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

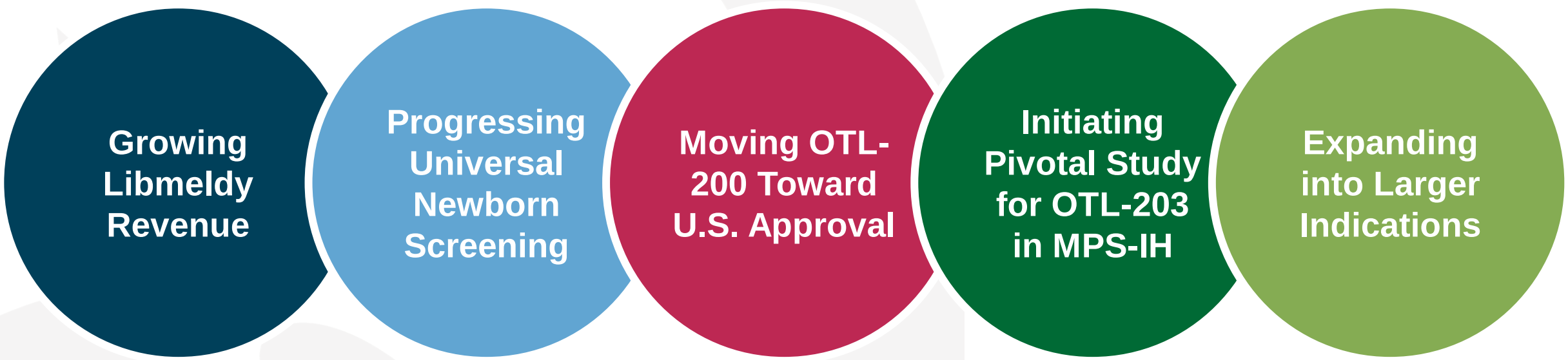
Forward-looking Statements

This presentation and statements made in this presentation contain forward-looking statements, which are made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. All statements that are not statements of historical facts are, or may be deemed to be, forward-looking statements. Such forward-looking statements may also be identified by words such as “anticipates,” “potential,” “expects” and other similar expressions. Forward-looking statements include express or implied statements relating to, among other things: Orchard’s estimates and expectations with respect to its financial performance, including revenue, expenses, trend of cash-burn rates and cash-runway; the incidence rate of diseases that our products and product candidates are intended to treat, including the incidence of MLD; the therapeutic potential of Orchard’s products and product candidates, including the ability of HSC gene therapy to address larger indications; Orchard’s expectations regarding the timing of regulatory submissions and approvals of its product candidates, including the timeline for acceptance of Orchard’s BLA submission for OTL-200; Orchard’s expectations regarding the timing of U.S. approval for OTL-200; the additional proceeds receivable by Orchard upon exercise of the warrants issued pursuant to its previously announced strategic financing; the number of newborns expected to be screened for MLD, and the timing and likelihood of additional newborn screening studies; and Orchard’s ability and expectations to meet its anticipated 2023 milestones, as further described in this release.

These statements are neither promises nor guarantees and are subject to a variety of risks and uncertainties, many of which are beyond Orchard’s control, which could cause actual results to differ materially from those contemplated in these forward-looking statements. In particular, these risks and uncertainties include, without limitation: Orchard’s anticipated cash runway assumes U.S. FDA approval of OTL-200 in the first half of 2024, which may be delayed or not occur, and achievement of net sales in the U.S. and Europe in line with management’s forecasts, which may not happen; the risk that Orchard’s OTL-200 BLA submission is not accepted on the timeline we expect or at all; the risk that our revenues will be less than we anticipate; the risk that our expenses will be greater than we anticipate; the risk that Orchard is unable to set up additional qualified treatment centers and newborn screening or is delayed in doing so; the risk that Orchard will not maintain marketing approval; the risk that long-term adverse safety findings may be discovered; the risk that the warrants issued pursuant to Orchard’s previously announced strategic financing are not exercised, that only a subset of the warrants are exercised, or that the exercise price of the warrants is lower than anticipated due to a delay in OTL-200’s U.S. approval. Given these uncertainties, the reader is advised not to place any undue reliance on such forward-looking statements. Other risks and uncertainties faced by Orchard include those identified under the heading "Risk Factors" in Orchard’s most recent annual or quarterly report filed with the SEC, as well as subsequent filings and reports filed with the SEC. The forward-looking statements contained in this press release reflect Orchard’s views as of the date hereof, and Orchard does not assume and specifically disclaims any obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, except as may be required by law.

