English translation for reference purposes only

FY2022
Financial Results

In case of any discrepancy,
the Japanese version shall prevail

MODALIS

Modalis therapeutics Corporation
(TSE：4883)
February 13, 2022

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

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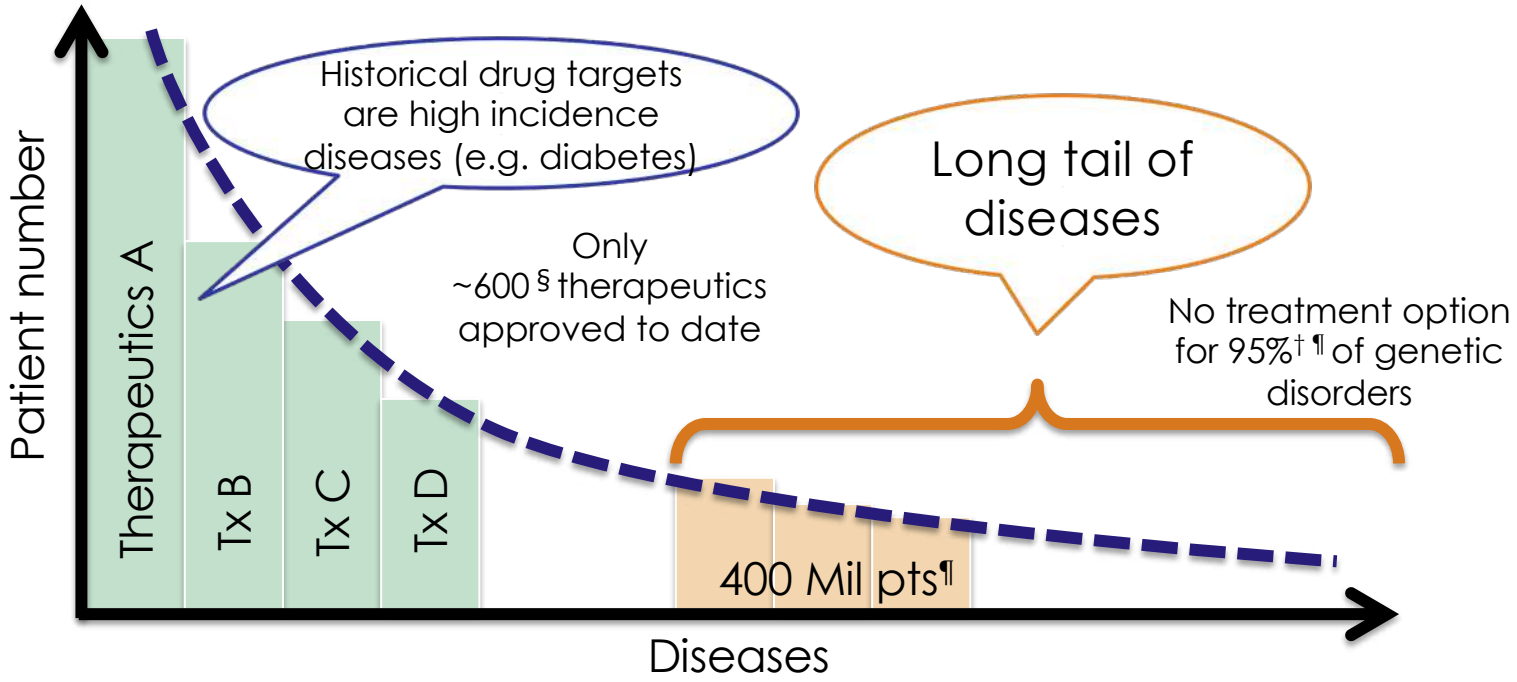
Corporate Philosophy

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.

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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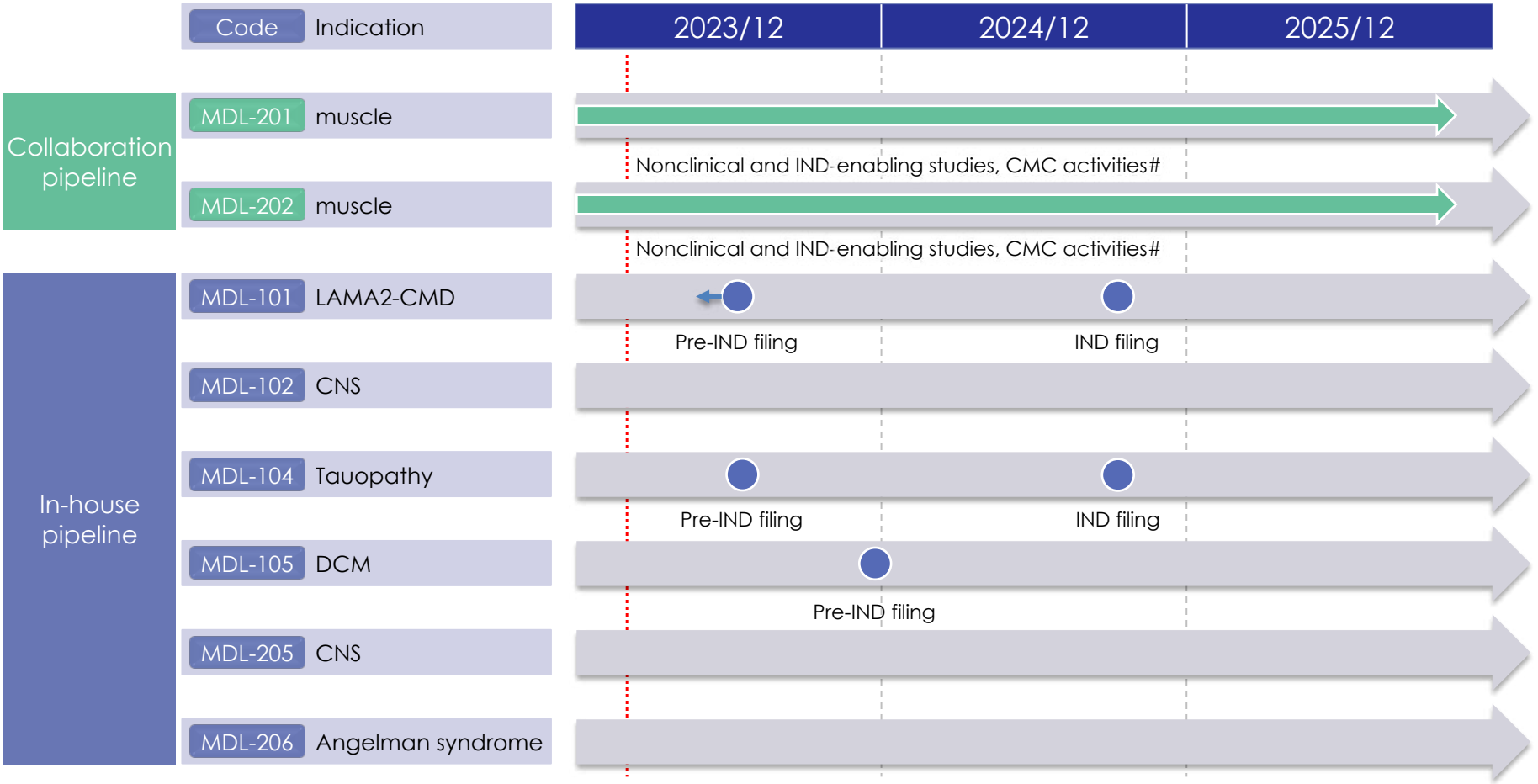
1. Key Topics

