

UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): August 3, 2023

ORCHARD THERAPEUTICS PLC

(Exact name of Registrant as Specified in Its Charter)

England and Wales  
(State or Other Jurisdiction  
of Incorporation)

001-38722  
(Commission File Number)

Not Applicable  
(IRS Employer  
Identification No.)

245 Hammersmith Road  
London W6 8PW  
United Kingdom  
(Address of Principal Executive Offices; Zip Code)

Registrant's Telephone Number, Including Area Code: +44 (0) 203 808 8286

Not Applicable  
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
American Depositary Shares, each representing ten ordinary shares, nominal value £0.10 per share	ORTX	The Nasdaq Capital Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

**Item 2.02 Results of Operations and Financial Condition.**

On August 3, 2023, Orchard Therapeutics plc (the “Company”) announced its financial results for the quarter ended June 30, 2023 and other business updates. A copy of the press release is furnished as Exhibit 99.1 to this current report on Form 8-K (the “Report”).

**Item 7.01 Regulation FD Disclosure.**

On August 3, 2023, the Company updated its corporate presentation for use in meetings with investors, analysts and others. A copy of the presentation is furnished as Exhibit 99.2 to this Report. The Company undertakes no obligation to update, supplement or amend the materials attached hereto as Exhibit 99.2.

*The information contained in Item 2.02, Item 7.01, Exhibit 99.1 and Exhibit 99.2 shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.*

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits.

<b>Exhibit Number</b>	<b>Description</b>
99.1	<a href="#">Press release, dated August 3, 2023</a>
99.2	<a href="#">Presentation of Orchard Therapeutics plc</a>
104	Cover page interactive data file (embedded within the Inline XBRL document)

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**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

**ORCHARD THERAPEUTICS PLC**

Date: August 3, 2023

By: /s/ Frank E. Thomas

Frank E. Thomas

President and Chief Operating Officer

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**Orchard Therapeutics Completes Submission of Biologics License Application for OTL-200 in MLD to U.S. FDA**

*Reported \$6.6M in Q2'23 Libmeldy net sales, representing the highest quarter to date*

*\$34.0M of additional capital from second closing of strategic financing extends runway to mid-2025*

*Four MLD patients identified from ~150,000 newborns screened in prospective studies suggests significantly higher incidence than previously estimated in the medical literature*

*Six presentations at ASGCT demonstrate the ability of HSC gene therapy to address neurometabolic and CNS disorders, as well as larger indications*

*Company to host conference call and live webcast today at 8:00 a.m. EDT*

BOSTON and LONDON, August 3, 2023, (GLOBE NEWSWIRE) -- Orchard Therapeutics (Nasdaq: ORTX), a global gene therapy leader, today announced several business accomplishments along with its financial results for the quarter ended June 30, 2023.

"With the completion of the rolling BLA submission for OTL-200 to the FDA, we are now one significant step closer to bringing this important therapy to families in the U.S. affected by MLD who currently have no treatment options beyond supportive care," said Bobby Gaspar, M.D., Ph.D., chief executive officer. "We look forward to working with the agency throughout the filing and review process and expect to hear from the FDA regarding acceptance of the BLA in the third quarter of this year."

Dr. Gaspar continued, "In addition, the \$34 million in proceeds from the second closing of our strategic financing ensures we are well-capitalized to progress U.S. launch preparations, continue investing in initiatives aimed at accelerating commercial growth in Europe, and advance our next-in-line neurometabolic programs in MPS disorders. The next 12 months have the potential to provide Orchard Therapeutics several breakout opportunities as we work to cement our leadership position in the HSC gene therapy field."

**BLA Submission Completed for OTL-200 in the U.S.**

The company has completed the rolling submission of its Biologics License Application (BLA) to the U.S. Food and Drug Administration (FDA) for OTL-200, in children with early-onset metachromatic leukodystrophy (MLD). OTL-200 previously received both Rare Pediatric Disease (RPD) and Regenerative Medicine Advanced Therapy (RMAT) designations from the FDA. Orchard Therapeutics has requested priority review, which if granted, would put OTL-200 on track for a potential U.S. approval in the first half of 2024.

