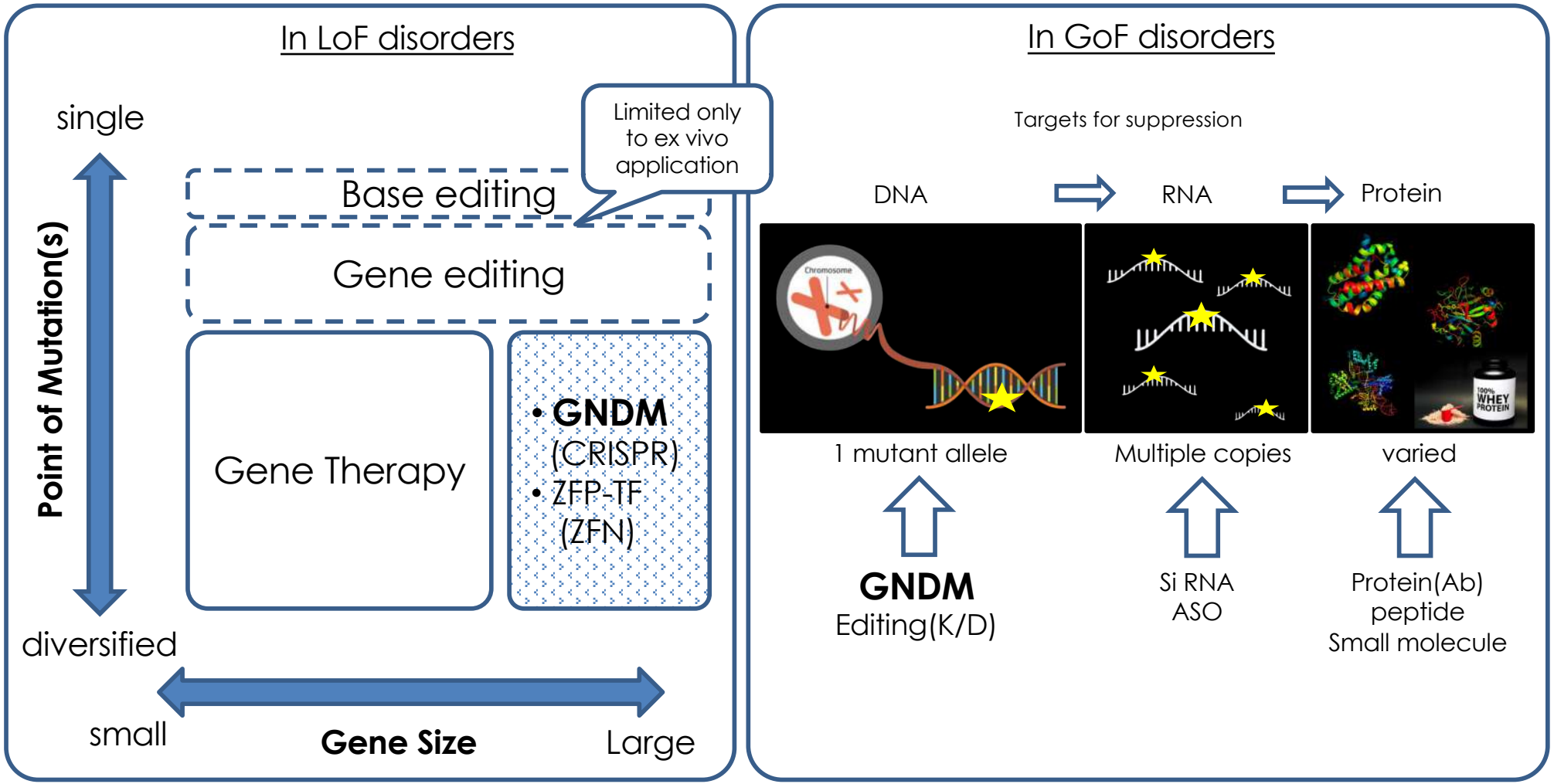
GNDM is efficient approach both for LoF and GoF mutation