Pipeline Status

MDL-101 on track to file PreIND in 1H 2023
Portfolio under review for the acquisition of assets related to MDL-205



*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

Summary of MDL-101 for LAMA2-CMD

- Reported by 3Q/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
  - Process development initiated for the GMP campaign in collaboration with a CDMO.
  - INTERACT meeting with FDA (Jul)
  - Capsid change (Sep)
- Progress thereafter
  - Evaluation of new constructs with new capsids in rodents and NHPs(started in Dec)
    - On a preliminary basis, positive results including meaningful LAMA2 expression have been obtained.
  - Redesigning the manufacturing process for the new version molecule
  - KOL meetings and drafting clinical synopsis and protocol
- Next steps:
  - Filing pre-IND meeting (mid-2023→Mar-Apr)
  - Continue IND enabling GLP tox and PK/PD
  - Continue process development and pilot productions for GMP campaign

KOL: Key Opinion Leader

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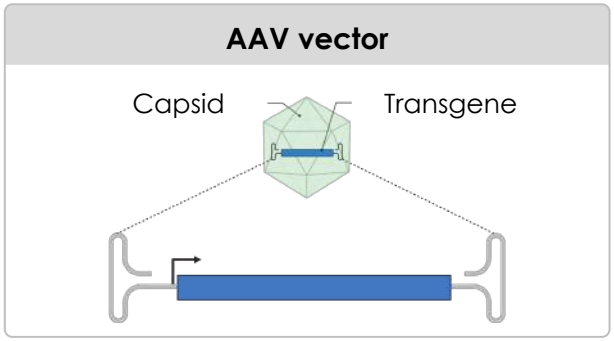
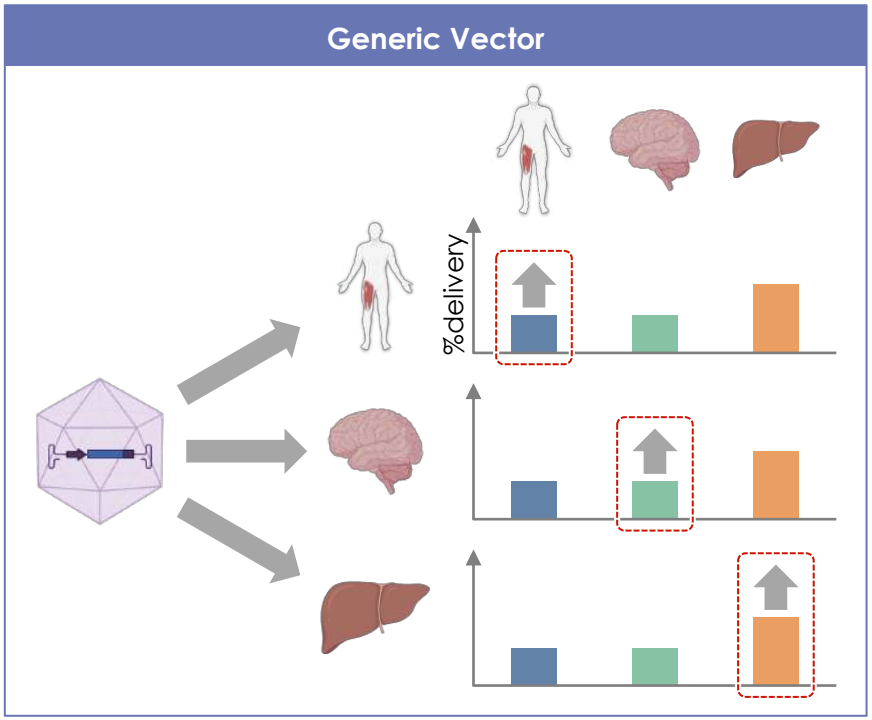
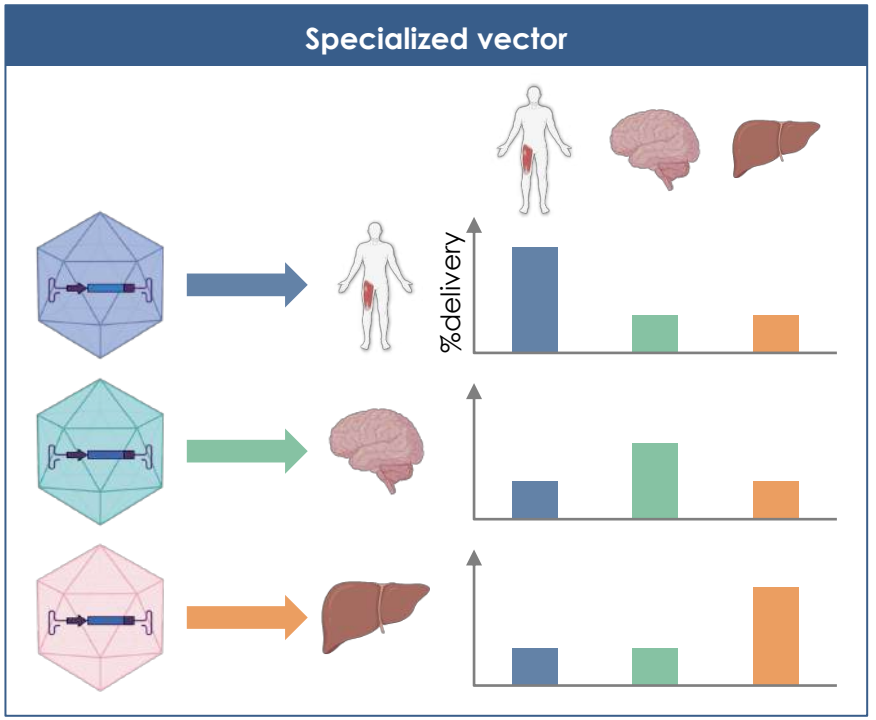
Big innovations have been brought to AAV vectors recently