OTL-200 is approved as Libmeldy<sup>®</sup> (atidarsagene autotemcel) by the European Commission (EC) and Medicines and Healthcare products Regulatory Agency (MHRA). The clinical development program for Libmeldy comprises data spanning 39 children and encompassing more than 10 years follow-up in the earliest treated patients.

**Second Closing of Strategic Financing Resulted in \$34.0M of New Capital**

In June 2023, the company completed the second closing of its previously announced strategic financing, resulting in \$34.0 million of new capital before placement agent and transaction fees, bringing the total raised to \$68.0 million. These securities were sold at a significant premium to the company's share price on the date of issuance. Orchard Therapeutics expects funding from the first and second closing to provide cash runway to mid-2025.

The company could bring in up to an additional \$120 million in proceeds in 2024 at a price of \$11.00 per American Depositary Share (ADS) following potential U.S. approval of OTL-200 if all warrants sold as part of the securities purchase agreement are exercised by participating investors.

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## Libmeldy Commercial Momentum and Newborn Screening Updates

- Orchard Therapeutics has secured reimbursement agreements for Libmeldy in four additional European countries in 2023. Most recently, The Decision Forum for New Approaches in Norway agreed to authorize Libmeldy for all eligible patients with early-onset MLD. Eligible MLD patients in Norway will be referred to the company's treatment center in Sweden, once it is fully qualified.
- To date, nine prospective newborn screening studies are active throughout Europe, the U.S. and the Middle East. By the end of 2023, more than 200,000 newborns are expected to have been screened.
  - Four confirmed cases of MLD have been identified following the screening of approximately 150,000 newborns globally as of June 30.
  - These preliminary findings suggest an incidence rate closer to one in 50,000 live births versus prior estimates in medical literature of one in 100,000.
  - Multiple eligible MLD patients identified in these studies have been or are expected to be treated commercially with Libmeldy in 2023, continuing to add to the pipeline of potential patients.
- In addition, efforts are underway to enable universal newborn screening for MLD, notably:
  - In the U.S., the Illinois state legislature passed the Newborn Metabolic Screening Act, also known as SB67, which requires the state Department of Public Health to screen all newborns for MLD. The bill was signed by the governor last week, and it is expected Illinois will start the process of implementing statewide screening for MLD this year.
  - In Germany, following the positive identification of three newborns with MLD from a prospective study, progress has been made toward an application for nationwide screening.

Chief Commercial Officer Braden Parker added, "Since launch, we have generated nearly \$26 million in total revenue for Libmeldy in Europe and continue to be successful treating eligible patients in countries with reimbursement agreements, while expanding our commercial reach geographically. We are proud to support newborn screening research for MLD to generate the data necessary to enable the implementation of universal MLD screening, which will help ensure timely diagnosis and treatment referral so children and their families can be offered the opportunity for the best possible outcomes. The data generated thus far from these studies suggests a significantly higher incidence than was previously estimated in the literature and may lead to a greater commercial opportunity for Libmeldy. We remain on track to meet our goal of year-over-year revenue growth in 2023, and with the completion of our rolling BLA submission for OTL-200 in MLD, we are ramping up our U.S. pre-launch activities."

## Recent Data Presentations

Six presentations demonstrating the company's leadership in neurometabolic and CNS disorders, as well as the ability of hematopoietic stem cell (HSC) gene therapy to address larger indications were featured at the 26th Annual Meeting of the American Society of Gene and Cell Therapy (ASGCT) in Los Angeles. The totality of the data highlights the ability of gene modified HSCs to migrate into multiple organ systems including bone, central nervous system and gastrointestinal tract and deliver therapeutic enzymes and proteins locally to effect disease correction.