Orchard therapeutics

Strong Operational Execution in 1H of 2023



Q2'23: Highest quarterly sales to date; Cumulative net sales of $25.9M

Four cases of MLD identified following ~150k newborns screened

BLA submission completed; potential approval in 1H'24

Global RCT in 40 patients following IND clearance by FDA

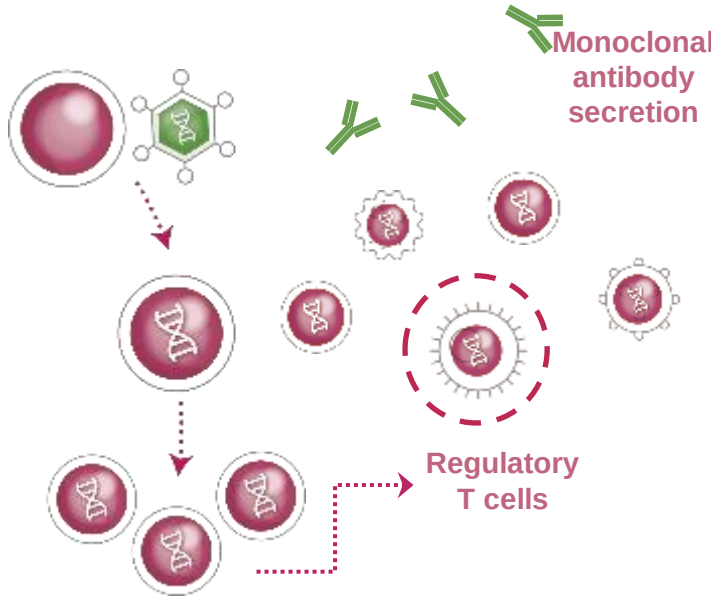
Preclinical PoC data in GRN-FTD and NOD2-Crohn's presented at ASGCT

Strategic financing resulted in $68M of new capital, extending cash runway into mid-2025

Potential for up to an additional $120M in proceeds could further offset financing needs for foreseeable future

Orchard therapeutics

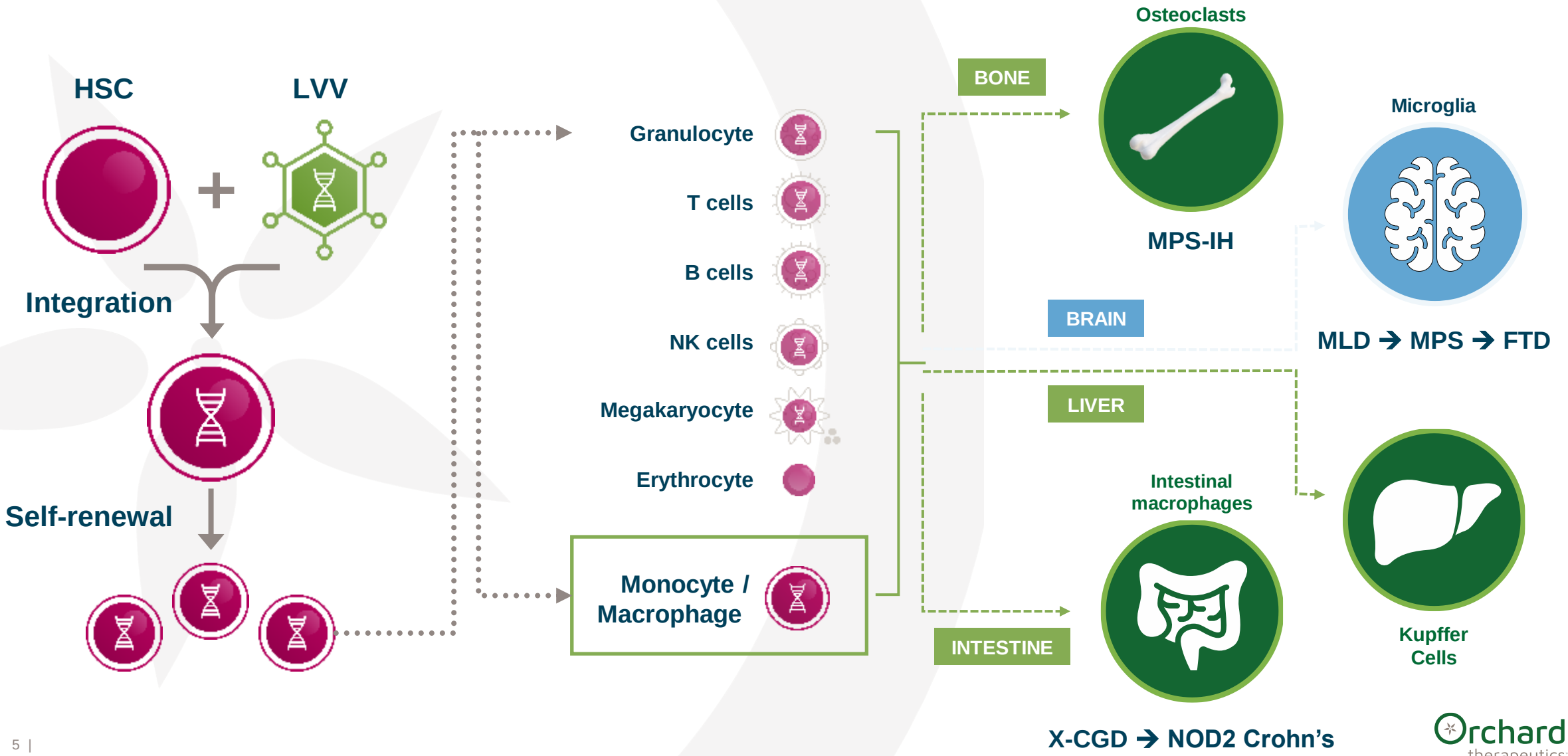
Orchard's HSC Gene Therapy Offers a Highly Differentiated, Validated Approach with Opportunities for Expansion

Validation in Rare Diseases	Larger Indications	Future Applications
libmeldy® (atidarsagene autotemcel)	OTL-104 NOD2-Crohn's	
OTL-200 MLD (US)	OTL-204 FTD	
OTL-203 MPS-I OTL-201 MPS-IIIA	OTL-105 HAE	
Other undisclosed programs		

Multiple opportunities for near-term data and inflection points through internal investment and business development