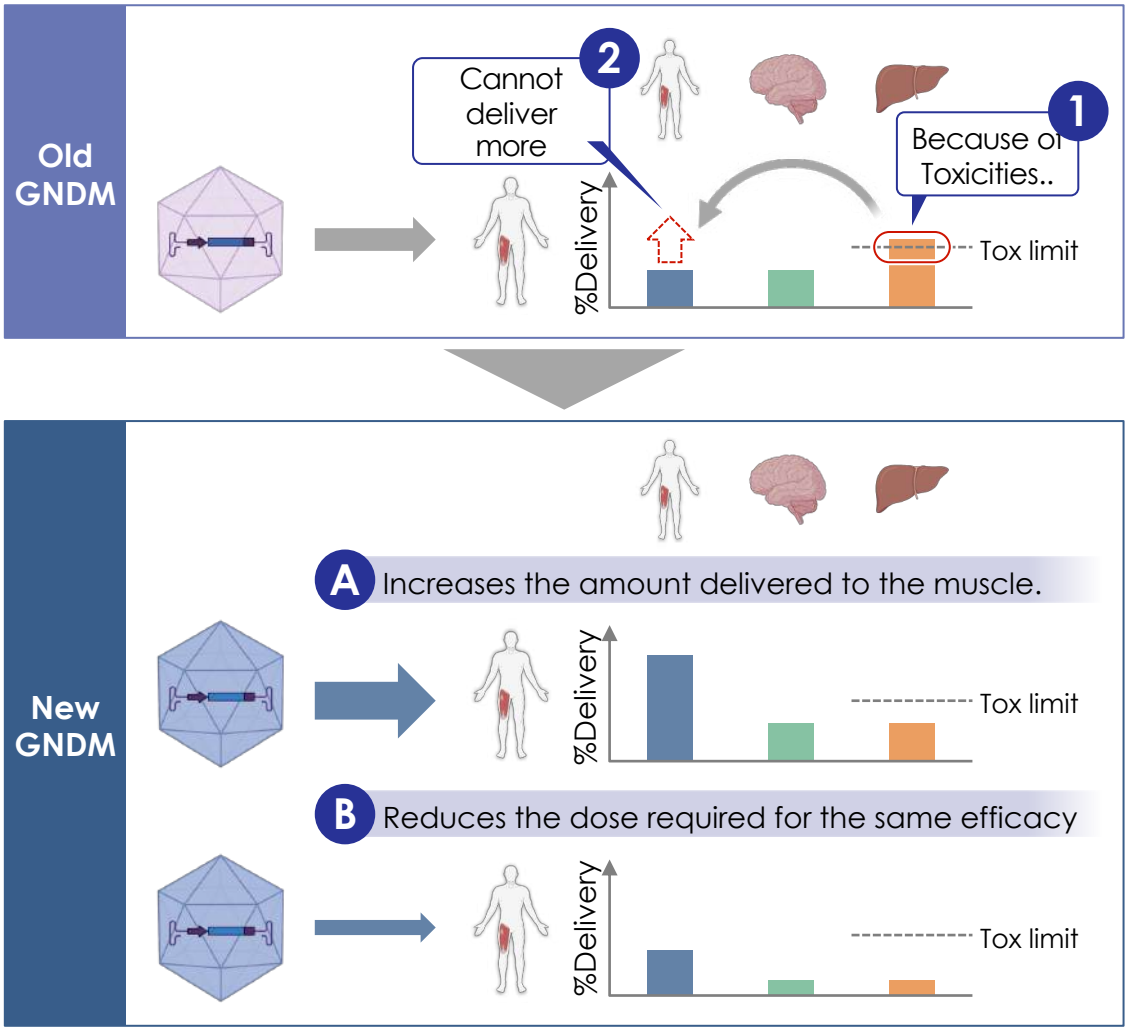
- Previously, generic vectors such as AAV2, 6, 8, and 9 were universally used for all target diseases
- Those capsids are predominantly sequestered in the liver after systemic injection, and cause hepatotoxicity which limits dose of AAVs.
- Recently developed engineered vectors have a much higher tropism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





Transition to specialized capsid is the need of the field and will be beneficial in the long run

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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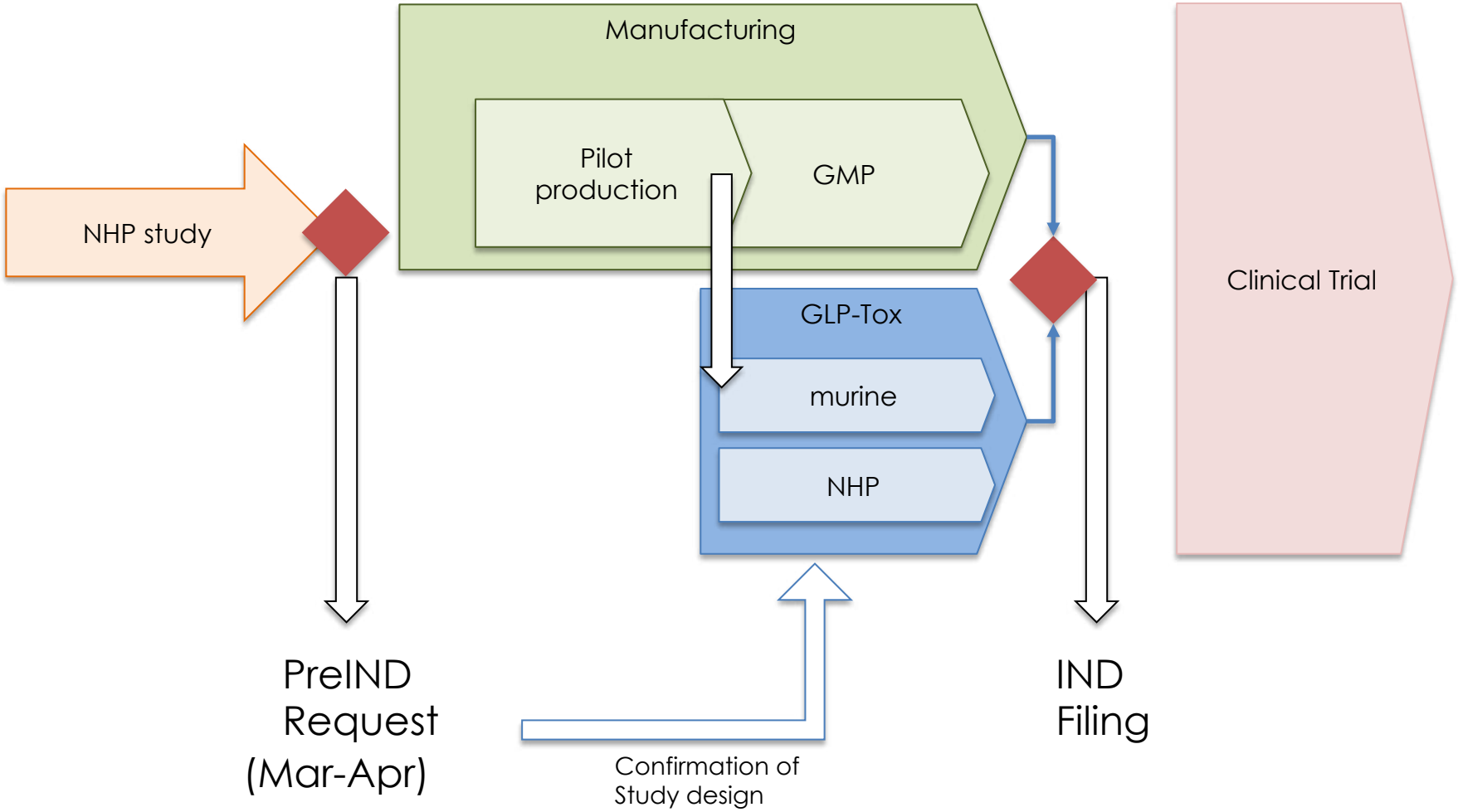
Development plan of MDL-101



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Summary of other R&D activity

- MDL-104（Tau）
  - Evaluation of the human version molecule with hTau and humanized Tau mice
    - Initiation of biodistribution study in NHP
  - Discussion on target indications with KOLs
    - Alzheimer's disorder(AD) and/or Frontotemporal dementia(FTD)
- MDL-105（TTN）
  - Got access to TTNtv mice model
  - Initiated evaluation of GNDM-TTN in the animals
- MDL-205
  - Upon the end of the research collaboration with Eisai, Modalis decided to regain the rights on MDL-205 and in negation with Eisai for the condition
  - As soon as we agree on the terms, Modalis will share the target, development status as well as plan for the development.

