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In case of any discrepancy, the Japanese version shall prevail

1Q/2024
Business and Financial report



MODALIS

(TSE：4883)

Modalis therapeutics Corporation

May 8, 2024

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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 in multiple species (mouse, cyno) resulting in functional efficacy without toxicities
- Pipeline of preclinical assets in muscular dystrophies, additional programs in CNS, cardiovascular and unlimited therapeutic potential in other areas
- Manufacturing established for challenging AAV capsids to enable tissue tropic delivery for lead programs
- Experienced team with deep knowledge of platform
- Strong IP portfolio and strategy that includes granted patents
- Regulatory and clinical path in place based on recent FDA guidance

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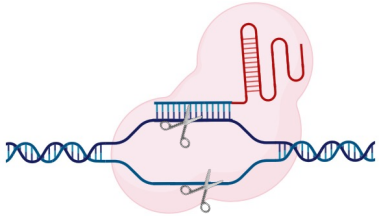
Non-cleaving CRISPR = CRISPR-GNDM®

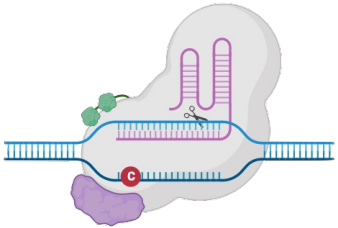
Enables treatment of genetic disorders by controlling epigenetic ON/OFF switch

GTx Technologies

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



Permanent Removal



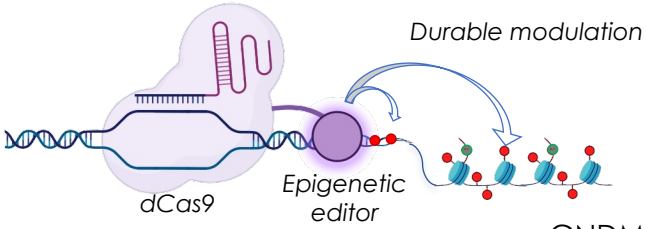
Permanent Replacement



Temporal silencing

Epigenome Editing(CRISPR-GNDM®)

Bind without cleaving
No DNA damage



GNDM=Guide Nucleotide Directed Modulation

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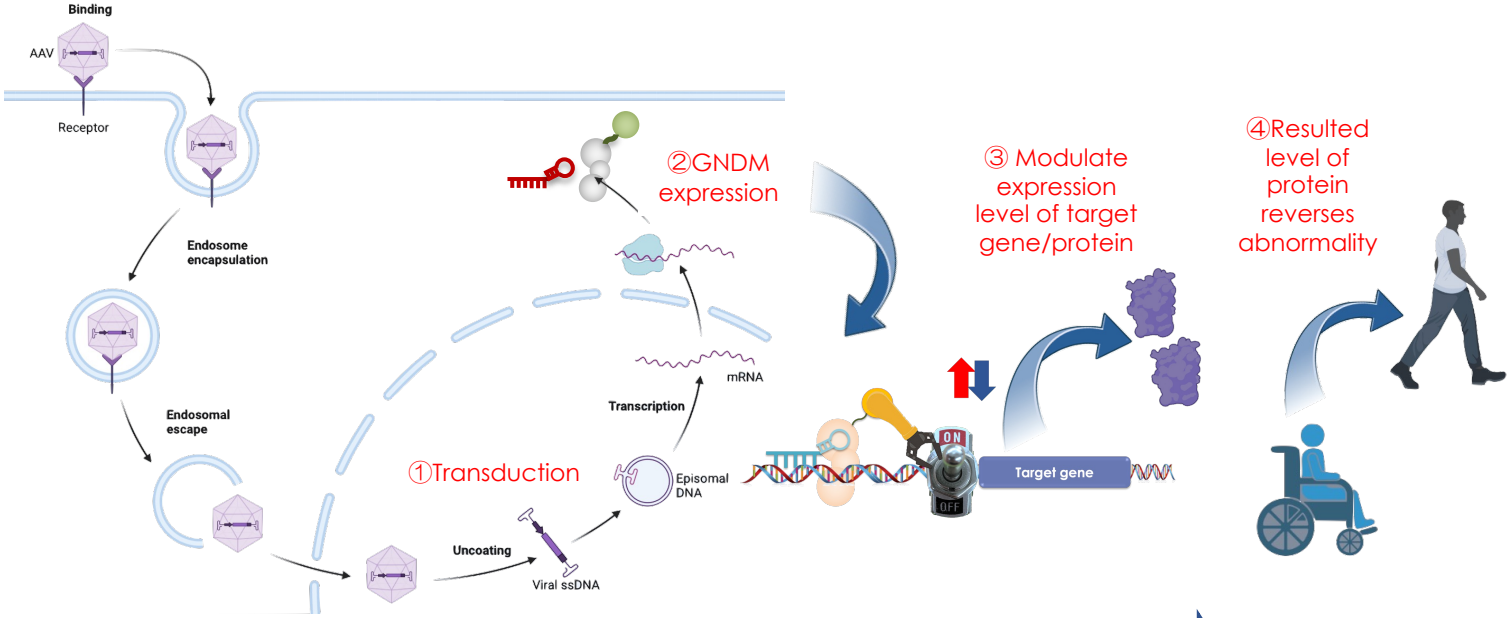
There are 3 steps for GNDM before providing efficacy