Orchard therapeutics

HSC Gene Therapy Allows Delivery of Gene-corrected Cells to Multiple Organ Systems



Orchard therapeutics

ASGCT Snapshot: Six Presentations (Three Oral) across Five Programs

OTL-203 for MPS-IH: Additional PoC data demonstrated extensive metabolic correction in the skeletal system resulting in normal growth, skeletal remodeling, improved joint function and progressive acquisition of motor skills

OTL-201 for MPS-IIIA: Updated data from ongoing PoC study show additional favorable neurocognitive outcomes compared to disease natural history with median follow-up of 2.5 years

OTL-204 for GRN-FTD: First preclinical data highlighting ability of HSC gene therapy to express progranulin in the CNS, modulate neuroinflammation, and normalize predictive biomarkers

OTL-104 for NOD2-Crohn's: Preclinical PoC data show the therapeutic potential in a severe and treatment-refractory form of the disease

HSC CAR-Treg: *In vivo* data demonstrated the feasibility of utilizing HSC gene therapy to provide stable and targeted immunotherapy as a potential one-time treatment for autoimmune disorders

OTL-200 (MLD): Potential Significant Clinical Benefit for a Devastating Genetic Disease

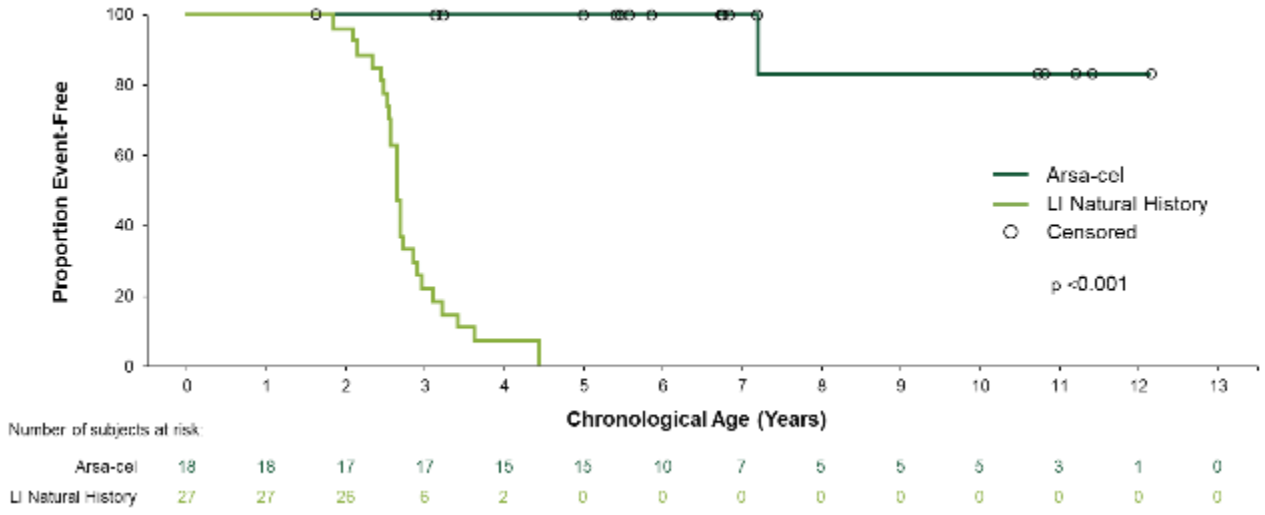
Age 5, pre-diagnosis

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]

Kaplan-Meier Plot of Severe Motor Impairment-Free Survival Pre-Symptomatic Late Infantile Subjects (n=18)



Data presented at 19th Annual WORLD*Symposium*™, February 2023

GMFC-MLD=Gross Motor Function Classification-Metachromatic Leukodystrophy.
Note: Severe motor impairment-free survival is defined as the interval from birth to the earlier of loss of locomotion and sitting without support (GMFC-MLD level 5 or higher) or death from any cause; otherwise, subject is censored at the last GMFC-MLD assessment date.

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

OTL-200 (MLD): BLA Submission Completed; Moving Toward Potential Approval in 1H'24

BLA Submission and Approval Timeline

Oct. 2022
Externally-led patient focused drug development meeting with the FDA held by MLD patients and families with significant engagement from members of the BLA review team

Jan. 2023
Productive Type B meeting with the FDA to align on clinical package, including natural history, *etc*.

Apr. 2023
Pre-BLA meeting held with multi-disciplinary review team at the FDA to align on final BLA package, rolling BLA timeline and content of modules

Summary of Recent Regulatory Correspondence with the FDA

Nov. 2022
MLD Scientific Workshop held with the FDA by KOLs and treating physicians of the MLD community

Feb. 2023
Informal feedback meeting with the FDA after comprehensive CMC comparability reports submitted in 4Q '22

May 2023
Rolling BLA submission initiated

Rolling BLA Submission Completed

- ***BLA acceptance anticipated in Q3' 23***
- ***Potential approval in 1H' 24 assuming priority review***