hTau mouse(mMAPT K/O, hMAPT Tg)
humanized MAPT mouse (aka MAPT(H2.1)-GR = mMAPT replaced with hMAPT)

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Tau is strongly suppressed in the brain regions that GNDM is transduced

humanized MAPT

ICV@P2

1.4e+11 vg/helm

8wk

RNA-FISH

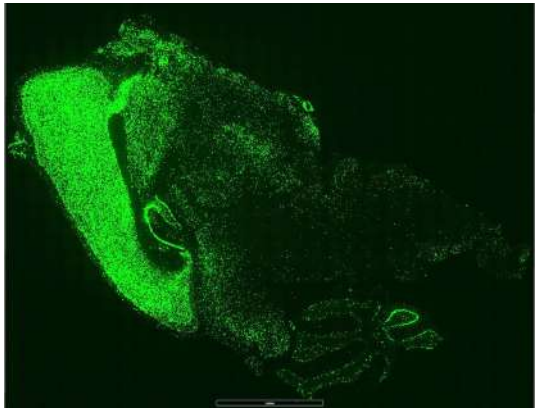
GNDM

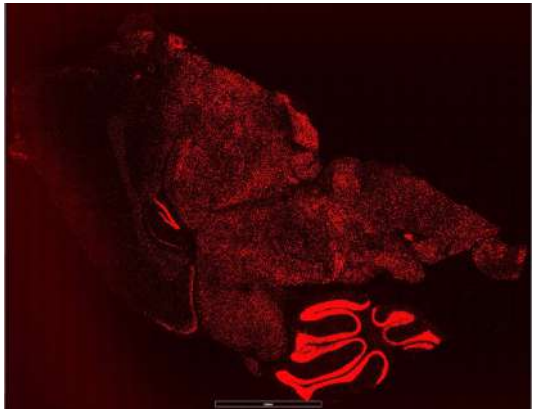
Tau

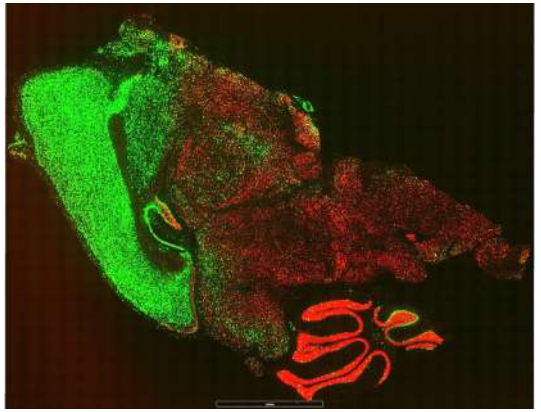
GNDM+Tau

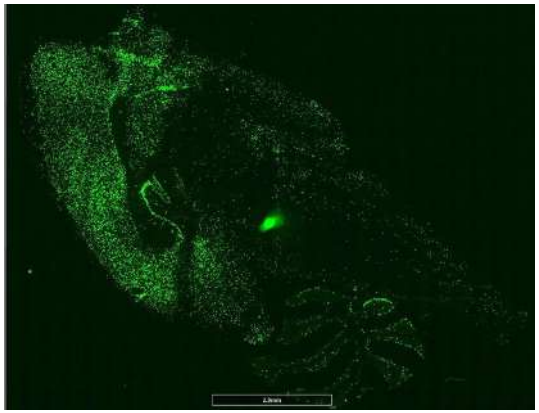
GNDM -Tau

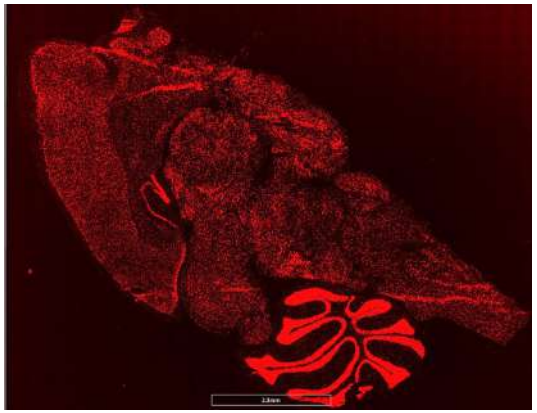
GNDM -control

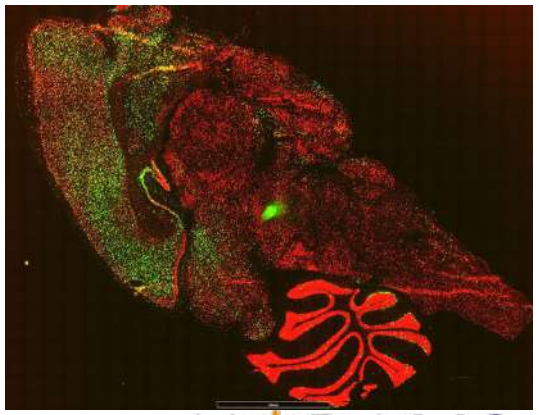












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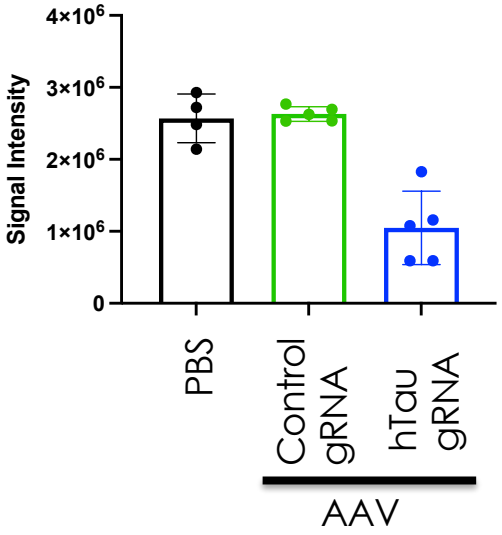
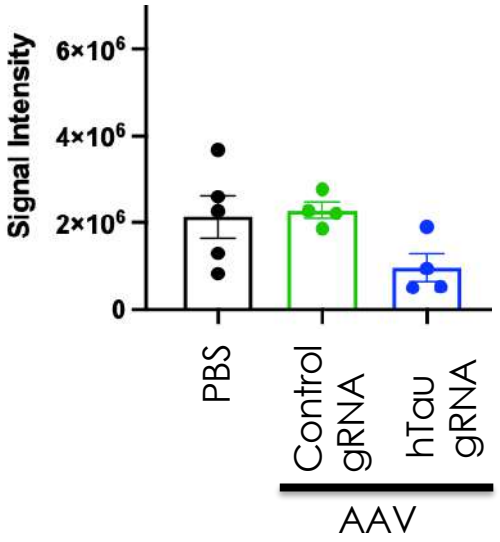
hTau protein is suppressed to ~50% in both Cortex and Hippocampus

CORTEX



Hippocampus



P2 ICV 8wk takedown
Jess Simple Western

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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 (Perkinson like symptom)	~7yrs
FTD	2-10% of dementia	frontal and temporal lobes	apathy, change in personality, lack of inhibition, obsessive behavior	~8yrs
AGD	18.8% to 80% of PSP 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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Other updates on business

- Progress on intellectual property
  - A patent which Modalis is licensed from Univ. Tokyo, JP2019-217431 (PAM Flex Cas9 patent), was granted in Japan(Dec)