The GNDM is transduced, expressed and engages to the target to show efficacy



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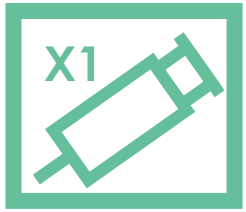
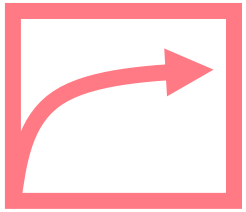
CRISPR-GNDM® is a promising new therapeutic modality

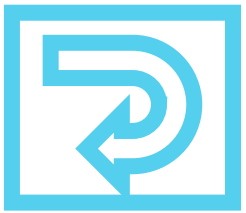
Potential benefits of CRISPR-GNDM® Technology



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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Epigenome editing competitive landscape

Modalis is in the lead

Company	Year Founded	Funding	Platform	Pipeline/Target indication	Stage of Development
Modalis Therapeutics	2016	Public	CRISPR-GNDM x AAV	• MDL-101/LAMA2-CMD • MDL-202/Myotonic Dystrophy Type 1(DM1)	IND enabling PreIND completed
Tune Therapeutics	2020	Series A ($40M, Dec 2021)	DNMT-KRAB fusion dCas9 x LNP	PCSK9 for hypercholesterolemia? HBV	NHP study reported at ASGCT2023
Chroma Medicine	2021	Series B ($135M, Mar 2023)	DNMT-KRAB fusion dCas9 x LNP	PCSK9 for cardiovascular disease	Mice study reported at ASGCT2023
Epic Bio	2022	Series A ($55M Jul 2022)	Cas12f-fused with demethylation enzyme x AAVrh74	EPI-321/FSHD	Mice study reported at ASGCT2023
Moonwalk Bioscience	2023	Series A ($57M 2023)	Not known	Not known	Not known

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Adding 2nd FDA approval in 2024, Gene Therapy Enters Harvest Period

Based on recent successes, gene therapy is expanding its target from local to systemic administration

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	Spark/Roche	2 per 100,000	$65M[#3]
Zolgensma	2018	$2.1M	SMA	Novartis (Avexis)	1 in 10,000 live births (Approx. 10,000 to 25,000 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]
ELEVIDYS		$3.2M	DMD	Sarepta	1 in 3,500 male birth	$4.1B[#4]
Roctavian		$2.9M	Hemophilia A	BioMarin	1 in 5,000 male	$262M[#4]
Casgevy		$2.2M	SCD	CRISPR Tx/Vertex	100,000 in America	>$2B[#5]
LYFGENIA		$3.1M		Bluebird		
Lenmeldy	2024	$4.25M	Metachromatic Leukodystrophy	Orchard/KyowaKirin	1 in 100,000 live birth	?
beqvez		$3.5M	Hemophilia B	pfizer	1 in 30,000 male	$88M[#3]

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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- Topics of the 1Q/2024
- Financial update
- Growth strategy

Key Takeaway of the 1Q outcome

01

Business consolidation and prioritization

02

MDL-101 moving forward to IND

03

Research collaboration initiated with JCR



strategic pipeline prioritization and corporate restructuring

- Focus primarily on MDL-101
  - These actions are on top of the previously announced portfolio prioritization which resulted in the decision to seek a partner for the other programs.
- Modalis has reduced its US workforce by approximately 40%, or 15 FTE
  - Downsized with manufacturing teams that have completed their missions
- Joint research will be maintained as is.