Data highlights included:

- Additional OTL-203 proof-of-concept data demonstrated extensive metabolic correction in the skeletal system of patients with mucopolysaccharidosis type I Hurler syndrome (MPS-IH) resulting in normal growth rates, skeletal remodeling, improvement in joint function and progressive acquisition of motor skills.
  - Updated OTL-201 data from the ongoing proof-of-concept study in mucopolysaccharidosis type IIIA (MPS-III A) patients showed additional favorable neurocognitive outcomes compared to disease natural history with median follow-up of 2.5 years.
  - The first preclinical data for OTL-204 highlighted the ability of HSC gene therapy to express progranulin in the CNS, modulate neuroinflammation, and normalize predictive biomarkers in the progranulin form of frontotemporal dementia (GRN-FTD).
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- Preclinical proof-of-concept data showed the therapeutic potential of OTL-104 for nucleotide-binding oligomerization domain containing protein 2 (NOD2) Crohn's, a severe and treatment-refractory form of the disease.
- *In vivo* data demonstrated the feasibility of utilizing HSC gene therapy to provide stable and targeted immunotherapy, through the ability of HSCs to differentiate into T regulatory (Treg) cells engineered to express chimeric antigen-specific receptors (CAR). This approach combines the proven durability of HSC gene therapy with the specific suppressive activity of CAR-Treg cells as a potential one-time treatment for autoimmune disorders.

### Remaining 2023 Expected Milestones

Orchard Therapeutics has outlined the following key milestones expected for the remainder of 2023:

- Libmeldy: Continue to establish additional qualified treatment centers and expand newborn screening activities throughout Europe, the U.S. and the Middle East.
- OTL-200 for MLD: Secure acceptance of the BLA submission by FDA in advance of a potential U.S. approval in the first half of 2024.
- OTL-203 for MPS-IH: Initiate a global, multi-center registrational trial by year end.
- OTL-104 for NOD2-Crohn's disease: Commence IND- and CTA-enabling studies in the second half of 2023, ahead of a potential filing in 2025.
- Advance the company's other pre-clinical programs, which includes OTL-204 in the progranulin form of FTD and OTL-105 partnered with and funded by Pharming Group N.V. in hereditary angioedema (HAE).

### Second Quarter 2023 Financial Results

Total revenue was \$7.3 million for the three months ended June 30, 2023, comprising \$6.6 million in Libmeldy revenue and \$0.7 million in collaboration revenue. This compares to total revenue of \$4.4 million, comprising \$3.2 million in Libmeldy revenue, \$0.6 million of Strimvelis revenue and \$0.6 million in collaboration revenue in the same period in 2022. Libmeldy revenue increased 111% compared to the corresponding period in the prior year. The cost of product sales, which includes the cost of manufacturing, royalties to third parties and non-cash amortization, was \$2.2 million during the second quarter of 2023 compared to \$1.1 million in the same period in 2022. The company reported gross margins of approximately 70% for the three months ended June 30, 2023.

For the three months ended June 30, 2023, the company reported research and development (R&D) expenses of \$16.7 million, compared to \$22.0 million in the same period in 2022, a decrease of 24%. The decline primarily resulted from the reprioritizing the company's portfolio in 2022 and the realignment of its R&D organization with a more focused strategy. R&D expenses include the costs of clinical trials and pre-clinical work on the company's portfolio of investigational gene therapies, as well as costs related to regulatory, manufacturing, license fees and milestone payments under the company's agreements with third parties, and personnel costs to support these activities.

For the three months ended June 30, 2023, the company reported selling, general and administrative (SG&A) expenses of \$11.0 million compared to \$13.7 million in the same period in 2022, a decrease of 20%. The decline resulted primarily from the realization of savings in SG&A expenditures from the restructuring announced in March 2022.

Loss from operations was \$22.6 million in the three months ended June 30, 2023, compared to a loss from operations of \$32.4 million in the corresponding period of 2022, a decrease of 30%. The reduction resulted from a combination of higher Libmeldy product sales as well as lower operating expenses. The company expects its operating loss will continue to decline as Libmeldy revenue grows in Europe combined with a potential commercial launch in the U.S. in 2024.

