Kyowa Kirin - Orchard Therapeutics IR Meeting

April 8th, 2024

協和キリン株式会社

Today's Agenda

- **The Background of Acquiring Orchard Therapeutics**
  – President and Chief Executive Officer　Masashi Miyamoto, Ph.D.
- **About Orchard Therapeutics and HSC-GT***
  – The CEO of Orchard Therapeutics plc, Bobby Gaspar, M.D., Ph.D.
- **Future Plans Regarding HSC-GT**
  – President and Chief Executive Officer　Masashi Miyamoto, Ph.D.

*Hematopoietic stem cell gene therapy

Our Vision toward 2030

Our Vision toward 2030

Kyowa Kirin will realize the successful creation and delivery of life-changing value* that ultimately makes people smile, as a Japan-based Global Specialty Pharmaceutical company built on the diverse team of experts with shared passion for innovation.

Provide pharmaceuticals for unmet medical needs

We are focused on developing medicines for diseases where there is a clear patient need for new options. We make full use of multiple therapeutic modalities, including biotechnology such as antibody technology, and beyond, building on our Kyowa Kirin established strengths.

Address patient-centric healthcare needs

We will meet the needs of patients and society by providing value across the entire patient care pathway, delivering cutting-edge science and technology, grounded in our in-depth pharmaceutical knowledge and expertise.

Retain the trust of society

We pursue world-class product quality and operational excellence to grow our business in ways which build long-term trust with our stakeholders.

* Make patients smile through dramatic improvements in quality of life by identifying the unmet medical needs of people battling with medical conditions and by creating and supplying new drugs or services that help them overcome those challenges.

Story for Vision 2030

Strategies for creating and delivering life-changing value

Disease Science

Focus disease areas: bone & mineral, intractable hematological diseases/hemato oncology, and rare diseases

- Explore UMN, causes and mechanisms of disease in depth
- Pursuit of molecular and cellular regulatory mechanisms for therapeutic realization

Drug Discovery Technology

Strengthening Innovative Modalities: Advanced Antibody Technologies, Hematopoietic stem cell gene therapy

- Application of optimal modalities for therapeutic realization
- Evolution of drug discovery methods through AI and data science

External Collaboration

- Open Innovation
- Partnering

Life-changing Value Creation

Assets in focus disease areas

Strategic Partnering Assets *

Value delivery on our own

Global deployment of products developed by taking full advantage of the company's strengths

Collaborative value delivery

Aim to maximize value by combining the strengths of the company and its partners

Full-licensing

Maximize the value of developed products and deliver them to patients faster by out-licensing to the most appropriate partners

***Assets outside of the disease areas of focus are designated as strategic partnering assets, and value maximization is achieved through collaboration with partners.**

Why Orchard Therapeutics?

Internal Changes

- Focus on disease areas with strengths in bone & mineral, hematologic cancers & intractable blood diseases, and rare diseases
- Portfolio evolution through maximizing the value of rocatinlimab and discontinuation of several pipelines
- Transition to a global structure incorporating diverse skills and mechanisms for organizational growth

External Changes

- Establishing treatments for diseases with no existing therapy
- Personalized medicine
- fundamental treatments

Social demand for realizing them is increasing

Challenges in Drug Discovery Research

- Exhaustion of drug discovery targets with existing modalities like antibodies and small molecules
- Genetic and rare diseases have targets but limited access methods

Focus on Orchard Therapeutics' Technology & Pipeline

- Libmeldy®/Lenmeldy™ - Aiming for fundamental treatments of diseases without SoCs
- Enhancing access to genetic and rare diseases through Hematopoietic Stem Cell Gene Therapy (HSC-GT)
- Anticipating new value creation through the integration of Kyowa Kirin's drug discovery R&D expertise

Bobby Gasper – the CEO of Orchard Therapeutics plc

Orchard therapeutics
A Kyowa Kirin Company

- **Bobby Gaspar, M.D., Ph.D.**
  - Co-founder and chief executive officer of Orchard Therapeutics
  - Studied medicine and surgery at Kings College in London
  - Completed Ph.D. at the UCL Great Ormond Street Institute of Child Health

Orchard therapeutics™

Imagine Limitless Possibilities

8 April 2024

Bobby Gaspar, M.D., Ph.D.

We aspire to end the devastation caused by genetic and other severe diseases through the curative potential of HSC gene therapy.

