

Q1 2022 Financial Results and Business Highlights

May 12, 2022



 **Orchard**
therapeutics™

Forward-looking Statements

Certain information set forth in this presentation and in statements made orally during this presentation contain “forward-looking statements”. Except for statements of historical fact, information contained herein constitute forward-looking statements and may include, but are not limited to, the Company’s expectations regarding: (i) the safety and efficacy of Libmeldy and its product candidates; (ii) the Company’s ability to establish the infrastructure necessary to enable the treatment of eligible MLD patients and the adequacy of the Company’s supply chain and ability to commercialize Libmeldy; (iii) the expected development of the Company’s business and product candidates; (iv) the timing of regulatory submissions for approval of its product candidates; (v) the timing of interactions with regulators and regulatory submissions related to ongoing and new clinical trials for its product candidates; (vi) the timing of announcement of preclinical data for its product candidates and the likelihood that such data will be positive and support further development and regulatory approval of these product candidates; (vii) the timing and likelihood of approval of such product candidates by the applicable regulatory authorities; (viii) the adequacy of the Company’s manufacturing capacity and plans for future investment and commercialization; (ix) execution of the Company’s vision and growth strategy, including with respect to global growth; (x) the size and value of potential markets for Libmeldy and the Company’s product candidates; and (xi) expected financial performance and financial condition, including its cash runway. The words “may,” “should,” “expects,” “intends,” “plans,” “anticipates,” “believes,” “estimates,” “predicts,” “potential,” “continue,” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Forward-looking statements are provided to allow investors the opportunity to understand management’s beliefs and opinions in respect of the future so that they may use such beliefs and opinions as one factor in evaluating an investment.

These statements are neither promises nor guarantees of future performance. Such forward-looking statements necessarily involve known and unknown risks and uncertainties, many of which are beyond the Company’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, the risk that Libmeldy will not be successfully commercialized, including the risk that the Company may not secure adequate pricing or reimbursement to support continued development of Libmeldy or its product candidates, if approved; the risk that any one or more of the Company’s product candidates, including OTL-200, will not be approved, successfully developed or commercialized; the risk that prior results, such as signals of safety, activity or durability of effect, observed from preclinical studies or clinical trials of Orchard’s product candidates will not be repeated or continue in ongoing or future studies or trials involving its product candidates; the risk that the market opportunity for Libmeldy or its product candidates may be lower than estimated; and, the severity of the ongoing and evolving impact of the COVID-19 pandemic on Orchard’s business, including on preclinical and clinical development, its supply chain and commercial programs. You are cautioned not to place undue reliance on forward-looking statements. For additional disclosure regarding these and other risks faced by the Company, see the disclosure contained in the Company’s most recent annual or quarterly filed with the U.S. Securities and Exchange Commission (the “SEC”), as well as subsequent filings and reports filed with the SEC. These forward-looking statements speak only as of the date of this presentation. The Company undertakes no 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.

Non-GAAP Financial Information

Orchard has presented certain non-GAAP financial measures, including research and development costs and selling, general and administrative expenses, each excluding certain one-time charges. Management believes this non-GAAP information is useful for investors, taken in conjunction with Orchard’s GAAP financial statements, because it provides greater transparency regarding Orchard’s operating performance. Management uses these measures, among others, to assess and analyze operational results and trends and to make financial and operational decisions. Non-GAAP information is not prepared under a comprehensive set of accounting rules and should only be used to supplement your understanding of Orchard’s operating results as reported under GAAP, not as a substitute for GAAP information. In addition, these non-GAAP financial measures are unlikely to be comparable with non-GAAP information provided by other companies. Reconciliation between these non-GAAP financial measures and the most comparable GAAP financial measures is included in the financial results section of this presentation.