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MDL-101 is moving toward to IND

- The manufacturing process has been established
- Planning of GLP-tox completed
  - Determining clinical dose based on preclinical outcomes
- Organization and coordination of clinical trial operations



Established manufacturing process

- Adopted to the engineered AAV capsid
- Feasible productivity, yield, and quality have been achieved
- Major analytics are also developed
- A production plan has been developed for clinical trials



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LAMA1 was upregulated to the potentially effective level

LAMA1 elevated in monkeys to the level of functional improvement at the mouse pathological condition observed



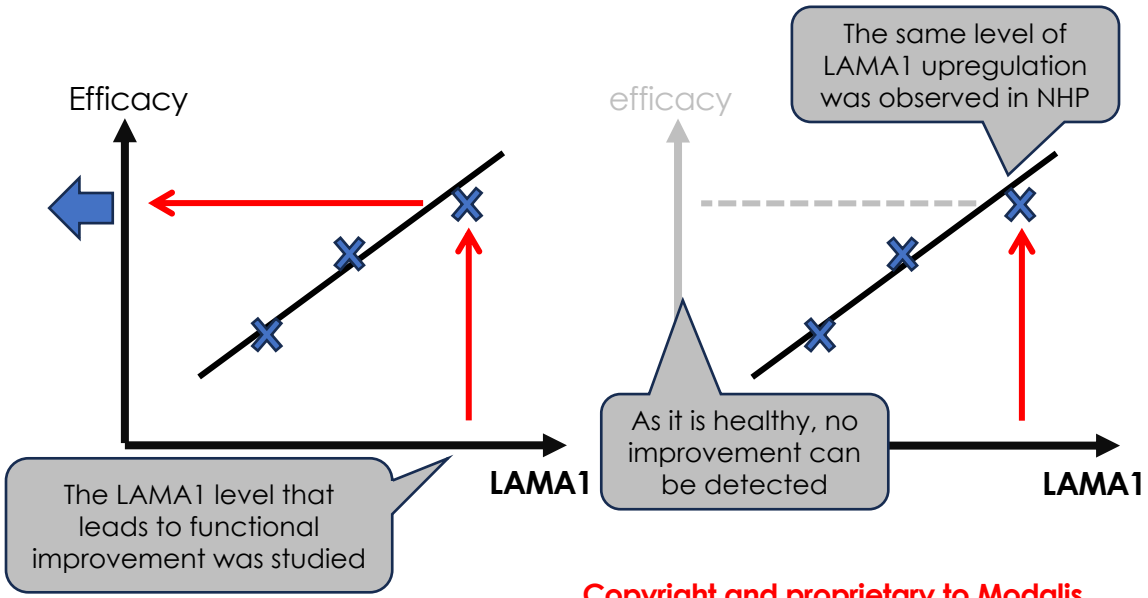
Disease model mice



Wildtype NHP



patient



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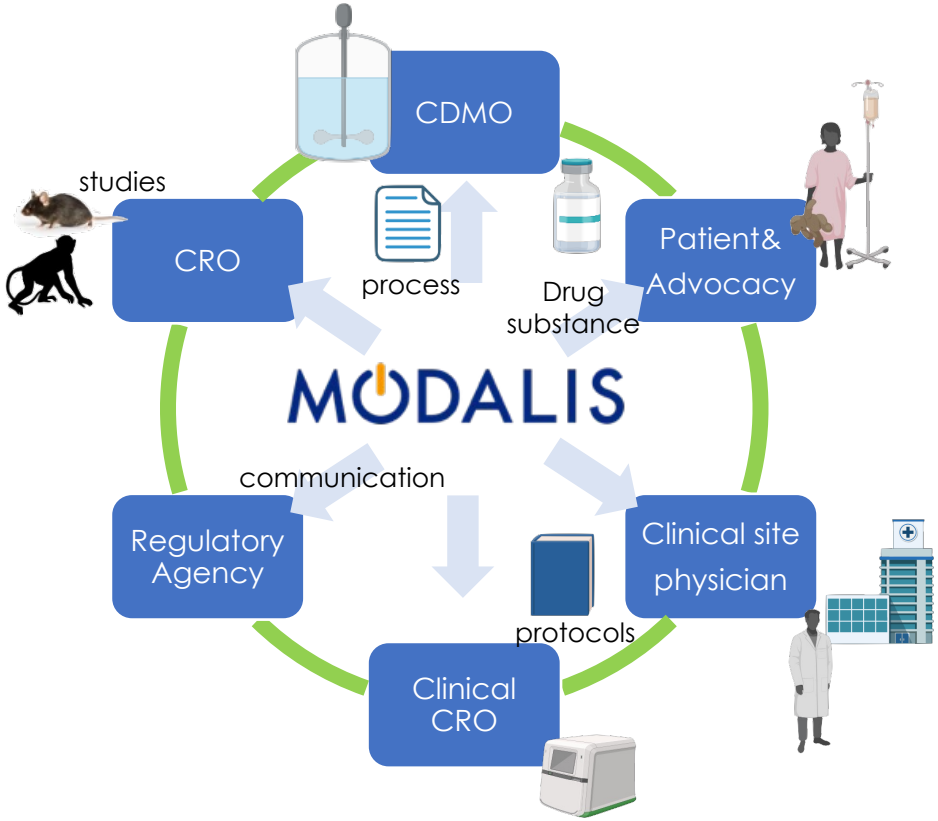
Modalis has set up the network for the clinical trial and is working with them





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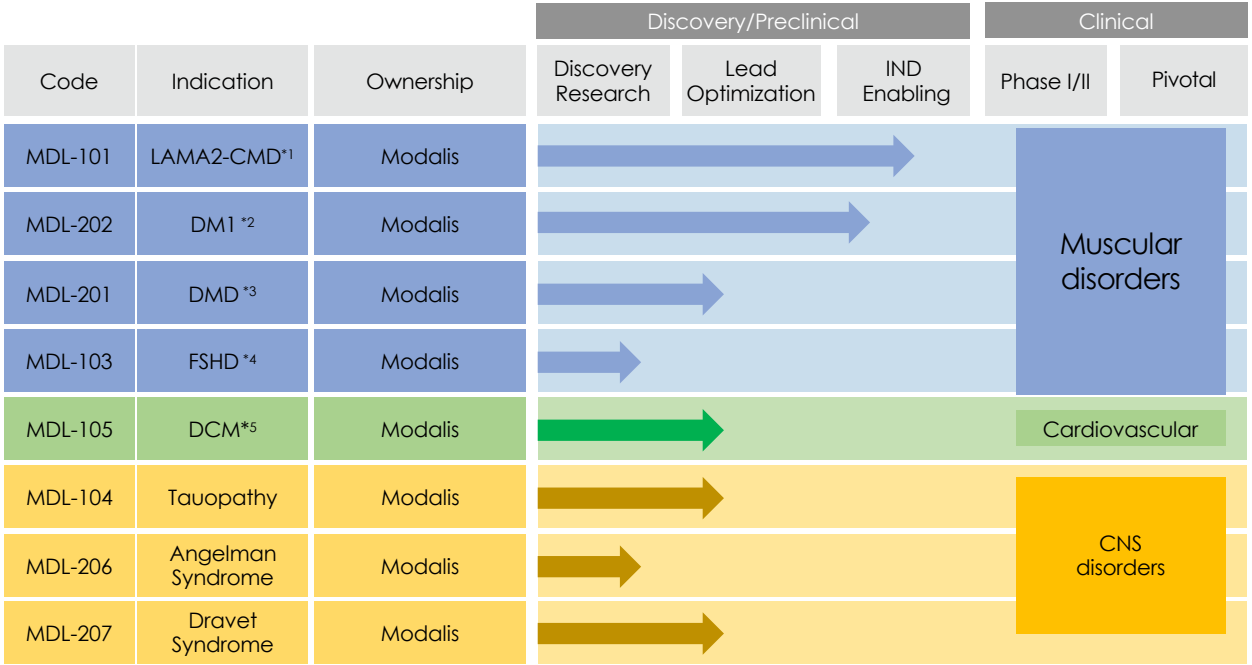
Updated