Orchard Therapeutics: A global gene therapy leader

Our Mission

Dedicated to ending the devastation caused by severe genetic diseases through the curative potential of hematopoietic stem cell (HSC) gene therapy

Our Approach

Our approach harnesses the unique power of a patient's own genetically modified HSCs, **to potentially correct the underlying cause of a genetic disease permanently** with a one-time treatment.

Our Focus

We are focused on treating severe genetic disorders **where the disease burden on children, families and caregivers is immense** and current treatment options are limited or do not exist.

Global headquarters
London

U.S. headquarters
Boston

101 Seaport Blvd
U.S. headquarters

245 Hammersmith Road
Office, laboratories and global HQ

Global footprint:

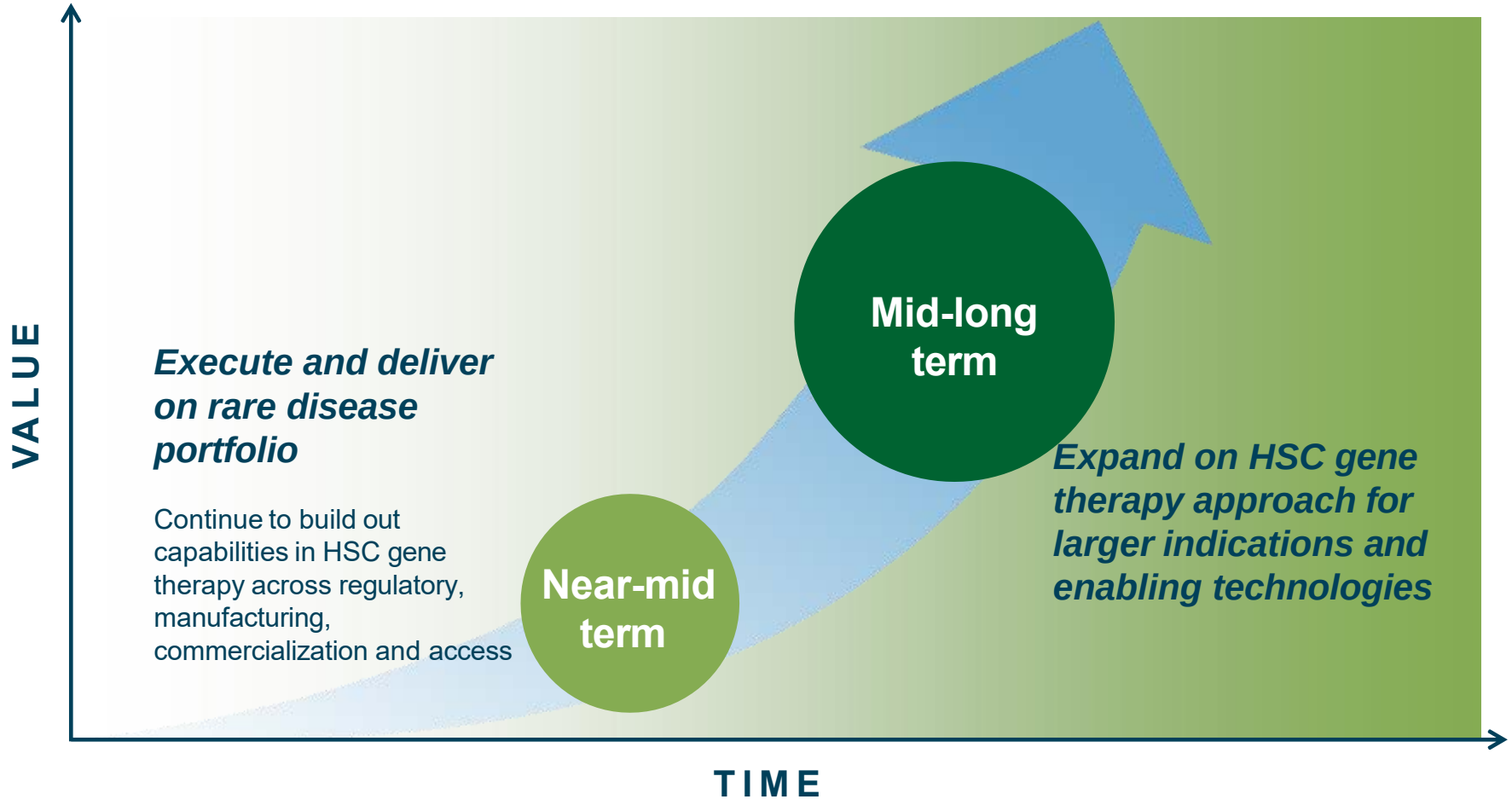
~170
Employees

Established presence in:

- France
- Germany
- Italy
- Netherlands
- Sweden
- Switzerland

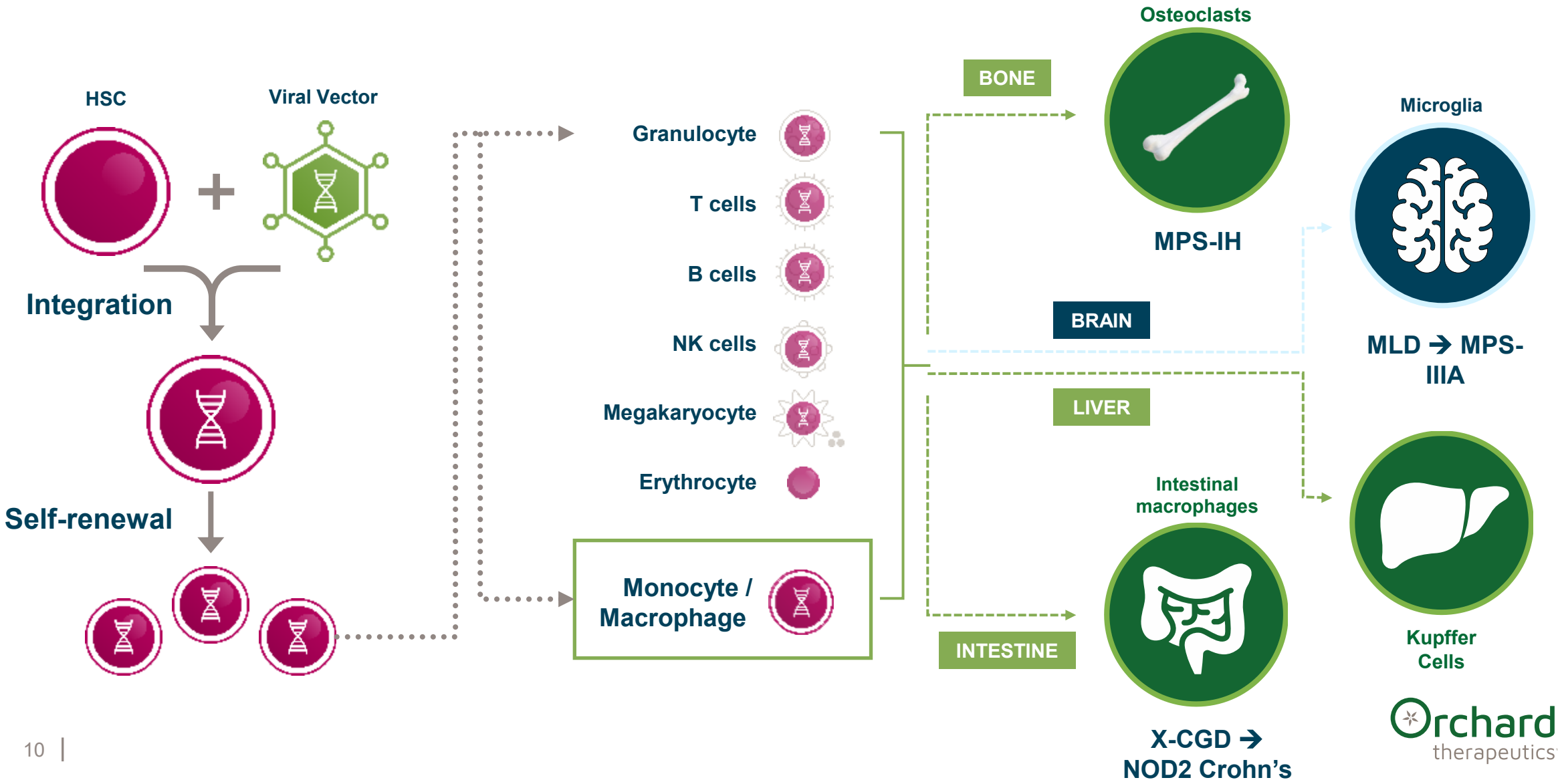
Orchard therapeutics

Strategic long-term growth and value creation with expansion into larger indications