Total other income was \$10.3 million for the three months ended June 30, 2023. The company reported an \$8.2 million gain relating to the fair value remeasurements of warrants and other liabilities that were issued in connection with the first and second closings of the strategic financing entered into in March 2023. The

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outstanding warrants will continue to be remeasured in future periods resulting in non-cash gains or losses based on a number of valuation assumptions on the underlying financial instruments.

Net loss was \$12.3 million for the three months ended June 30, 2023, compared to \$51.1 million in the same period in 2022, a reduction of 76%. The company had approximately 227.2 million ordinary shares, equivalent to 22.7 million American Depositary Shares, outstanding as of June 30, 2023.

The company expects its cash used to fund operations in 2023 to decline as compared to 2022 due to an anticipated increase in revenue from Libmeldy product sales and ongoing management of operating expenses.

As of June 30, 2023, the company reported cash, cash equivalents and investments of approximately \$155.0 million, with \$27.9 million of debt outstanding, compared to \$148.0 million and \$32.4 million of debt outstanding as of December 31, 2022. Orchard Therapeutics expects that its existing cash, cash equivalents and investments will fund its anticipated operating, debt service and capital expenditure requirements to mid-2025.

#### **Conference Call and Webcast**

The company will host a conference call and live webcast today at 8:00 a.m. EDT to review business updates and its second quarter 2023 financial results.

A live webcast will be available under "News & Events" in the Investors & Media section of the company's website at [www.orchard-tx.com](http://www.orchard-tx.com). Analysts wishing to participate in the question and answer session should use this link to register. A replay of the webcast will be archived on the Orchard website following the presentation.

#### **About Libmeldy / OTL-200**

Libmeldy (atidarsagene autotemcel), also known as OTL-200, has been approved by the European Commission for the treatment of MLD in eligible early-onset patients characterized by biallelic mutations in the ARSA gene leading to a reduction of the ARSA enzymatic activity in children with i) late infantile or early juvenile forms, without clinical manifestations of the disease, or ii) the early juvenile form, with early clinical manifestations of the disease, who still have the ability to walk independently and before the onset of cognitive decline. Libmeldy is the first therapy approved for eligible patients with early-onset MLD.

The most common adverse reaction attributed to treatment with Libmeldy was the occurrence of anti-ARSA antibodies. In addition to the risks associated with the gene therapy, treatment with Libmeldy is preceded by other medical interventions, namely bone marrow harvest or peripheral blood mobilization and apheresis, followed by myeloablative conditioning, which carry their own risks. During the clinical studies of Libmeldy, the safety profiles of these interventions were consistent with their known safety and tolerability.

For more information about Libmeldy, please see the Summary of Product Characteristics (SmPC) available on the European Medicines Agency (EMA) website.

Libmeldy is approved in the European Union, UK, Iceland, Liechtenstein and Norway. OTL-200 is an investigational therapy in the U.S.

Libmeldy was developed in partnership with the San Raffaele-Telethon Institute for Gene Therapy (SR-Tiget) in Milan, Italy.

#### **About Orchard Therapeutics**

At Orchard Therapeutics, our vision is to end the devastation caused by genetic and other severe diseases. We aim to do this by discovering, developing and commercializing new treatments that tap into the curative potential of hematopoietic stem cell (HSC) gene therapy. In this approach, a patient's own blood stem cells are genetically modified outside of the body and then reinserted, with the goal of correcting the underlying cause of disease in a single treatment.

In 2018, the company acquired GSK's rare disease gene therapy portfolio, which originated from a pioneering collaboration between GSK and the San Raffaele Telethon Institute for Gene Therapy in Milan,

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Italy. Today, Orchard is advancing a pipeline spanning pre-clinical, clinical and commercial stage HSC gene therapies designed to address serious diseases where the burden is immense for patients, families and society and current treatment options are limited or do not exist.

Orchard has its global headquarters in London and U.S. headquarters in Boston. For more information, please visit [www.orchard-tx.com](http://www.orchard-tx.com), and follow us on Twitter and LinkedIn.