Orchard therapeutics

Building Global Momentum for Libmeldy Commercial Potential

Commercial Activities

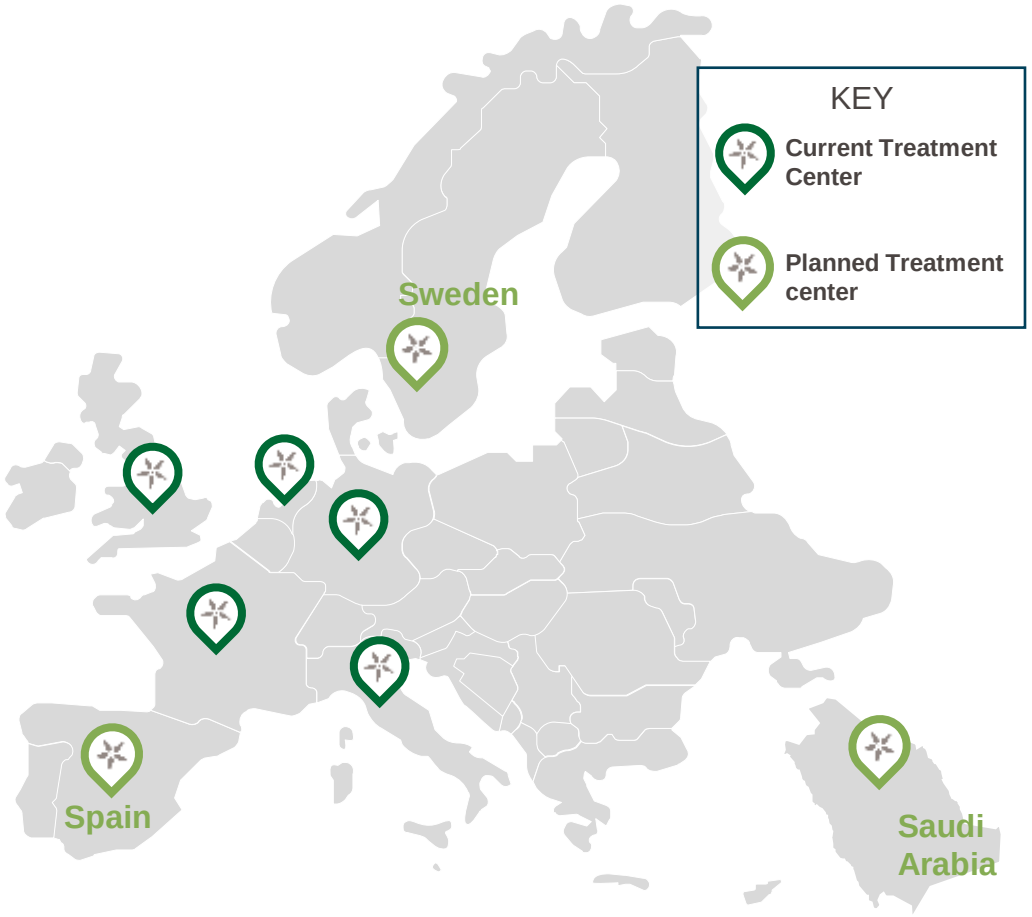
1) Newborn screening and disease awareness to drive patient ID
2) Broad access through qualified treatment center (QTC) network
3) Reimbursement through various pathways

Staged Areas of Focus

Orchard therapeutics

Expanding Reimbursed Access Throughout Europe

Access



Reimbursement

Secured for all eligible MLD children

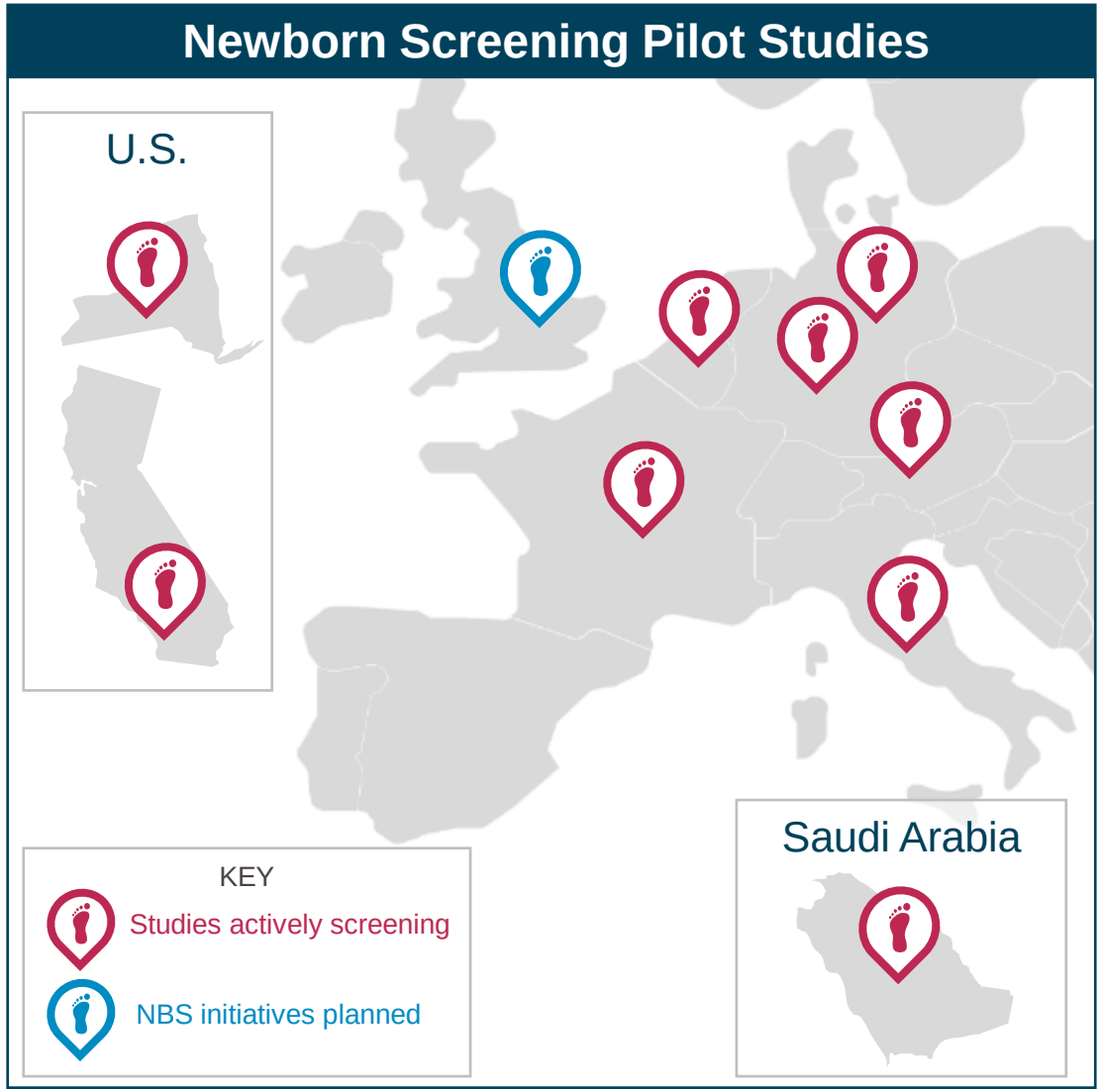
Reimbursed early access (*e.g.*, France)