- Progress on partnering
  - MDL-101, 104, and 105: Partnering discussion ongoing with pharma/biotech companies
  - Research collaboration: In discussion with pharma/biotech companies on new targets

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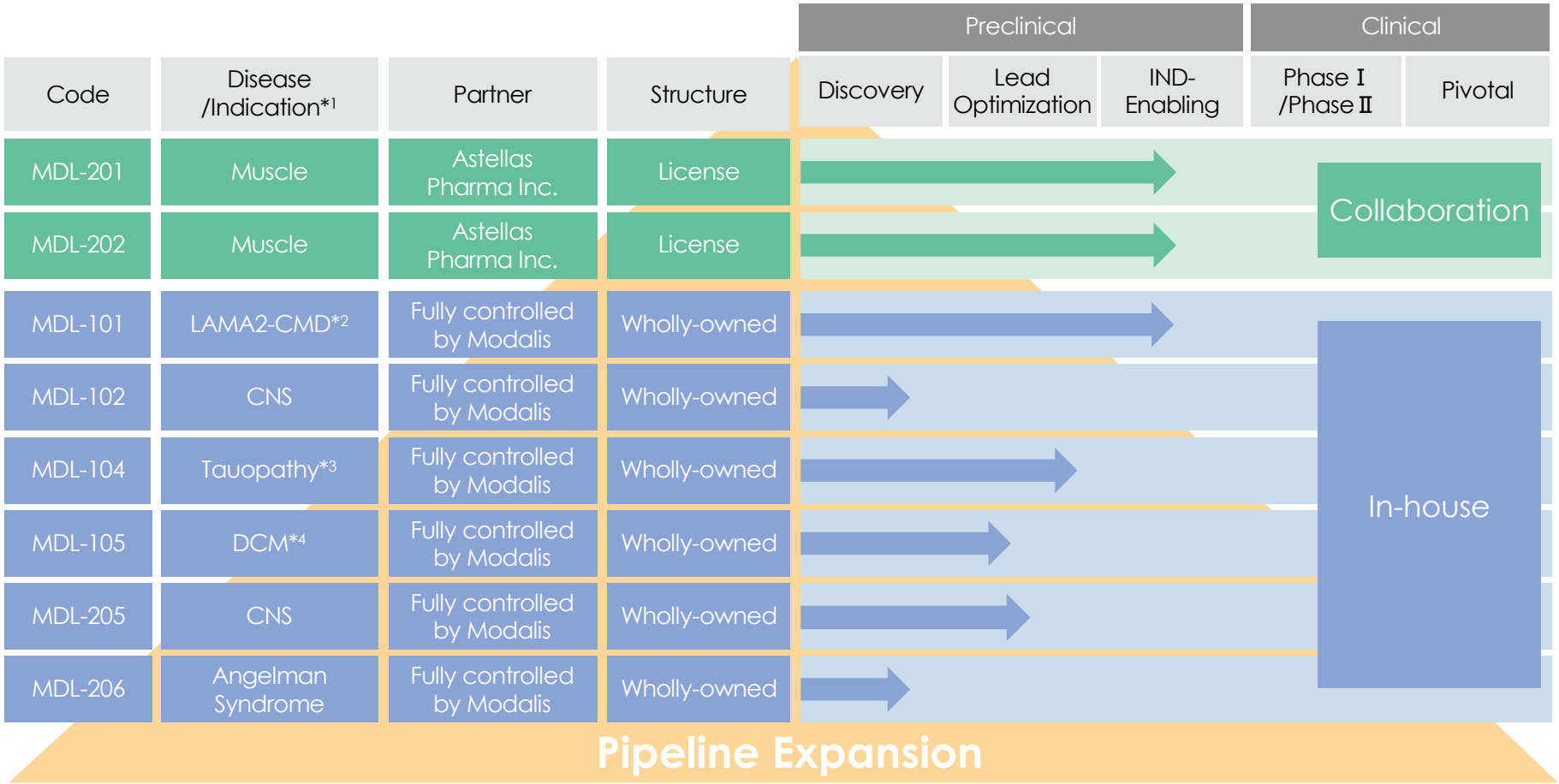
2. Financial Highlights

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)

	FY2021 4Q (Twelve Months) (A)	FY2022 4Q (Twelve Months) (B)	(B)−(A)
Operating revenue	1	40	39
Operating expenses	1,240	2,103	863
R&D	1,009	1,861	852
SGA	231	242	11
Operating income	(1,239)	(2,063)	(824)
Ordinary income	(1,231)	(1,995)	(764)
Current Profit	(738)	(2,702)	(1,964)

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, expenses for conducting clinical trials of MDL-101 and yen depreciation against US dollar)

Extraordinary profit/loss

- Impairment loss on fixed assets as extraordinary loss (996 million yen), gain on reversal of advances received as extraordinary profit (285 million yen)

SGA: Selling and Generally Administrative Expenses

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BS & Financial Position

(Million Yen)

	FY2021 (A)	FY2022 (B)	(B) – (A)
Current assets	5,067	3,061	(2,006)
Cash & deposits	4,936	2,933	(2,006)
Non-current assets	1,002	68	(934)
Property, plant and equipment	223	-	(223)
Right to use patent	704	-	(704)
Total assets	6,069	3,129	(2,940)
Current liabilities	181	141	(40)
Non-current liabilities	339	47	(292)
Total liabilities	520	188	(332)
Total net assets	5,549	2,941	(2,608)
Total liabilities and net assets	6,069	3,129	(2,940)
Capital adequacy ratio	91.4%	93.4%	

- 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, Reversal of advances received from partners for patent license due to impairment loss (refer to p.22)

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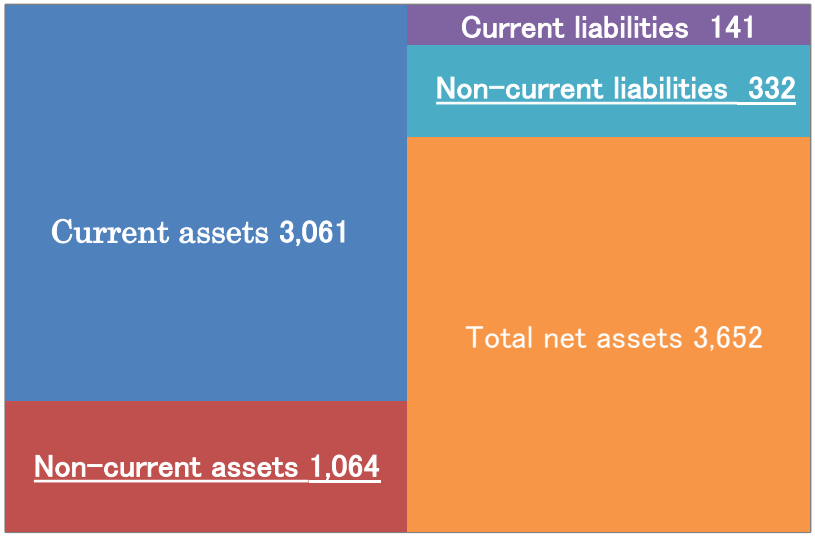
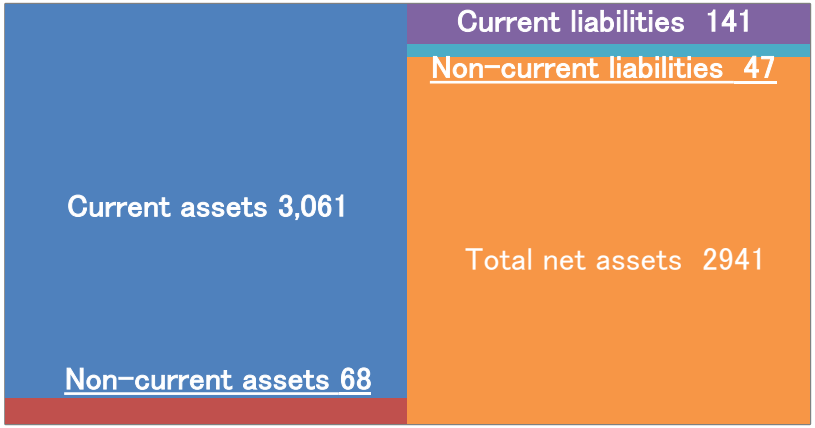
Impairment loss and gain on reversal of advances received