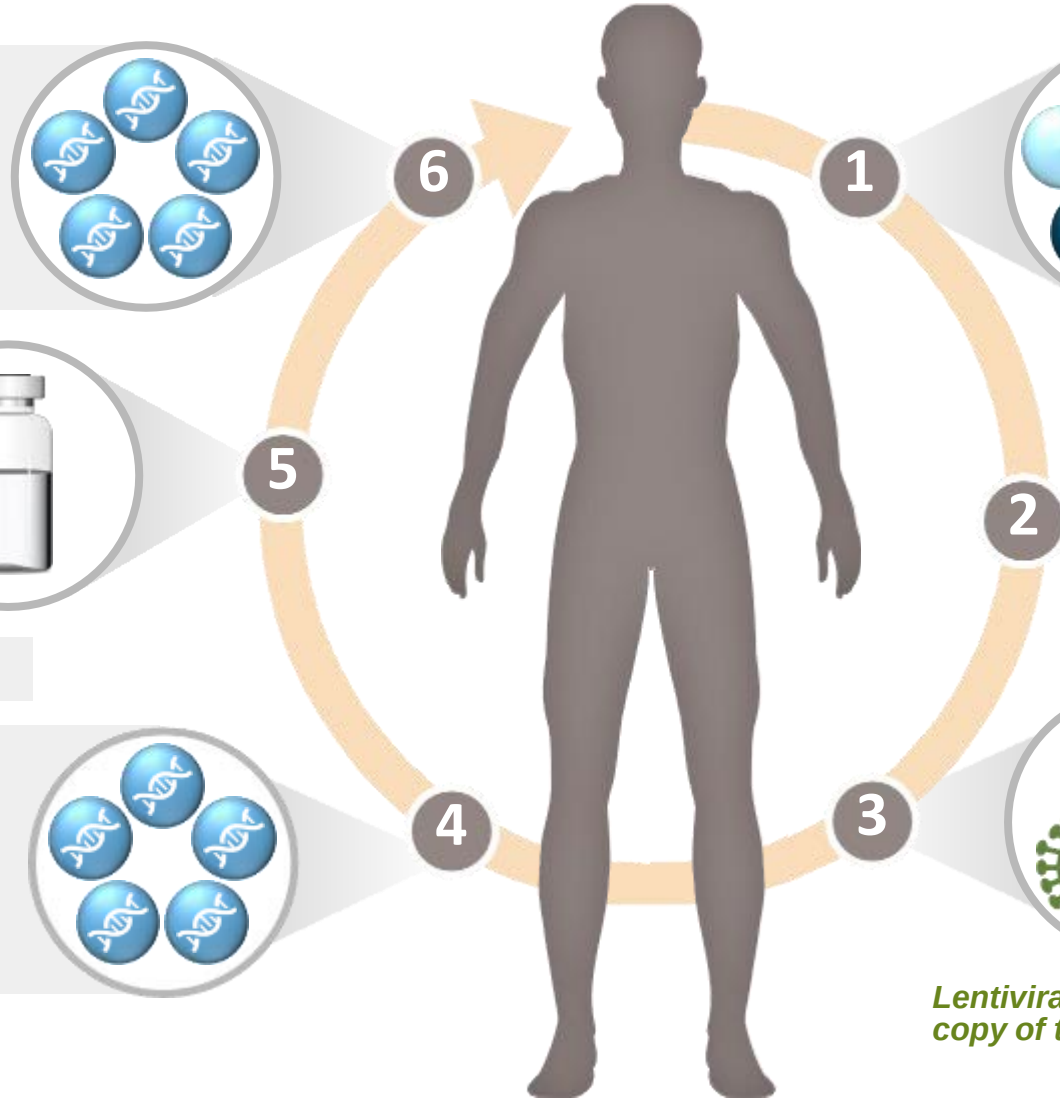
Orchard therapeutics

HSC gene therapy enables delivery of gene-corrected cells to multiple organ systems



Orchard therapeutics

Autologous *ex vivo* gene therapy approach



Blood cell collection:
Blood hematopoietic stem and progenitor cells (HSPCs) are taken from the patient via leukapheresis

Patient can return home

HSPC selection and purification:
HSPCs, identified by the CD34+ cell surface marker, are selected and purified by magnetic bead selection

Transduction:
HSPCs are genetically-modified outside of the body (*"ex vivo"*) via exposure to a lentiviral vector carrying a functional copy of the gene

Lentiviral vector carrying a copy of the functional gene

Cryopreserved genetically-modified HSPCs:
Drug product is certified that it meets manufacturing standards and sterility