Cross border (S2) pathway: (*e.g.*, Central & Eastern Europe)

Treatment abroad: (*e.g.*, Middle East)

Orchard therapeutics

Implementing Newborn Screening to Identify MLD Patients

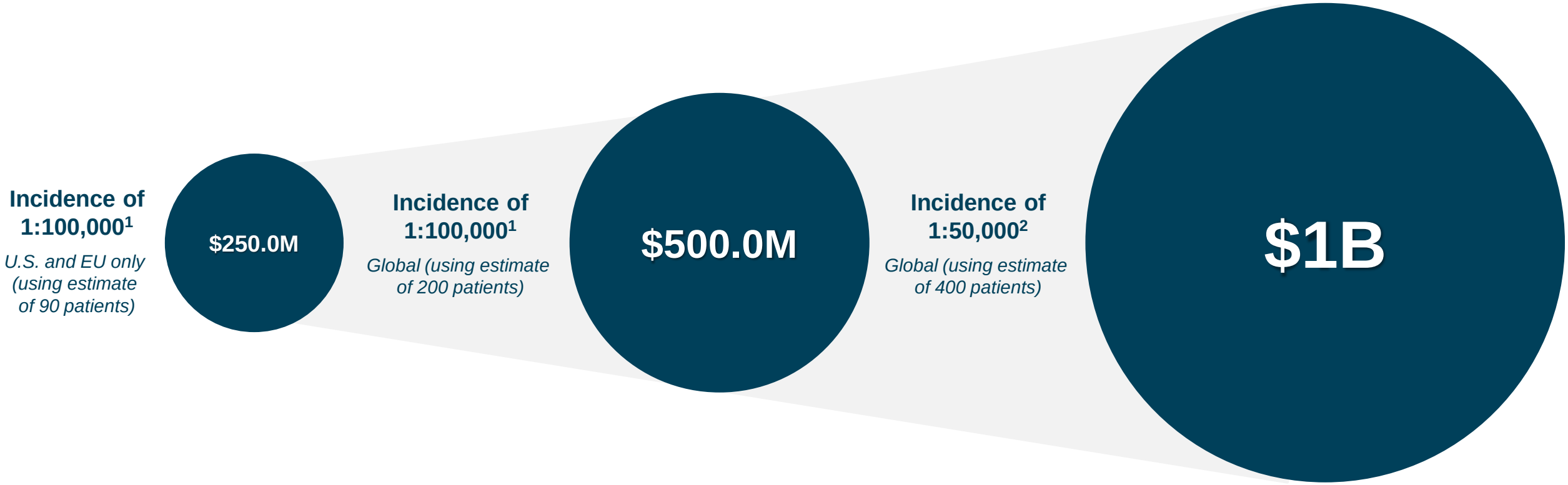


4 Confirmed cases of MLD following screening of **~150k** newborns

- ✓ Advancing universal newborn screening for MLD
  - Newborn Metabolic Screening Act (SB67) enacted in Illinois, MLD being added to statewide panel
  - Following study data, application for nationwide screening progressing in Germany
- ✓ Continuing to expand NBS initiatives in Europe, the U.S. and the Middle East