For the Fiscal Year Ended December 31, 2022, the Company recorded impairment loss on fixed assets of 996 million yen as an extraordinary loss. In conjunction with this, the Company recorded gain on reversal of advances received of 285 million yen as an extraordinary gain, as the Company had recorded the portion of the licensee's portion of patent licensing rights as a liability.
Since impairment is an accounting matter, there is no actual cash out, and business value and these assets themselves do not disappear even it is applied.

B/S before reflection



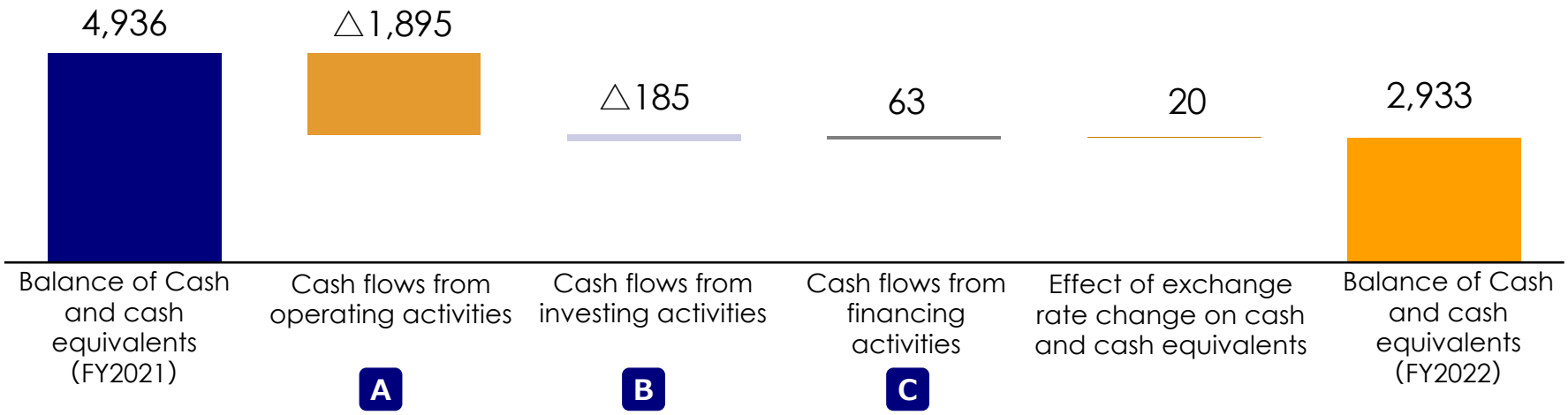
B/S after reflection (million yen)



285 (Extraordinary income)
-996 (Extraordinary loss) =△711 (NET)

Cash Flow Status

(Million Yen)



A Cash flows from operating activities	• Loss before income taxes （△2,710） • Impairment loss （996）
B Cash flows from investing activities	• Purchase of property, plant and equipment （△197）
C Cash flows from financing activities	・Proceeds from issuance of stock resulting from exercise of subscription right to shares （60）

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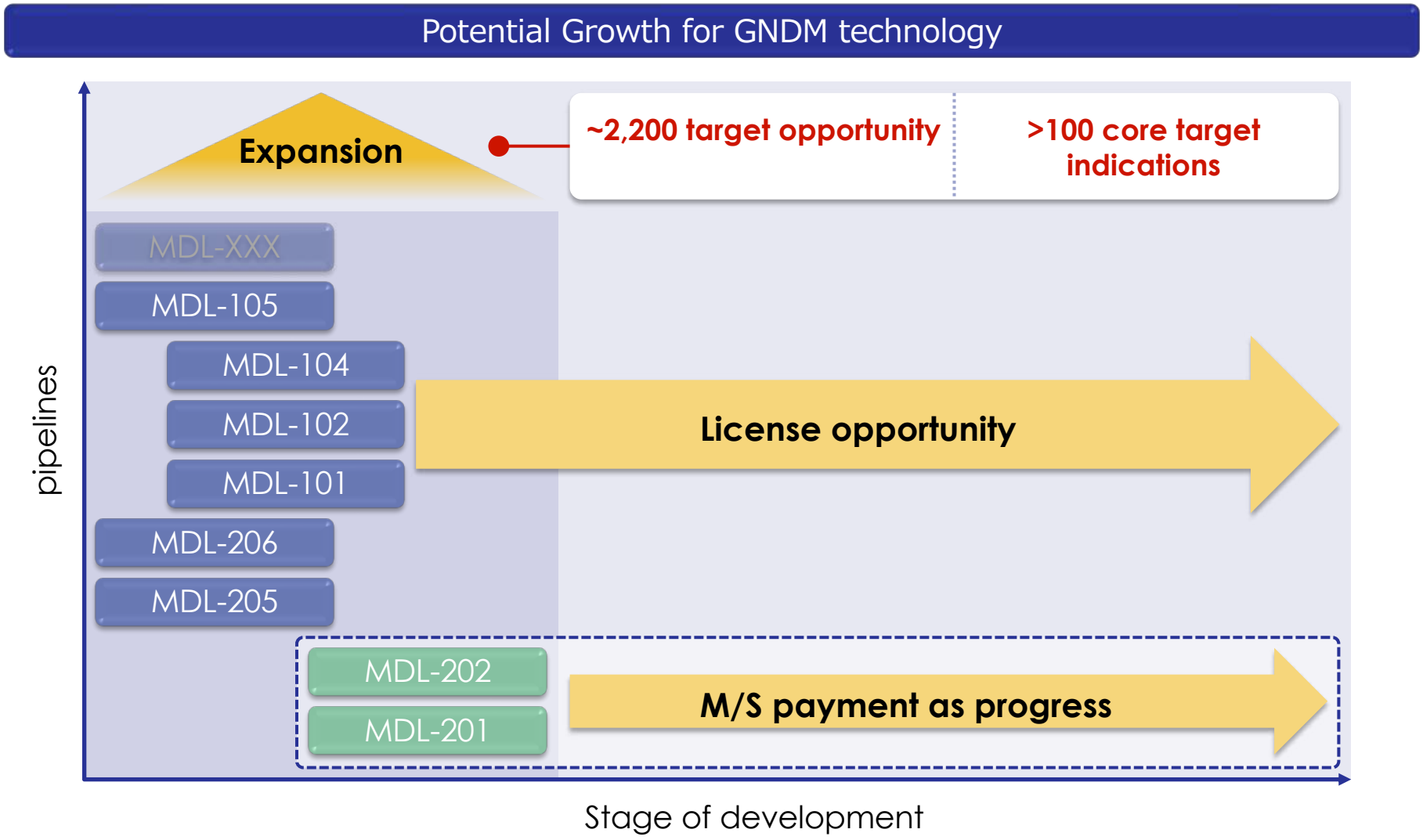
3. Growth Strategy