#### **Availability of Other Information About Orchard**

Investors and others should note that Orchard communicates with its investors and the public using the company's website ([www.orchard-tx.com](http://www.orchard-tx.com)), the investor relations website ([ir.orchard-tx.com](http://ir.orchard-tx.com)), and on social media (Twitter and LinkedIn), including but not limited to investor presentations and investor fact sheets, U.S. Securities and Exchange Commission (SEC) filings, press releases, public conference calls and webcasts. The information that Orchard posts on these channels and websites could be deemed to be material information. As a result, Orchard encourages investors, the media, and others interested in Orchard to review the information that is posted on these channels, including the investor relations website, on a regular basis. This list of channels may be updated from time to time on Orchard's investor relations website and may include additional social media channels. The contents of Orchard's website or these channels, or any other website that may be accessed from its website or these channels, shall not be deemed incorporated by reference in any filing under the Securities Act of 1933.

#### **Forward-Looking Statements**

This press release contains 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.

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**Condensed Consolidated Statements of Operations Data**  
(In thousands, except share and per share data)  
(Unaudited)

	Three Months Ended June 30,	
	2023	2022
Product revenue, net	\$ 6,651	\$ 3,781
Collaboration revenue	663	587
Total revenue	7,314	4,368
Costs and operating expenses:		
Cost of product revenue	2,189	1,122
Research and development	16,695	21,965
Selling, general and administrative	10,992	13,730
Total costs and operating expenses	29,876	36,817
Loss from operations	(22,562)	(32,449)
Other income (expense):		
Interest income	1,391	213
Interest expense	(975)	(672)
Changes in fair value of PIPE warrant and unit liabilities	8,206	—
Other income (expense), net	1,658	(18,227)
Total other income (expense), net	10,280	(18,686)
Net loss before income taxes	(12,282)	(51,135)
Income tax benefit (expense)	(25)	219
Net loss attributable to ordinary shareholders	\$ (12,307)	\$ (50,916)
Net loss per ordinary share, basic and diluted	\$ (0.07)	\$ (0.40)
Weighted average ordinary shares outstanding, basic and diluted	189,286,329	127,854,596

**Condensed Consolidated Balance Sheet Data**  
(In thousands)  
(Unaudited)

	June 30, 2023	December 31, 2022
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 38,273	\$ 68,424
Marketable securities	112,468	75,326
Accounts receivable	9,547	8,467
Inventory	6,937	3,400
Prepaid expenses and other current assets	5,540	6,586
Research and development tax credit receivable	8,525	5,942
Total current assets	181,290	168,145
Non-current assets:		
Operating lease right-of-use-assets	21,018	22,774
Property and equipment, net	7,808	8,138
Research and development tax credit receivable, net of current portion	2,101	—
Restricted cash	4,215	4,215
Intangible assets, net	3,474	3,560
Other assets	12,396	12,075
Total non-current assets	51,012	50,762
Total assets	\$ 232,302	\$ 218,907
<b>Liabilities and Shareholders' Equity</b>		
Current liabilities:		
Accounts payable	\$ 6,950	\$ 9,318
Accrued expenses and other current liabilities	33,786	34,437
Deferred revenue, current	752	959
Operating lease liabilities	6,600	6,424
Notes payable, current	9,429	9,429
Total current liabilities	57,517	60,567
Notes payable, long-term	18,440	22,991
Deferred revenue, net of current portion	10,819	10,315
Operating lease liabilities, net of current portion	16,044	19,246
PIPE warrant liabilities	12,266	—
Other long-term liabilities	8,169	7,524
Total liabilities	123,255	120,643
Total shareholders' equity	109,047	98,264
Total liabilities and shareholders' equity	\$ 232,302	\$ 218,907

**Contact**

Benjamin Navon  
+1 857-248-9454  
Benjamin.Navon@orchard-tx.com





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

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# Forward-looking Statements

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## Strong Operational Execution in 1H of 2023