Set the muscular disease-centered strategy



*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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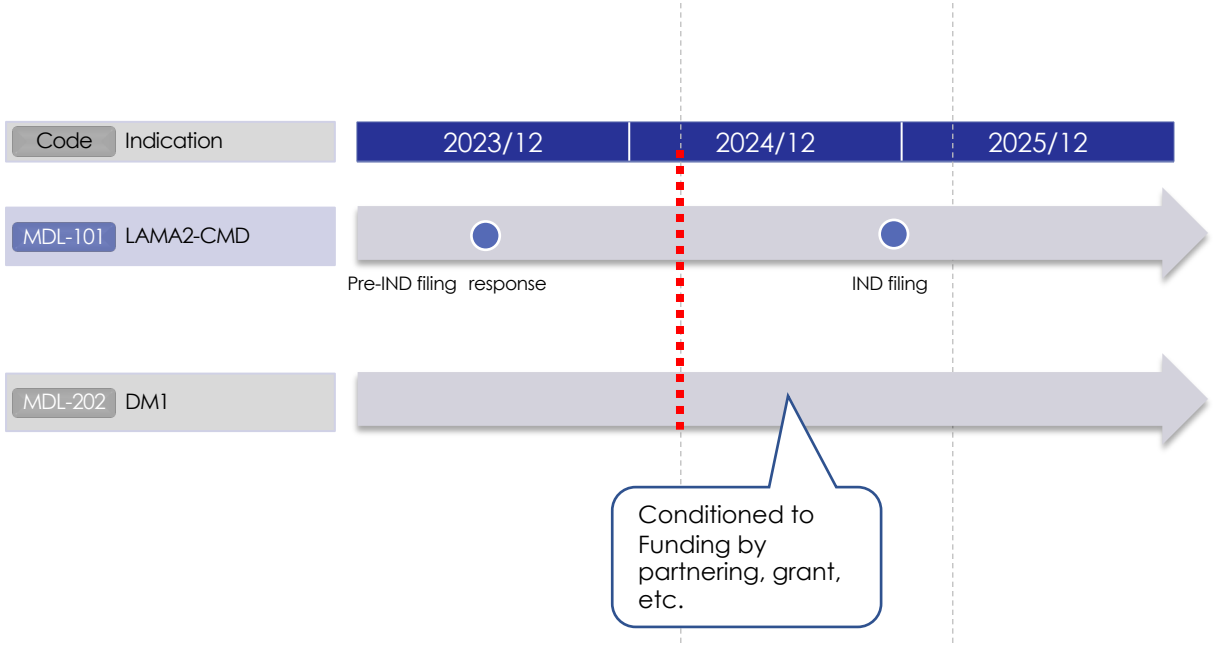
Status of the focused pipeline

MODALIS reorganized pipelines and put a higher priority on muscle disorder programs



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

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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 • Completion of process development	• GLP-Tox • GMP manufacturing • IND • Data presentation (June and July)
MDL-202 DM1	• Animal PoC in disease model mice • Regain rights of development • Transplantation to muscle tropic capsid	• Target engagement in NHP with new version molecule • Partnering

Other	• Animal PoC established
	  • MDL-201 (DMD)
	  • MDL-104 (Tauopathy)
	  • MDL-205 (Angelman Syndrome)
	  • MDL-207 (Dravet Syndrome)
	• MDL-103 (FSHD)
	• MDL-105 (DCM)
	• Research collaboration with JCR
		• Transition to the muscle tropic capsid
		• Exploration of new capsid and route of administration for CNS programs
		• Partnering to fund the program
		• Animal PoC (FSHD, DCM)
		• Continuing research

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Presentation

- 4th Annual Next Generation Gene Therapy Vectors Summit
  - June 12-14th, 2024 @Boston MA

    Title: "*Epigenetic Editing with CRISPR-GNDM®: MDL-101 is a Novel Muscle-Tropic AAV Vectors for the Treatment of LAMA2-CMD* "
  - June 14th 11:15AM EST
  - Session: Beyond AAV: HIGHLIGHTING BOUNDARY-PUSHING VECTOR PLATFORMS

- Cell and Gene Therapy Summit 2024
  - July 8-10th, 2024 @Boston MA

    Title: "*Epigenetic Editing with CRISPR-GNDM®: Novel Muscle-tropic AAV Vectors Deliver Promising Single-dose Treatment for LAMA2-CMD* "
  - July 8, 2024, 10-12AM EST
  - Session: Gene Editing Breakthroughs & Therapeutics Approaches