Joining Today's Call



Bobby Gaspar, M.D., Ph.D.
Chief Executive Officer



Braden Parker
Chief Commercial Officer

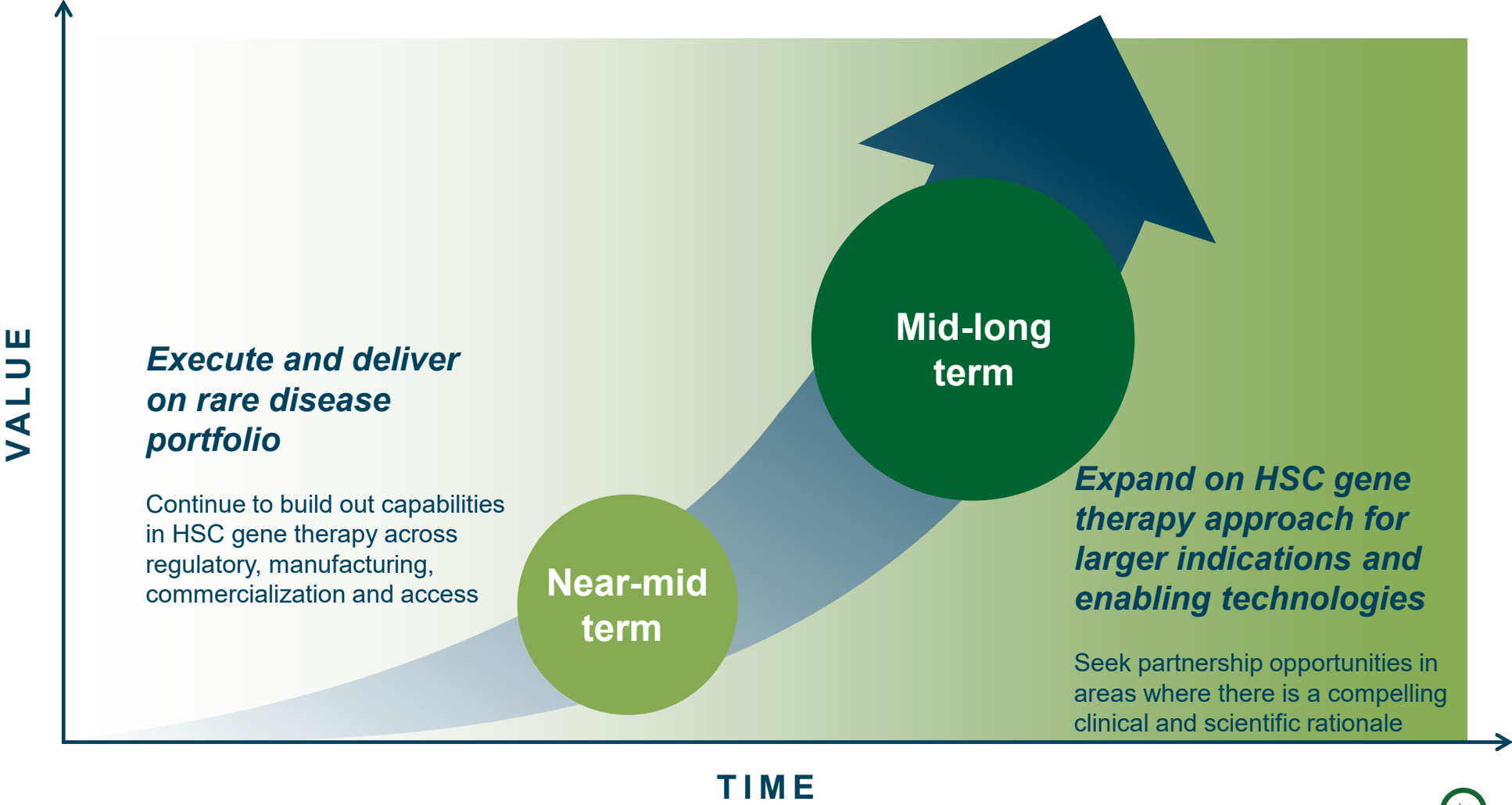


Frank Thomas
*President & Chief
Operating Officer*

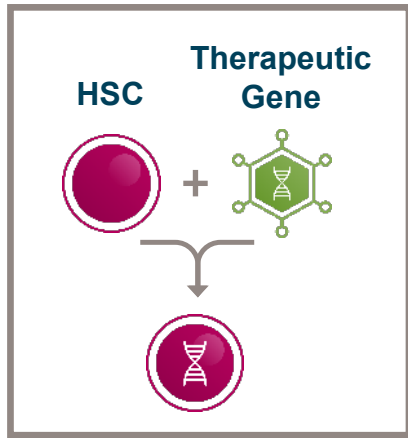


Leslie Meltzer, Ph.D.
Chief Medical Officer

Accelerating Long-term Growth and Value Creation By Expanding into Larger Indications