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

	Editing Gene	base	Modulation (epigenetic editing)
CRISPR	Editas CRISPR Tx Intellia	BEAM	MODALIS
Other (e.g. ZFN)	Sangamo		

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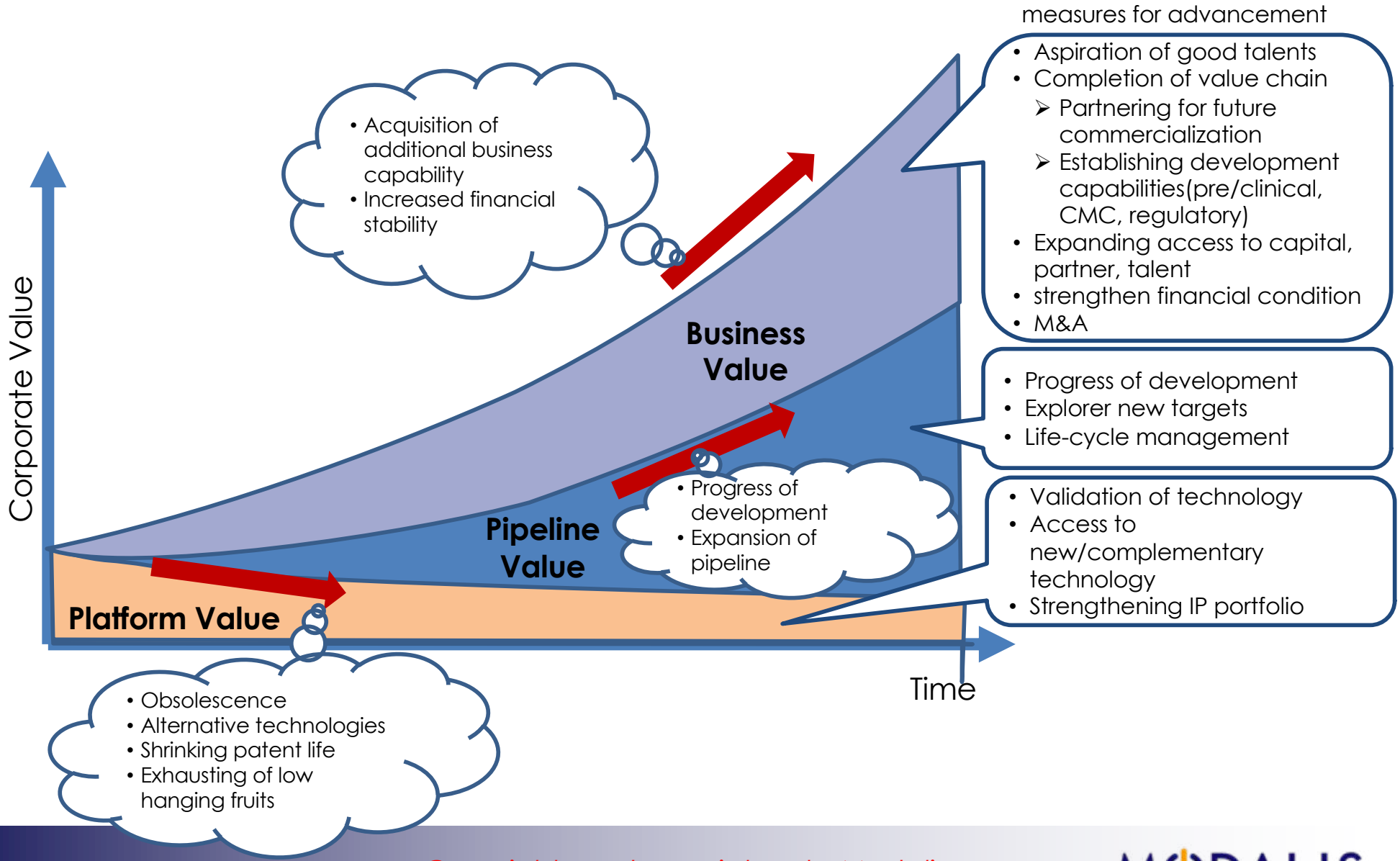
Composition of Modalis' value and measures for advance



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4. Q & A

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Q1 You had planned to license out MDL101 in the first half of 2022, how is the progress going?