Growth Strategy

opportunity expands two dimensionally



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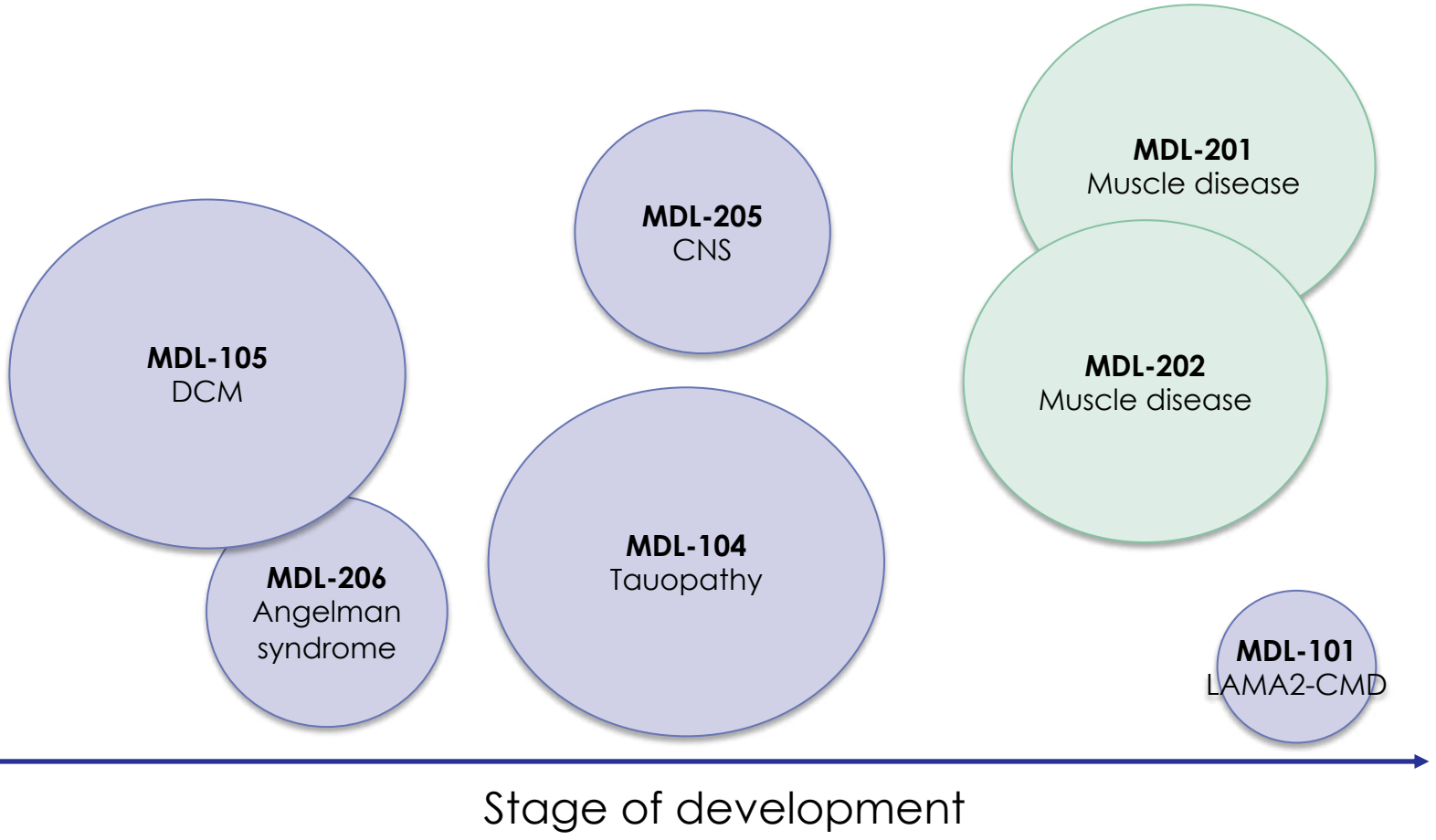
Modalis' pipelines and market size

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

The future Modalis envisioned

Short Term (2023)	Mid Term (3yrs)	Long Term (>3yrs)
•MDL-101 PreIND(1Q) •MDL-104	•Initiation of clinical trial •Clinical PoC（2024～25）	•Market approval and launch of GNDM-based product(S) •Plug-and-play GNDM technology

Partnering

Commoditization of genetic analysis

Public acceptance of gene therapy

Evolution of GTx technologies

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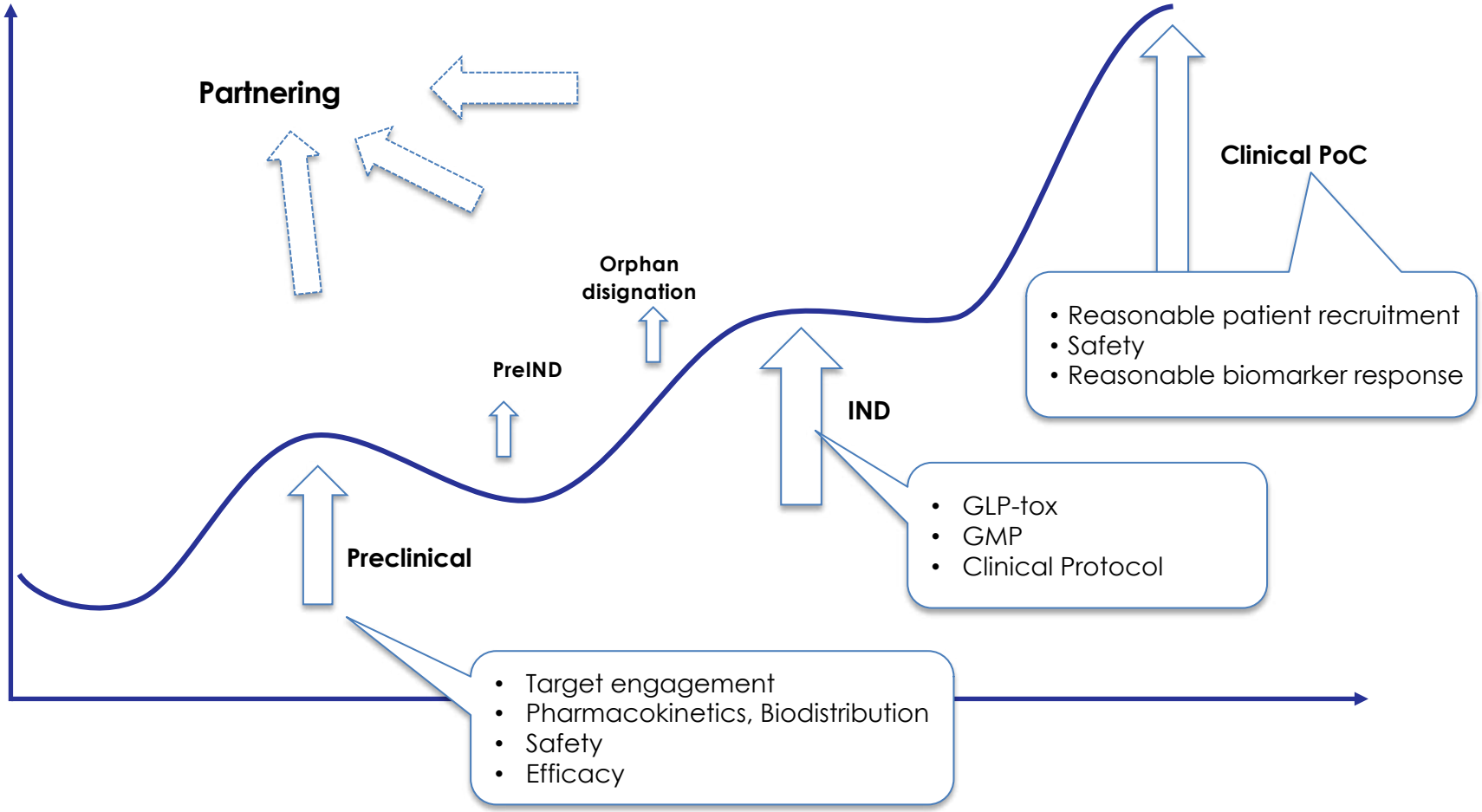
Future pre-clinical and clinical trials are expected to increase the value of the company.