Orchard therapeutics

MLD Represents a Significant Annual Global Market Opportunity



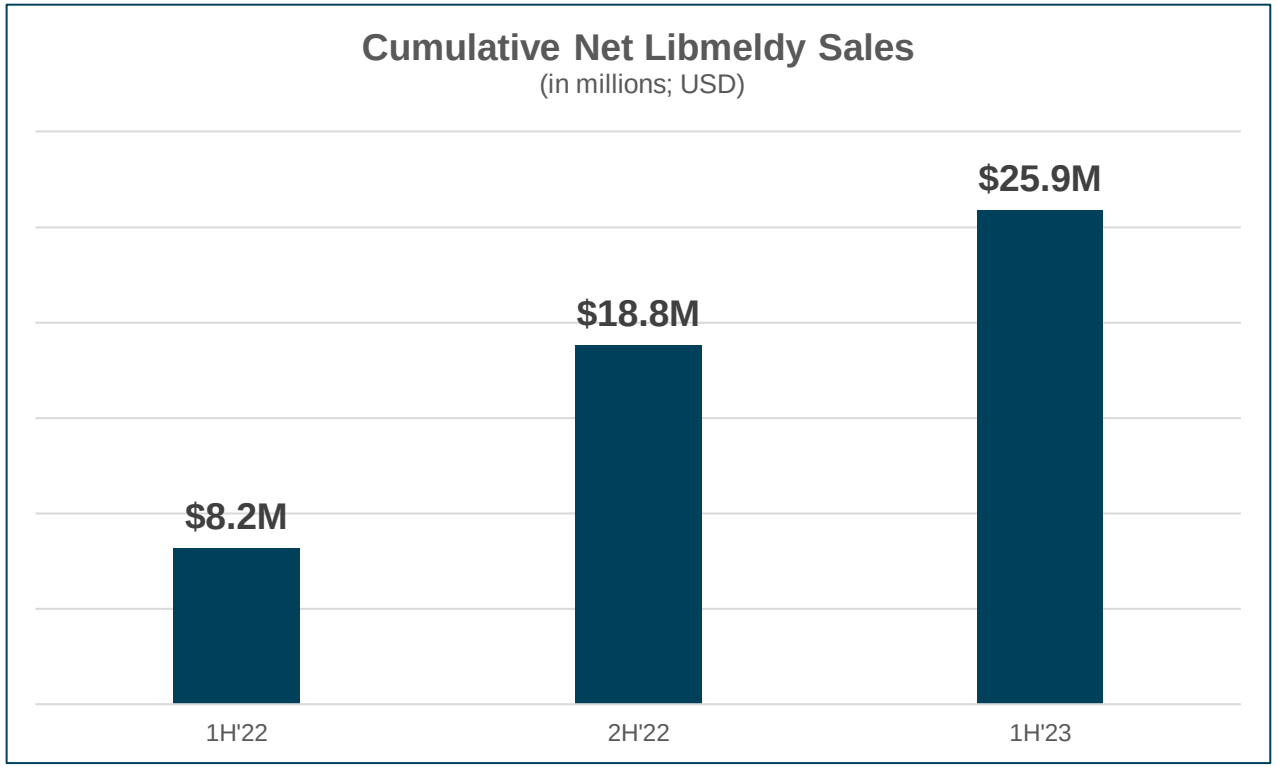
Potential annual market opportunity for Libmeldy across all patient segments assuming an average per patient net price of $2.5M and universal newborn screening[3]

1. *von Figura K, Jaeken J. Metachromatic leukodystrophy. In: Scriver CR, Valle D, WS S, eds. The metabolic and molecular bases of inherited diseases. Mac Graw-Hill; 2001:3695-3724, chap. 148.*
2. *Based on four MLD cases identified following ~150,000 newborns screened through ongoing research studies as of June 30, 2023.*
3. *The sale price of Libmeldy will vary from jurisdiction to jurisdiction and could vary for a variety of reasons, some of which are outside of the company's control. The net price utilized on this slide is for illustrative purposes only and is not an estimate or prediction of the average net price of Libmeldy globally.*

Orchard therapeutics

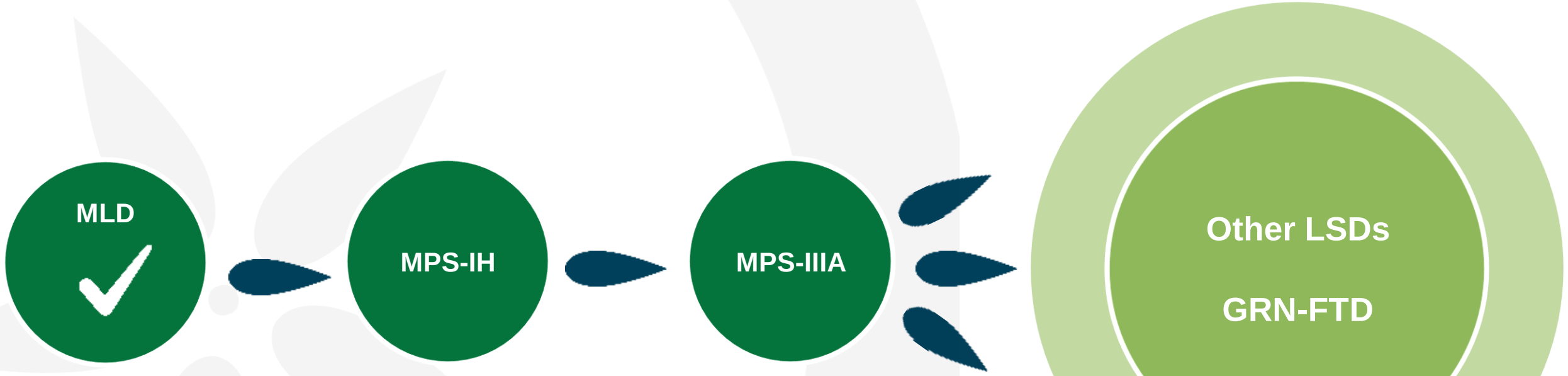
Steady Libmeldy Revenue Growth Since Launch