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2. Financial reports



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PL & Business Result

(Million Yen)

	1Q FY2023 (A)	1Q FY2024 (B)	(B)−(A)
Operating revenue	-	-	-
Operating expenses	514	490	△24
R&D	443	422	△21
SGA	71	67	△3
Operating income	△514	△490	24
Ordinary income	△509	△457	52
Current Profit	△532	△457	74

Operating expenses

- Advancement of clinical trial efforts for MDL-101 (process development costs for investigational drug manufacturing, etc., AAV change costs, etc.)
- Decrease in R&D expenses due to Decrease in in-house model pipeline including MDL-202 (mainly personnel expenses and research material expenses such as reagents)

Extraordinary loss

- Net loss increased due to lower impairment loss on fixed assets

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BS & Financial Position

(Million Yen)

	End of FY2023 (A)	End of 1Q FY2024 (B)	(B) – (A)
Current assets	1,956	1,485	△470
Cash & deposits	1,883	1,413	△470
Non-current assets	69	73	3
Total assets	2,025	1,559	△466
Current liabilities	198	151	△46
Non-current liabilities	447	395	△51
Total liabilities	645	547	△98
Total net assets	1,380	1,011	△368
Total liabilities and net assets	2,025	1,559	△466
Capital adequacy ratio	66.8%	62.9%	

Note

- Decrease in long-term liabilities due to conversion of convertible with stock acquisition rights (50 million yen)

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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