**Growing Libmeldy Revenue**

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

**Progressing Universal Newborn Screening**

*Four cases of MLD identified following ~150k newborns screened*

**Moving OTL-200 Toward U.S. Approval**

*BLA submission completed; potential approval in 1H'24*

**Initiating Pivotal Study for OTL-203 in MPS-IH**

*Global RCT in 40 patients following IND clearance by FDA*

**Expanding into Larger Indications**

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

Validation in Rare Diseases	Larger Indications	Future Applications
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**OTL-200**  
MLD (US)

**OTL-203**  
MPS-I

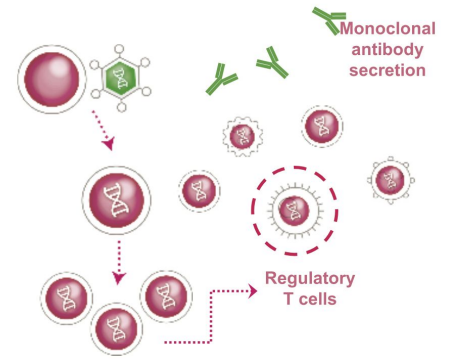
**OTL-201**  
MPS-III A

Other undisclosed programs

**OTL-104**  
NOD2-Crohn's

**OTL-204**  
FTD

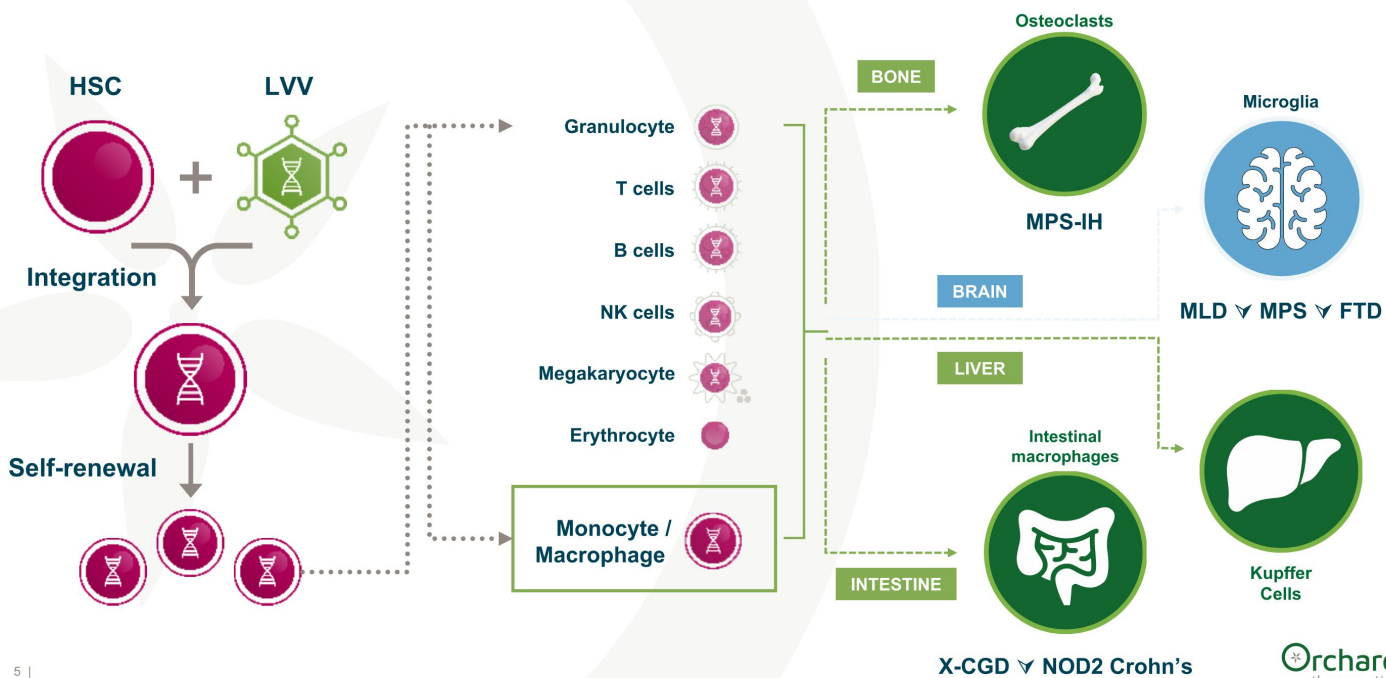
**OTL-105**  
HAE



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



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



# 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

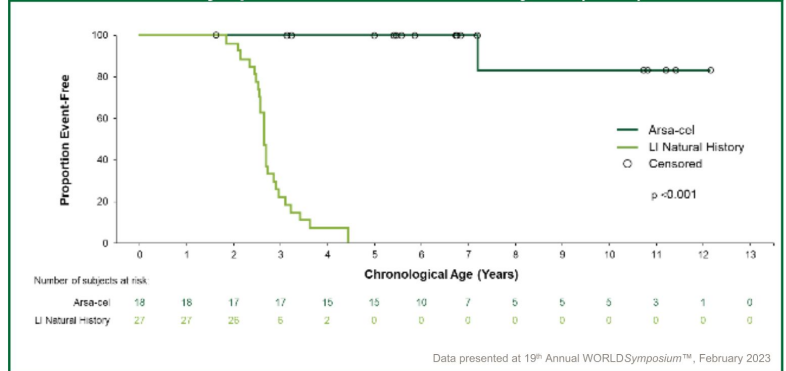


Age 9, advanced disease

## 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<sup>1</sup>

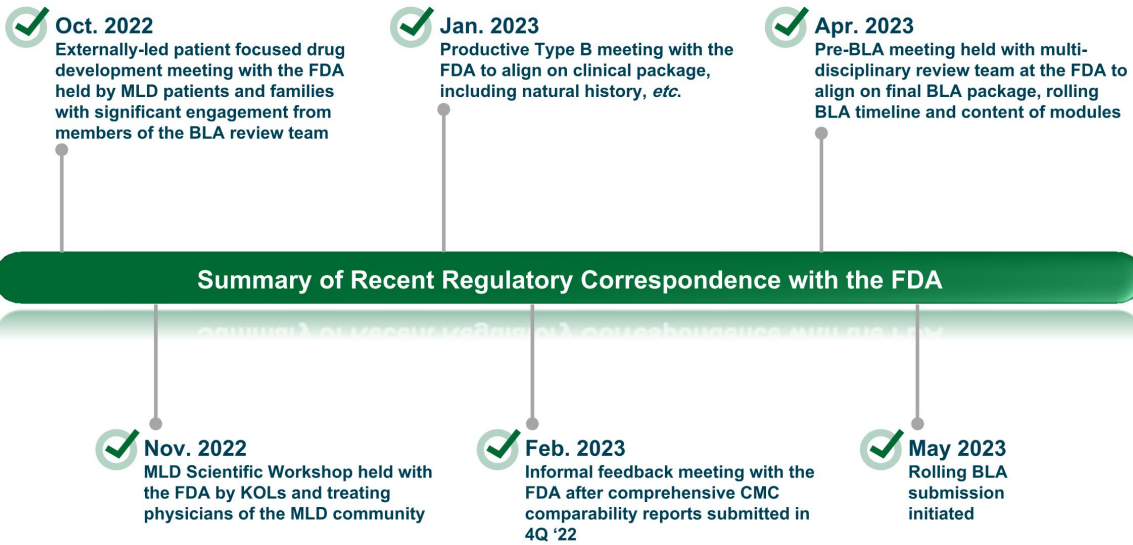
Kaplan-Meier Plot of Severe Motor Impairment-Free Survival Pre-Symptomatic Late Infantile Subjects (n=18)



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.