Patient returns to center

Conditioning:
The patient is given conditioning to "make space" for the genetically-modified cells

Administration:
Genetically-modified cells are given back to the patient intravenously

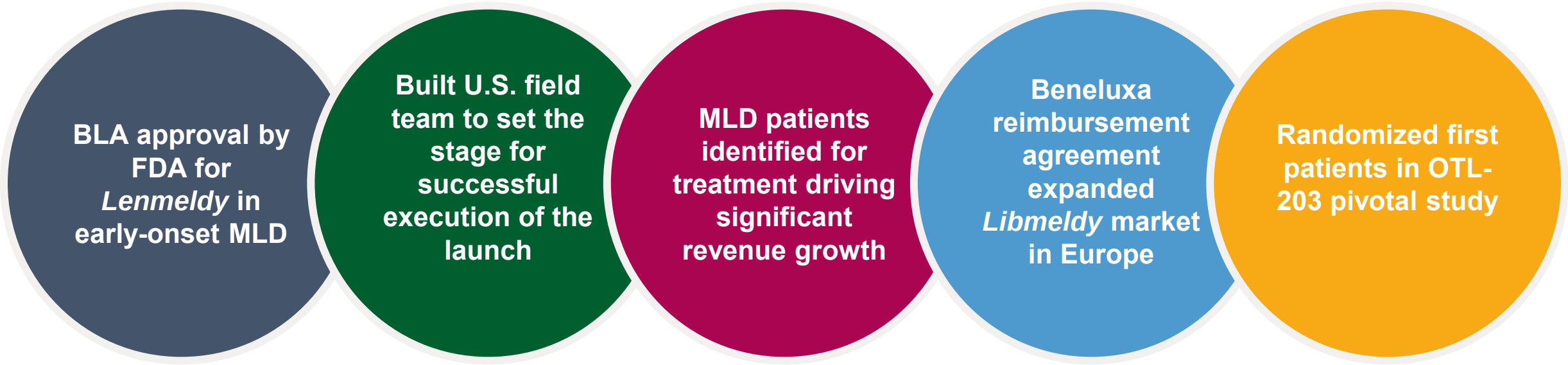
Orchard therapeutics

Advancing a pipeline to address serious genetic diseases

*Lenmeldy™ is approved in the U.S. for the treatment of children with pre-symptomatic late infantile, pre-symptomatic early juvenile, or early symptomatic early juvenile metachromatic leukodystrophy (MLD). Libmeldy® is approved in the European Union, UK, Iceland, Switzerland, Liechtenstein and Norway.

Orchard therapeutics™

Strong operational execution already in 2024



Orchard therapeutics™

Lenmeldy™ / Libmeldy® (MLD): Potential significant clinical benefit for a devastating genetic disease

Age 5, pre-diagnosis

Age 9, advanced disease

Disease Snapshot

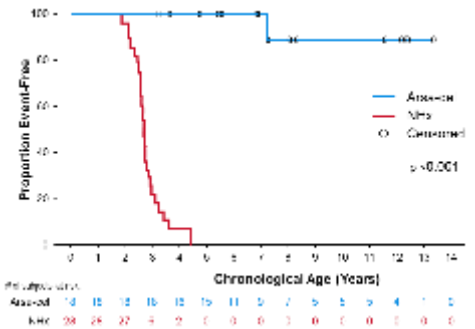
- Fatal genetic CNS disorder
- Rapid and irreversible loss of motor and cognitive function
- In its most severe form, most children pass away within five years of symptom onset[1]

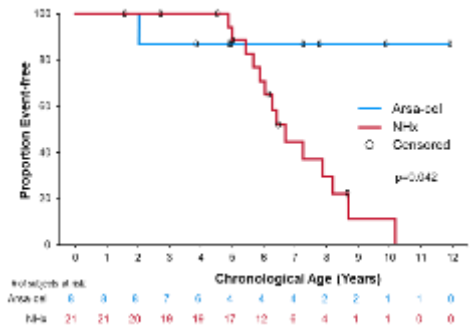
Severe Motor Impairment Free Survival (sMFS)

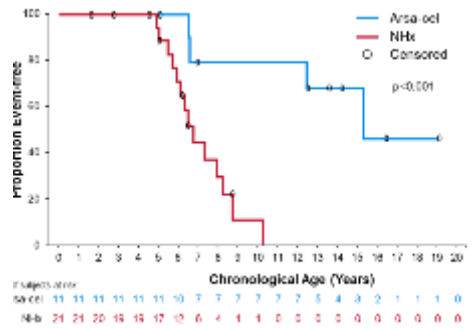
Interval from birth to first occurrence GMFC-MLD ≥ 5 (no locomotion and unable to sit) or death

Treatment with OTL-200 resulted in statistically significant and clinically meaningful improvement in sMFS in the PSLI (p<0.001), PSEJ (p=0.042) and ESEJ (p<0.001) MLD subgroups compared to disease natural history.