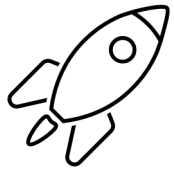
MDL-202

Further approach to challenging applications

Other programs

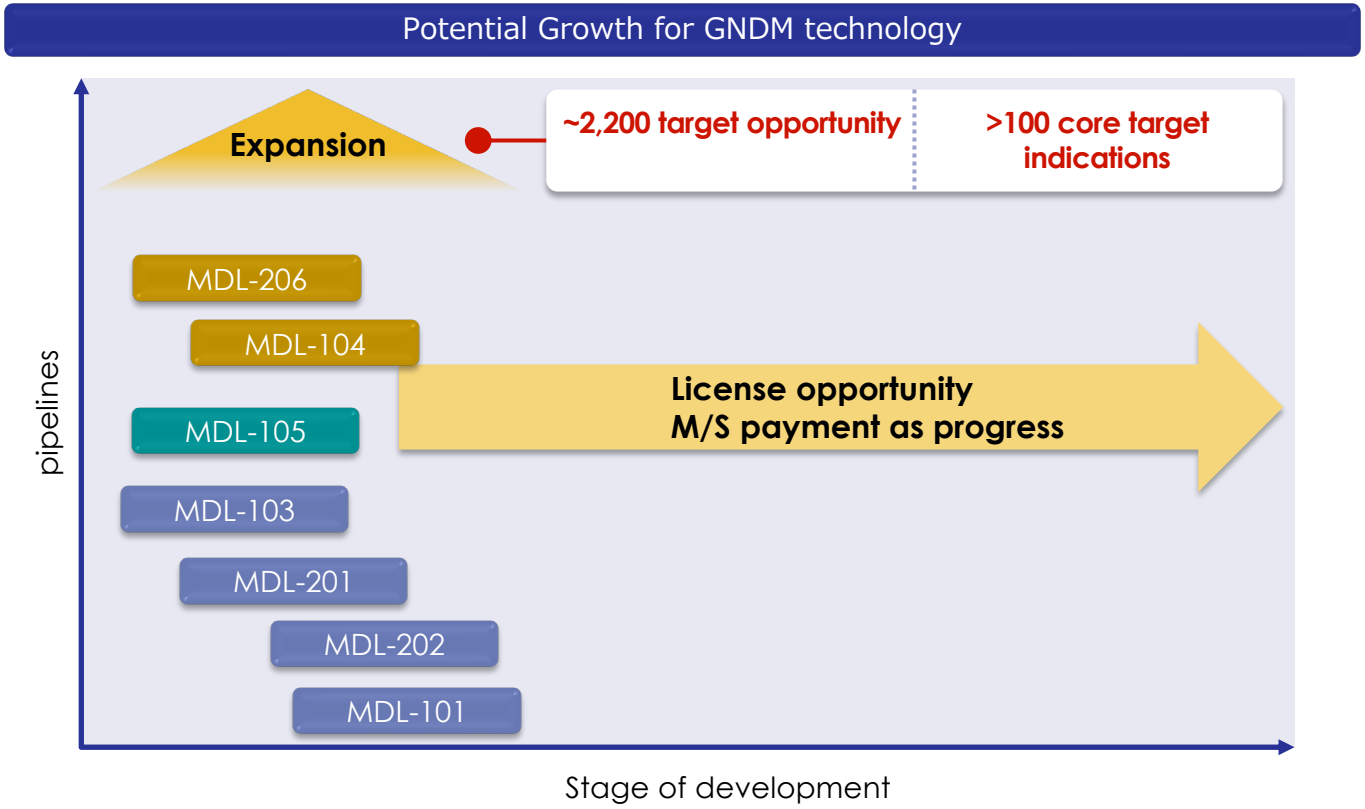






Growth Strategy

opportunity expands two dimensionally



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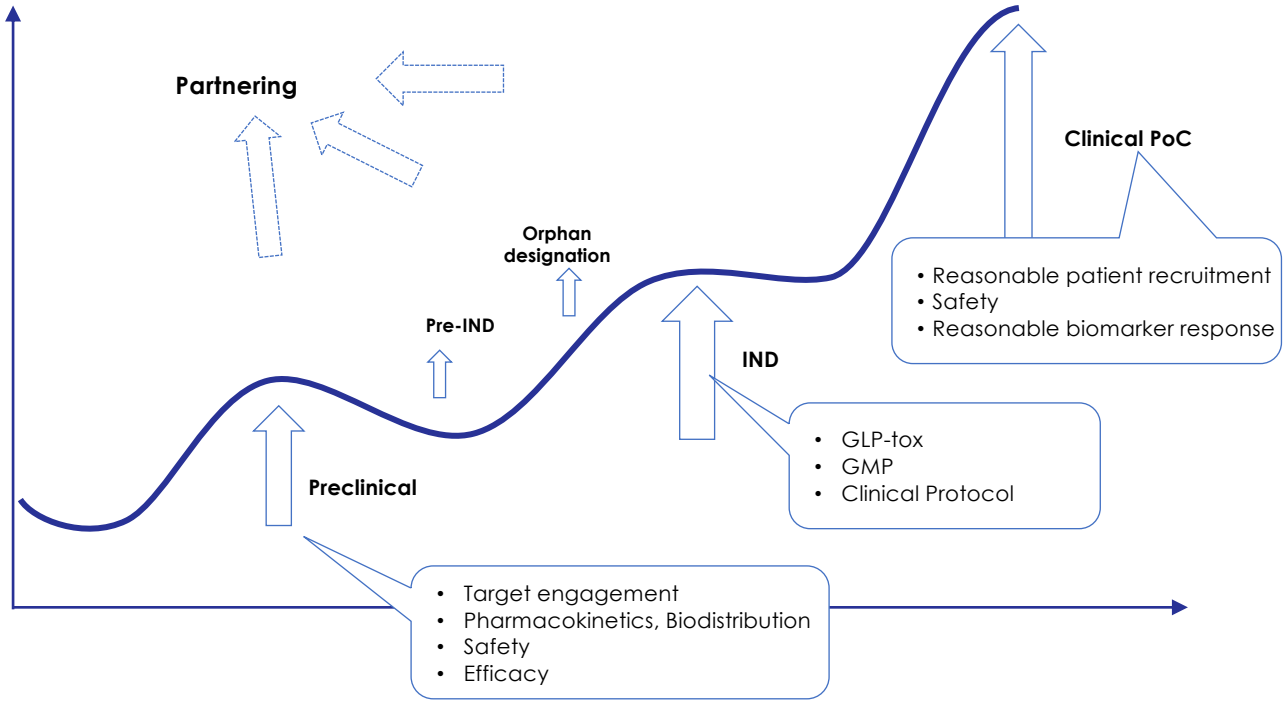
Future pre-clinical and clinical trials are expected to increase the value of the company.

Expected milestone events and impact on corporate value



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