- Patients from 6 different countries treated commercially at 4 of 5 qualified centers
- Reimbursement via access agreements, cross-border and named patient pathways
- Average vein-to-vein time of 55 days with 100% success in production
- Company on track for year-over-year revenue growth



Orchard therapeutics

Success in MLD Provides Roadmap, Common Infrastructure for Next-in-line Neurometabolic and CNS Programs



Approved in Europe;
BLA submitted to U.S. FDA

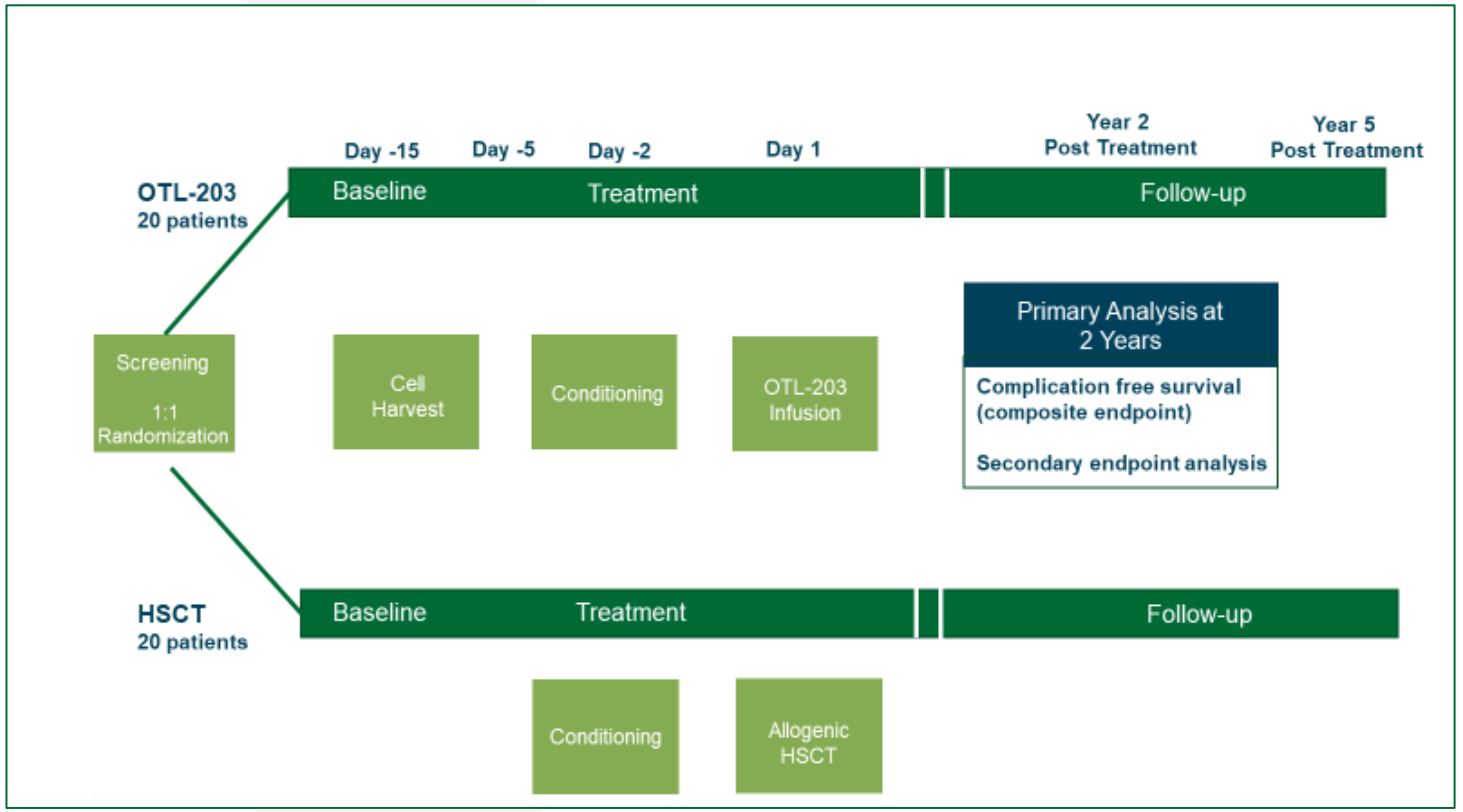
PLATFORM SYNERGIES

Regulatory	Supply Chain
Manufacturing	Treatment Sites
Distribution	Referral Networks