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

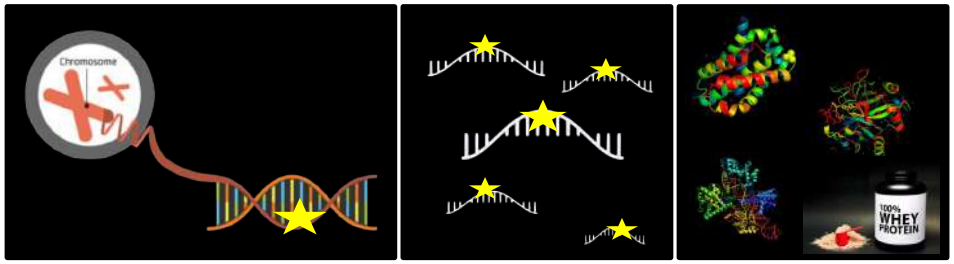
- **GNDM** (CRISPR)
- ZFP-TF (ZFN)

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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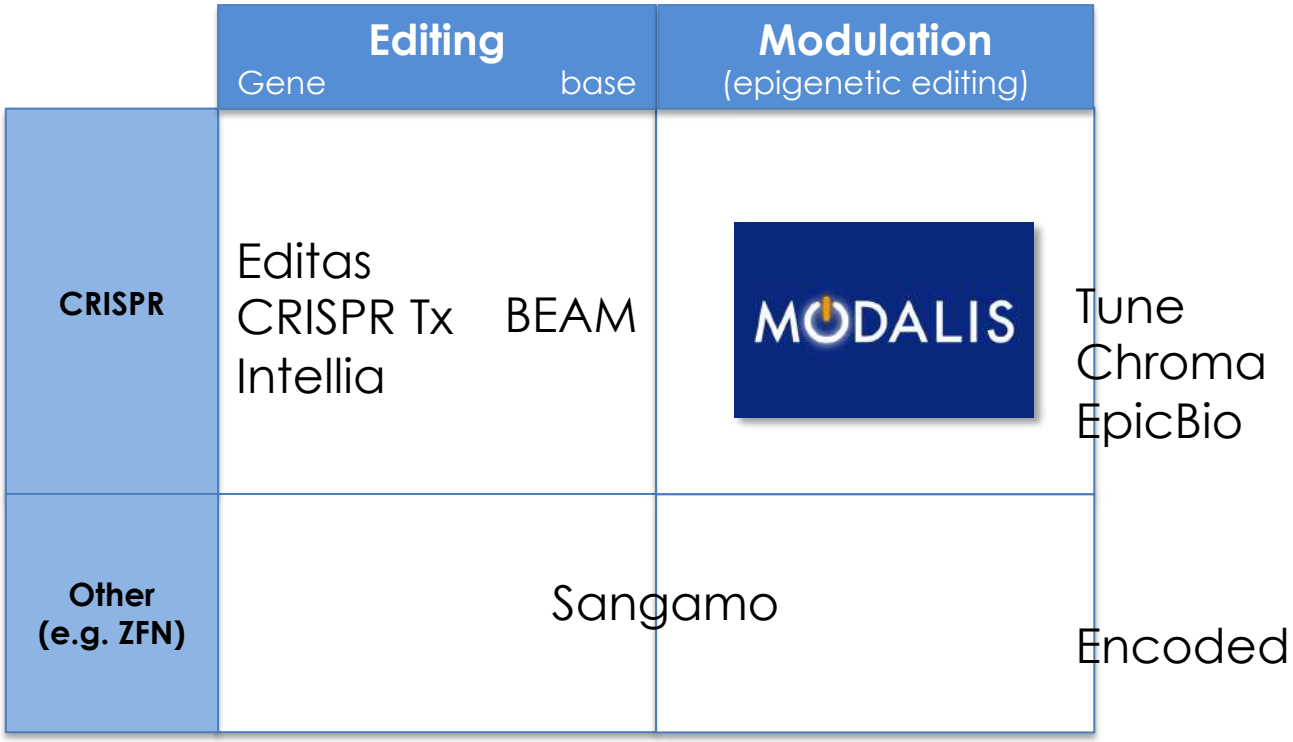
Modalis is uniquely positioned within the CRISPR field



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4. Q & A

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Q1 Can you share why the joint research of MDL-205 was terminated and why it is being reacquired as an in-house pipeline?

A) At the end of the originally agreed-upon collaboration, we were unable to reach an agreement with our partner, Eisai, regarding an extension or transition to another arrangement.

Although the details of the agreement nor the target cannot be disclosed until the reacquisition agreement is completed, We believe that there is a high unmet medical need and a large number of patient population in this disease area and that the results of the joint research can be sufficiently differentiated from other approaches. We are grateful for this collaboration opportunity to our partner, which has deep knowledge and research resources in this field, and for the excellent results achieved.

Q2 Does the recorded impairment loss matter to the future business ?

A) It doesn't.

This was recorded in accordance with the "*Accounting Standard for Impairment of Fixed Assets*" because the Company is in the research and development phase of its pharmaceuticals business, and therefore, the profit and loss arising from operating activities are continuously negative, and future projections are highly uncertain in terms of profitability considering the characteristics of the business.

However, since this is a numerical figure in accordance with the accounting standards, the business value and the fixed assets themselves do not disappear, and the fixed assets can still be used to conduct business as before. There will be no actual cash outflow, so there will be no significant change in the business situation. In addition, as a result, the depreciation expense corresponding to the impaired fixed assets will be reduced from the next fiscal year onward.

Q3 Why we marked "*gain on reversal of advances received*"?

A) We licensed the CRISPR/Cas9 basic patent from Editas Medicine Inc in 2020. In 2021, when we sublicensed the right to a partner, the partner paid a certain amount as a contribution to the license. The amount we received was booked as a liability for *Advances Received* on our B/S.

Along with the impairment loss marked this 4th quarter, the *Advances Received* in question and the corresponding asset, which is the right for the license, were offset both from the B/L.

As the result, the *Advances Received* was recorded as extraordinary gains.