Where HSC Gene Therapy is Scientifically and Clinically Differentiated



**Clinical PoC in
MLD & MPS**

**Neurodegenerative
disorders
GRN-FTD**

**Multilineage
potential of HSCs**

**HSC-generated Tregs
Vectorized mAbs**

Clinical PoC in
Rare PIDs

Immunological
disorders

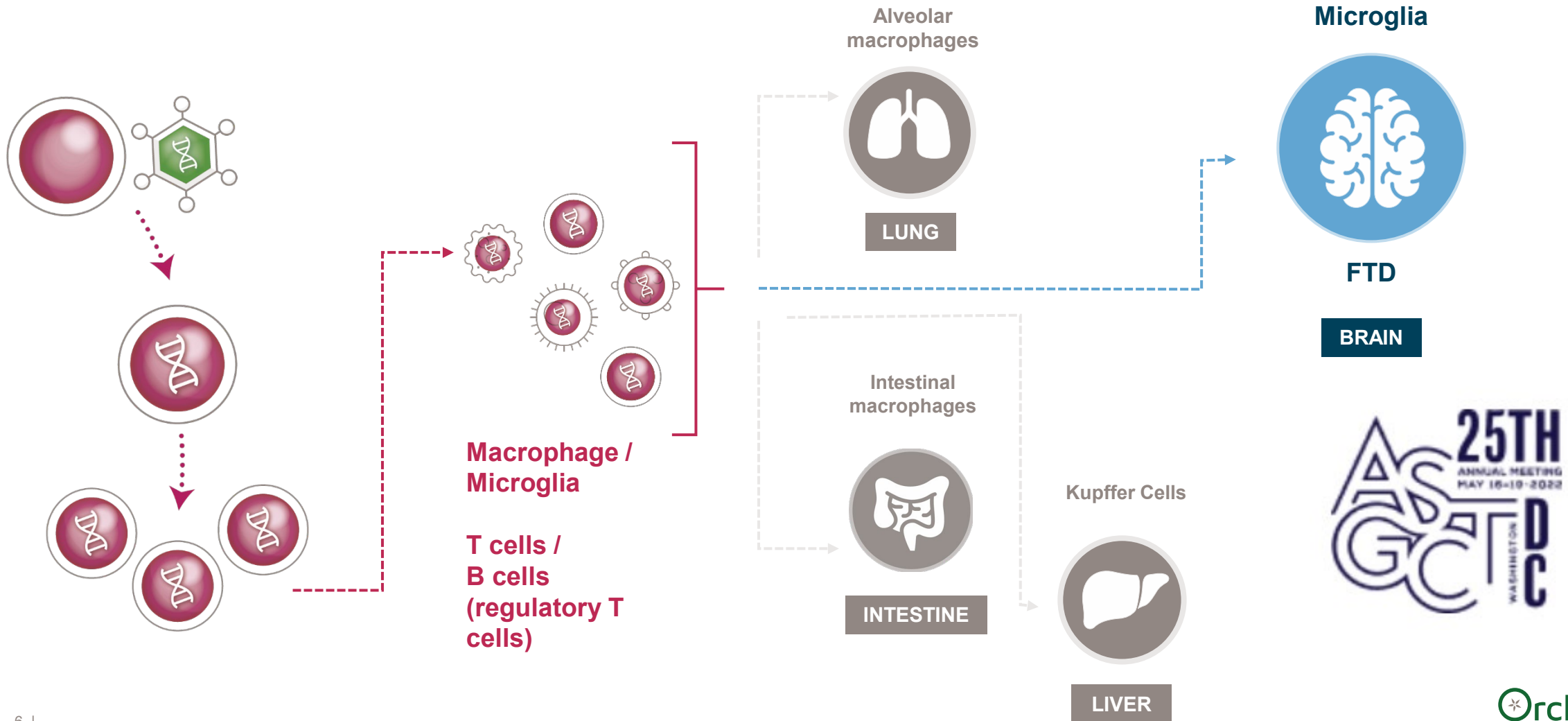
**NOD2- Crohn's
HAE**

Commercial Infrastructure

Manufacturing Innovations

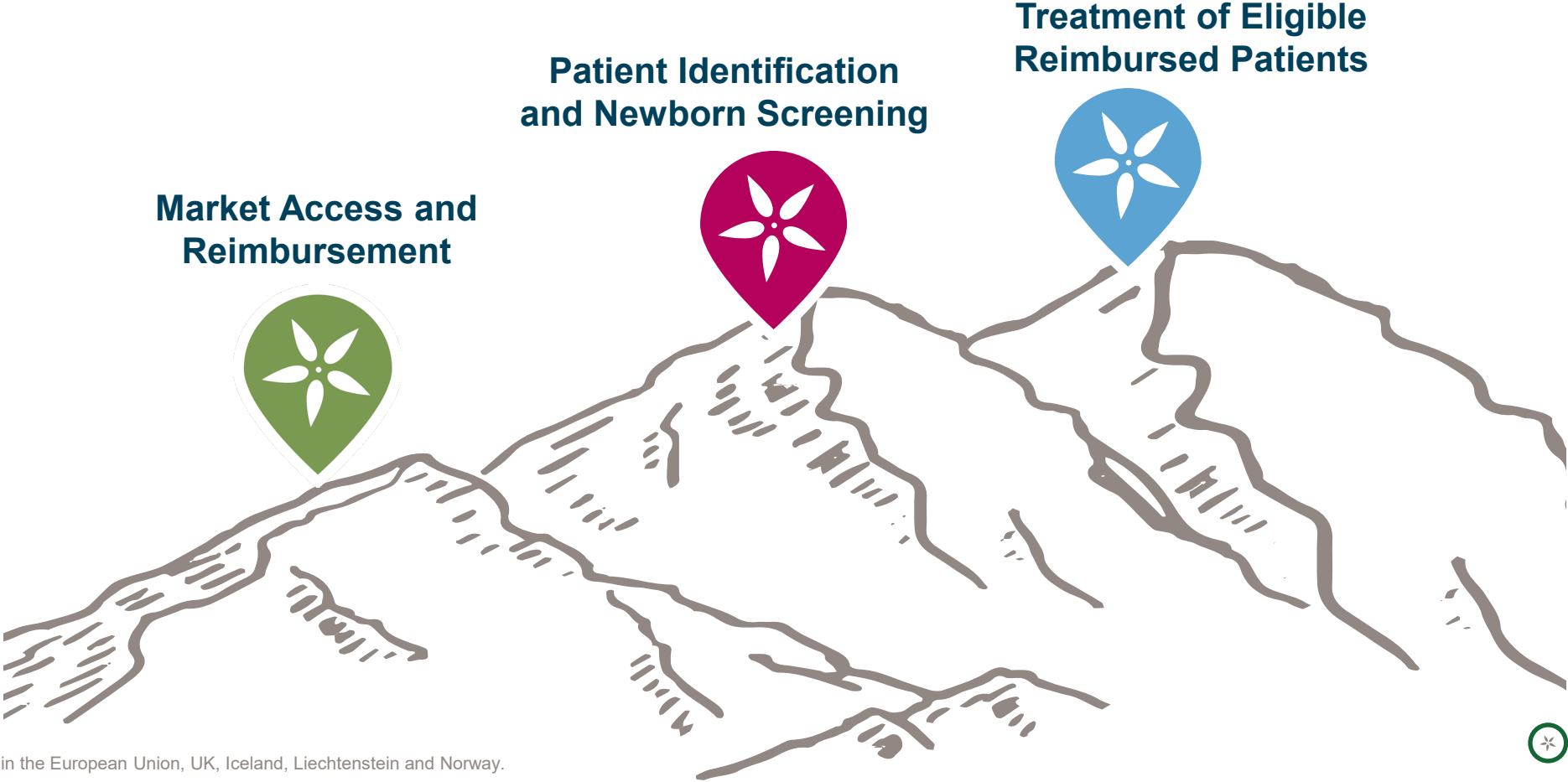
Enabling Technologies

The Power of HSC Gene Therapy: *Differentiation & Migration*



Commercializing Libmeldy

Strong Momentum for Libmeldy



Commercial Priorities to Maximize Libmeldy's Value

Market Access & Reimbursement

Reimbursement secured for all eligible MLD children

UK



Italy



Germany



- **France:** Reimbursed early access program secured
- **Nordics / Beneluxa / Spain:** HTA / reimbursement discussions underway

Newborn Screening



Expansion Opportunities

Expanded Footprint

Partnership

Regulatory Filings

Future Potential Launches

MLD US Regulatory & MPS Programs

Neurometabolic Rare Disease Programs Provide Platform Validation and Potential Near-term Milestones

Advancing U.S. regulatory discussions for OTL-200 (MLD)

- U.S. BLA submission, approval and launch over next 12-24 months



RMAT meeting for expected clinical package (June 2021)



Productive Type B CMC meeting (Nov 2021)



Clarity on mfg facility FDA inspection readiness (early 2022)



Treatment of patients in the U.S. on compassionate use basis (with EU CDMO manufacturing) (2021)



NEXT STEP: Pre-BLA submission meeting with FDA

Maturing next wave of neurometabolic programs to value-creating milestones

- OTL-203 (MPS-IH) pivotal trial initiation in 2023
- OTL-201 (MPS-IIIA) POC data by YE 2022