Pre-Symptomatic Late Infantile (PSLI)	Pre-Symptomatic Early Juvenile (PSEJ)	Early-Symptomatic Early Juvenile (ESEJ)







	PSLI	PSEJ	ESEJ
OTL-200	100%	87.5%	80%
NHx	0%	11.2%	11.2%

Data presented at the at the Society for the Study of Inborn Errors of Metabolism (SSIEM) Annual Symposium 2023, August 2023

1. van Rappard DF, Boelens JJ, Wolf NI. Metachromatic leukodystrophy: disease spectrum and approaches for treatment. Best Pract Res Clin Endocrinol Metab 2015; 29: 261–73.

Orchard therapeutics

All 7 surviving PSEJ patients maintained the ability to walk with normal performance for age (GMFC-MLD Level 0)

Untreated NHx sibling

GMFC-MLD Level 6
3 years post-onset
8 years of age

Treated Child

GMFC-MLD Level 0
8 years post-GT
12 years of age

Pioneering Commercial Operations Leading to Sustainability

Access

Reimbursement

Secured for all eligible MLD children

Early access program: AP2 granted and renewed (France)

Treatment abroad: Named patient program in the Middle East established (Saudi Arabia)

Cross border: European pathway (S2) leveraged in multiple CEE countries

Treatment

Europe & Middle East	2022	2023 (1H)	Total
Leads	98	54	152
Confirmed MLD	73	40	113
LI or EJ MLD	57	31	88

Patients treated across all six qualified treatment centers in Europe

Landmark agreements secured in a dozen European countries for all eligible MLD children

Alternative pathways for reimbursement successfully utilized

Focus on lead generation, disease awareness and diagnosis

Orchard therapeutics

OTL-203 (MPS-IH): Disease background & *NEJM* interim proof-of-concept results

Disease snapshot

- **Multisystemic neurometabolic condition affecting cognition, growth and skeletal function**
- **Current standard of care: HSCT and/or ERT as a bridging or chronic therapy**
- **~1:100,000 live births; NBS established in some geographies, including U.S.**

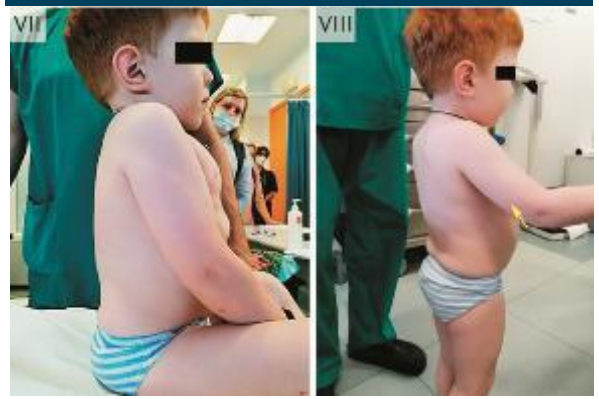
Next steps

Pivotal trial initiated

- Randomized controlled trial vs. HSCT (standard of care)
- 40 patients
- 2-year primary analysis
- Composite endpoint
- Initial six sites to be activated globally