A) Although we continue to have dialogues with potential partners, we are proceeding with our business with the belief that advancing development toward clinical trials as planned will ultimately add value to the program and technology and lead to the realization of an alliance on better terms.
Since the decision to enter into an alliance depends on the timing and intent of the other party as well as our own, it is not something that can be achieved solely through our efforts. On the other hand, as we recognized again at CureCMD conference, where we participated, MDC1A is a life-threatening disease, and given the current situation where the drug we are developing is a hope of the patients, the best thing we can do and manageable to us is to proceed with the development as fast as possible while we are waiting for a right partner who has strong commitment to develop the molecule together will make a decision at an appropriate time and under the appropriate conditions.

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Q2 Change in Policy on Non-Disclosure of Partnering Goals

A) We had been disclosing our intention and target timing of partnering goals for our own pipelines because we believed it would contribute to investment information.
However, since partnering depends not only on the progress of the development and our intentions, but also on the intentions and strategies of the other party, we have determined that disclosing information that is not within our control is not appropriate for investment information.
In addition, disclosing our partnering intentions and deadlines would not have a positive impact on negotiations, and in fact there have been cases where such an impact has occurred. Therefore, we have decided not to disclose our partnering goals.

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Q3 Any outcomes from the presentation at ASGCT?

A) This year's ASGCT was our first opportunity to present our technology and developments at a scientific conference, and we believe our presentations attracted a great deal of attention. This is consistent with the fact that our approach is quite new and unique even in the the rapidly developing field of gene therapy and genome editing, as well as with the emergence of new companies advocating epigenome editing and gene regulation.
As a result, we have received several inquiries about partnerships, which we believe has been very positive for our future business.

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Q4 How does the USPTO's Notice of Allowance to UTRN patent impacted on Modalis' business

A) The fact that the patent will be granted in the U.S. following Japan means that the product will be protected by the patent when the pharmaceutical product based on the patent is launched in that country. Therefore, we believe that the granting of the patent in the U.S., which is believed to account for about half of the pharmaceutical market, is of great significance.
We will continue to work with our partners to obtain patents in the remaining target countries.

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Q5 How did the INTERACT meeting go?

A) This meeting was the first opportunity for MDL-101 and CRISPR-GNDM technology to make a contact with the regulatory authorities.
While we do not have a policy for disclosing details, the meeting resulted in a better understanding on our part of

1. The position of the product and technology in gene therapy and applicable guidelines
2. Issues related to bridging the investigational drug with the product to be used in the GLP studies
3. Data to be demonstrated in the IND package
4. The rationale for the study design that we should present in the Pre-IND

As a result, the FDA's opinion is generally consistent with our original study design, and we do not believe that we need to make any significant changes to our study plan or strategy.

Refer to following for INTERACT meeting

https://www.fda.gov/vaccines-blood-biologics/industry-biologics/interact-meetings

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Q6 “ Gene therapy" is noted in the Kishida Cabinet's policy published on 6/7. What impact does this have?

A) We understand that budgetary and legal measures will be taken based on this decision, and the impact of this decision is still unknown at this time.
However, the fact that the areas in which we operate are related to the national interest and have been identified as priority areas in which to provide incentives is a tailwind, but not a headwind, for our business. Hopefully, appropriate selection will be made and budget allocations will be made among these areas.

Reference: Basic Policy on Economic and Fiscal Management and Reform 2022

https://www5.cao.go.jp/keizai-shimon/kaigi/cabinet/2022/summary_en.pdf

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