Libmeldy Platform Synergies



Manufacturing, distribution, supply chain



Regulatory learnings



Treatment sites and referral network

Q1 Financials, Business Development and Upcoming Milestones

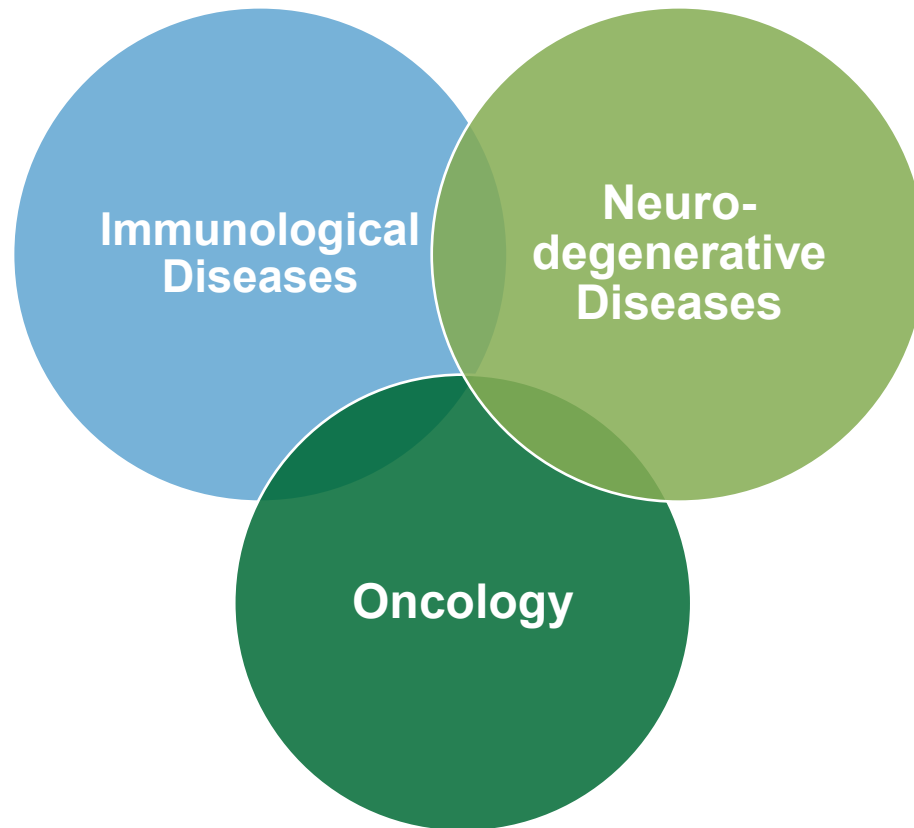
Key Financial Highlights with Cash Runway into 2024

<i>(in millions)</i>	Three Months Ended March 31,	
	2022	2021
Product revenue, net	\$5.1	—
Collaboration revenue	\$0.5	—
<i>Total revenues</i>	<i>\$5.6</i>	<i>—</i>
<i>Costs and operating expenses:</i>		
Cost of product sales	\$1.6	—
Research and development	\$28.2*	\$21.0M
Selling, general and administrative	\$13.3**	\$14.1M
<i>Total costs and operating expenses</i>	<i>\$43.1</i>	<i>\$35.1M</i>
<i>Loss from operations</i>	<i>\$37.6</i>	<i>\$35.1M</i>
Balance Sheet	As of 3/31/22	As of 12/31/21
Cash & investments	\$199.0	\$220.1
Long-term debt (notional amount)	\$33.0	\$33.0

*R&D includes one-time charges of \$4.3M related to the proposed restructuring and portfolio changes

**SG&A includes one-time charges of \$0.4M related to the proposed restructuring

Platform Provides Multiple Opportunities for Business Development



Partnerships in specific diseases

- **OTL-105** for HAE partnered with Pharming
- Leveraging ongoing programs in CNS (**FTD/ALS**) and colitis (**NOD2-Crohn's**)

Partnerships built on specific technologies

- **Antigen-specific Tregs** for autoimmune diseases
- **mAb vectorization technology** to target specific tumors or other targets

Runway Covers Multiple Anticipated Milestones of Significance to 2024

Spanning Commercialization and All Phases of Development

1H'22



Commercial

Libmeldy: Reach reimbursement agreement with at least two countries

- ✓ UK
- ✓ Italy
- ✓ Germany

2H'22



Development

OTL-200: Pre-BLA for MLD in 2H 2022; submission in late 2022 / early 2023

OTL-201: Report data from ongoing MPS-III A POC trial by year end

OTL-104: Report preclinical POC data for NOD2-CD

2023



Regulatory

OTL-200: Potential FDA approval by year end 2023

OTL-203: Initiate global registrational trial for MPS-IH by year end

2024



Preclinical

OTL-104: Submit IND filing in NOD2-CD

Libmeldy commercialization and revenue generation

Advance preclinical pipeline (OTL-105 for HAE, OTL-204 for GRN-FTD and work in Tregs)

Q&A