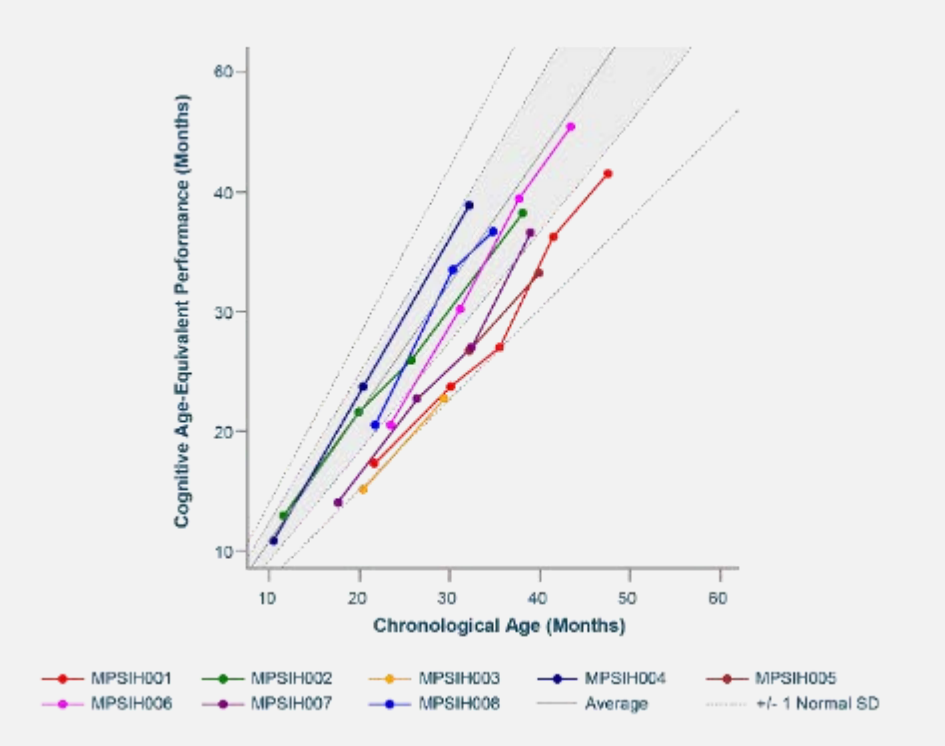
Before gene therapy

1.5 yrs. after gene therapy



Neuropsychological Tests over Time

Cognitive Age-Equivalent Score (Overall)



Interim Proof-of-Concept (PoC) Study Results Published in *NEJM*

SD = Standard Deviation; IQ(C) = Intelligence Quotient (Cognition);
Engl J Med 2021; 385:1929-1940 DOI: 10.1056/NEJMoa2106596

Orchard therapeutics

OTL-201 (MPS-IIIA): A progressive and devastating disease with no approved treatment options

Disease snapshot

- **Sanfilippo syndrome type A; pathogenic variants in *SGSH* gene**
- **Accumulation of substrate heparan sulfate leading to severe CNS degeneration w/ somatic manifestations**
- **Severe phenotype development slows from 3 years of age, followed by cognitive decline, behavioural disturbances, loss of skills and eventual death**
- **No successful treatment options**
- **Incidence: ~1 in 100,000 live births**

Early Neurocognitive Outcomes

- Change in cognitive function (age equivalent scores) against natural history of MPSIIIA
- Change in patient behavior, patient QoL and daily living
- Early follow-up in trial patients:
  - Gain of skills in line with development of normal children in 4 out of 5 pts.
  - Developmental gains not seen in untreated MPS-IIIA, *e.g.* acquisition of speech, continence and complex play
  - Longer follow up ongoing to assess safety and efficacy outcomes