Orchard therapeutics

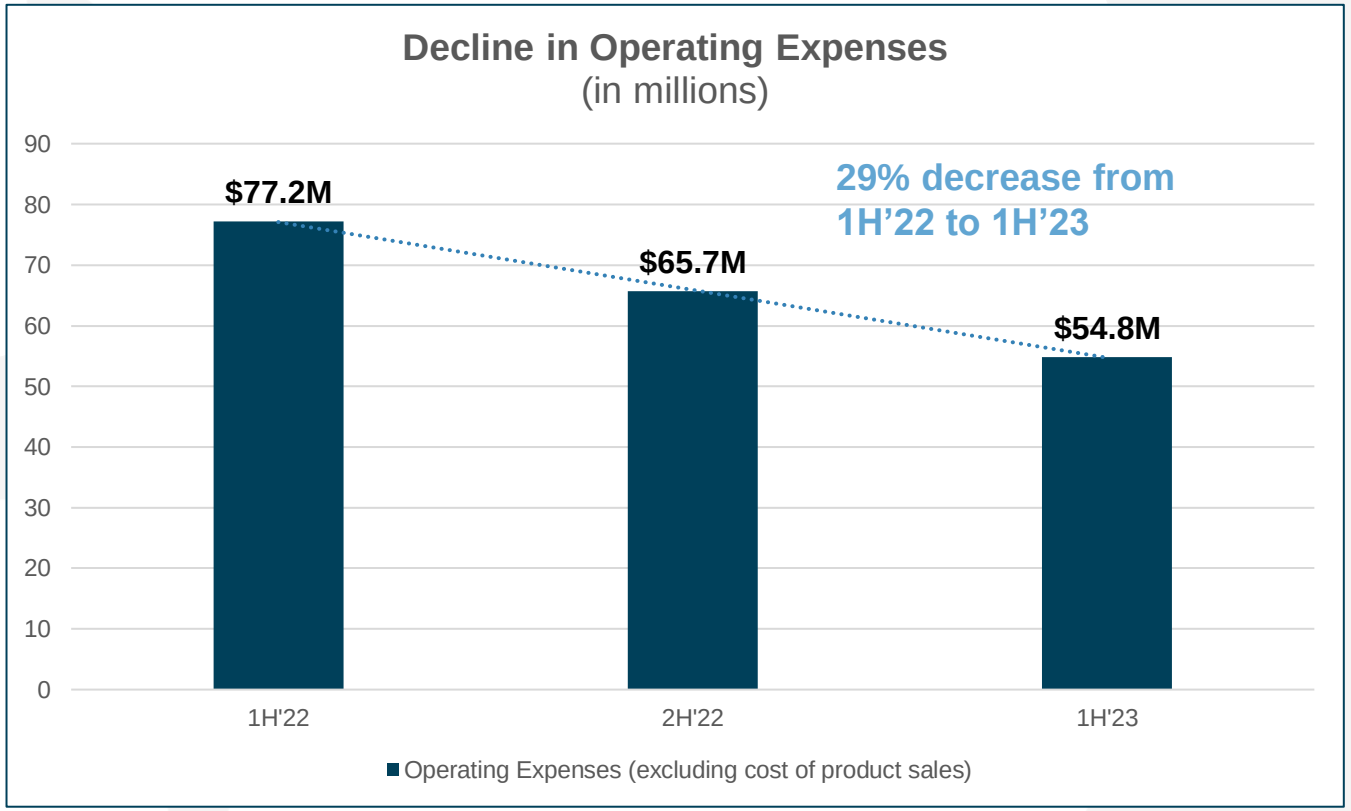
OTL-203 (MPS-IH): Moving into a Pivotal Trial in 2H 2023

- Randomized controlled trial vs. HSCT (standard of care)
- 40 patients
- 2-year primary analysis
- Composite endpoint
- Up to 6 U.S. / EU sites



Orchard therapeutics

Prioritizing Commercial Growth, Development of Pipeline and Expense Management to Generate Value



- **Anticipated year-over-year increase in Libmeldy product sales**
- **Ongoing management of operating expenses**
- **Annual burn rate expected to continue declining in 2023 vs. 2022**

Orchard therapeutics

Summary of Q2’23 Financial Results

	Three Months Ended June 30		
Statement of Operations:	**2023**	**2022**	**% Change**
Libmeldy product sales	$6.6M	$3.2M	+111%
Strimvelis product sales	-	$0.6M	-
Collaboration revenue	$0.7M	$0.6M	+13%
Total revenues	**$7.3M**	**$4.4M**	+67%
Cost of product sales	$2.2M	$1.1M	+95%
Research and development	$16.7M	$22.0M	-24%
Selling, general and administrative	$11.0M	$13.7M	-20%
Total costs and operating expenses	**$29.9M**	**$36.8M**	-19%
Loss from operations	$22.6M	$32.4M	-30%
Balance Sheet:			
Ending cash and investments	$155.0M	$175.2M	-12%
Ending ADS outstanding	22.7M	12.6M*	+80%

**Adjusted for post-ADS ratio change from one ADS to one ordinary share to the new ratio of one ADS to ten ordinary shares completed on March 10, 2023*

Orchard therapeutics

Executing on Key Corporate Milestones

Approximately $155.0M in Cash and Investments as of Q2'23 Supports Runway to mid-2025

Libmeldy - Commercial

- ✓ Secured reimbursed access in four additional European markets
- Add to qualified treatment center network
- Expand newborn screening activities to screen 200,000 babies by year-end
- Grow Libmeldy revenue year-over-year

Regulatory

- ✓ **OTL-200:** Completed rolling BLA submission to U.S. FDA in MLD
- **OTL-200:** BLA acceptance expected in Q3 w/ potential approval in 1H'24 assuming priority review

Development

- ✓ **OTL-201:** Report biochemical / clinical data from ongoing MPS-IIIA PoC study in 2023
- **OTL-203:** Initiate global registrational trial for MPS-IH in 2H 2023

Preclinical

- ✓ **OTL-204:** Report preliminary preclinical PoC data for GRN-FTD
- ✓ **OTL-104**: Report preclinical PoC data for NOD2-CD (1H 2023)
- **OTL-104:** Initiate IND-enabling activities ahead of 2025 planned IND submission

Advance other preclinical pipeline programs (*e.g.*, OTL-105) and enabling technologies (*e.g.*, HSC Tregs)

Orchard therapeutics

Strategic Anchors Represent Breakout Opportunities for Orchard

All based on a HSC GT scientific and clinical platform

Orchard therapeutics