Pre-treatment with GT | **Post-GT Treatment**

Post-GT Treatment

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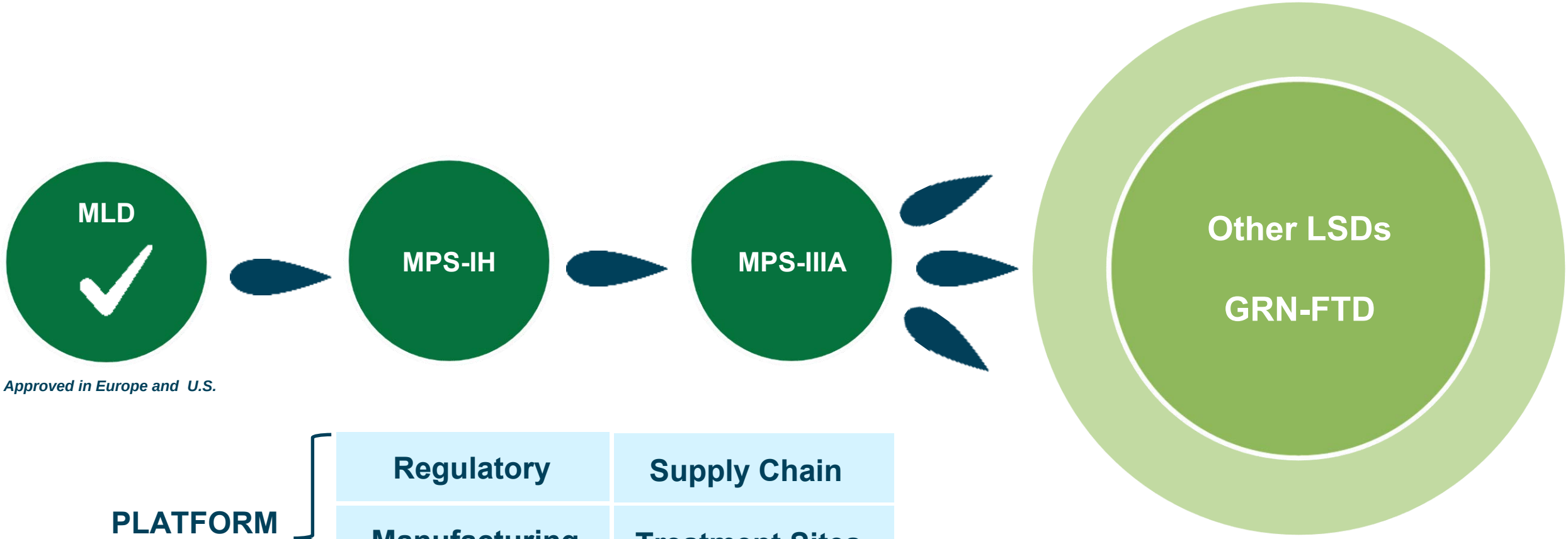
Success in MLD provides roadmap, common infrastructure for next-in-line neurometabolic and CNS programmes



Approved in Europe and U.S.

PLATFORM SYNERGIES		
	Regulatory	Supply Chain
	Manufacturing	Treatment Sites
	Distribution	Referral Networks

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Compelling fundamentals driving near-term value creation and long-term growth

Commercial Model	Diagnostics and Newborn Screening	Future Potential Regulatory Approvals	Manufacturing and Distribution	Other Applications
Establish scalable business and growth	Develop markets	Leverage success in rare diseases	Implement a sustainable process	Advance scientific platform

All based on a de-risked HSC GT scientific and clinical platform

Orchard therapeutics

The world’s leading gene therapy company

Orchard therapeutics™

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Future HSC-GT related business

Expansion of Libmeldy®/Lenmeldy™ usage in EU and US

- US approval on March 18, 2024, followed by launch
- Ten prospective NBS* studies for MLD are active throughout the U.S., Europe and the Middle East, w/ ~275k newborns screened as of 31 March
- Projected revenue for FY2024: 4.5 billion yen

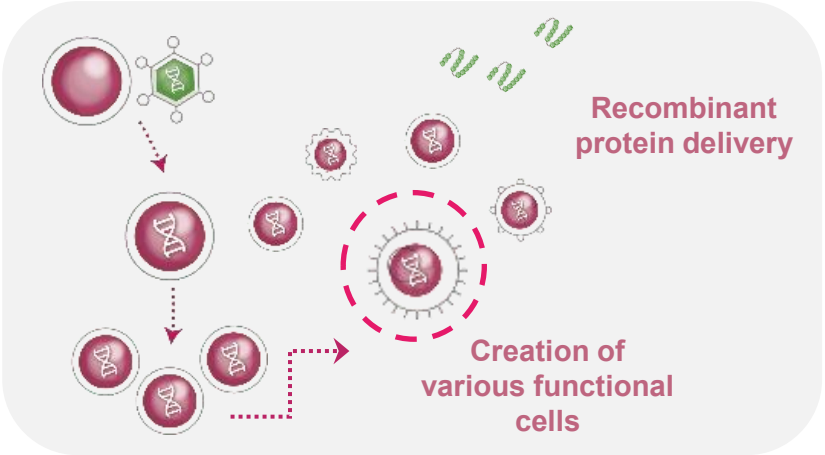
* Newborn screening

Steady progress in the current development pipeline

Code	Target disease	Status
OTL-203	MPS-IH (Hurler Syndrome)	Registrational study ongoing
OTL-201	MPS-IIIA (Sanfilippo Syndrome type A)	PoC study ongoing Planning for potential registrational study

Expanding into New Drug Discovery Technologies

- Fusion of our technology with HSC-GT: Recombinant protein delivery to sites typically difficult to reach
- Creation of functional cells utilizing the pluripotency of HSCs



Aiming for the successful creation and delivery of life-changing value through the integration of both companies' strengths

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