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

## BLA Submission and Approval Timeline



### Rolling BLA Submission Completed

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

# 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

EU Revenue Growth

U.S. Launch Prep

ROW Expansion Opportunities

# Expanding Reimbursed Access Throughout Europe

## Access



## Reimbursement

### Secured for all eligible MLD children

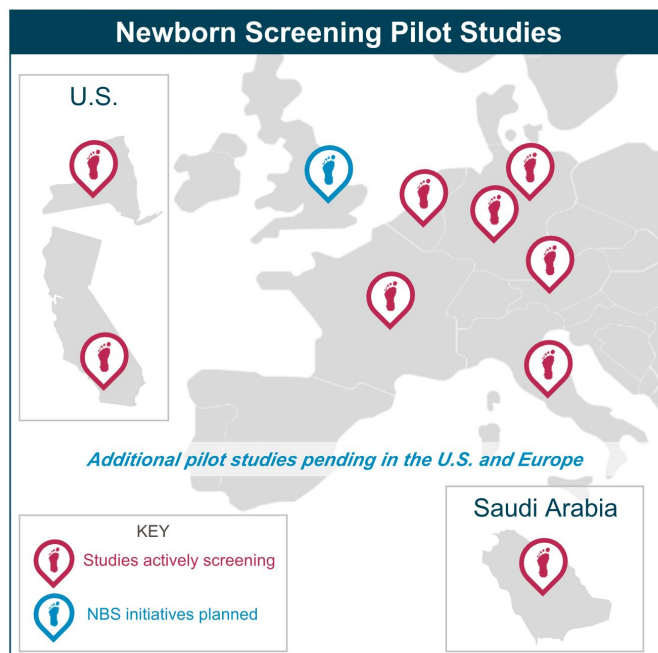


Reimbursed early access (e.g., France)

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

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

# Implementing Newborn Screening to Identify MLD Patients

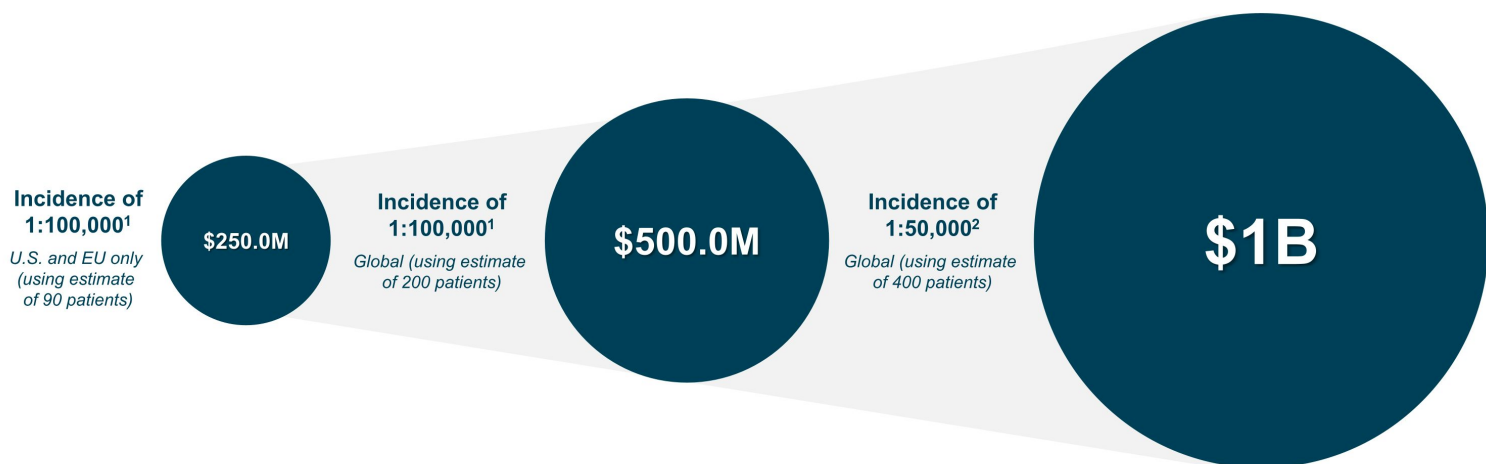


**4** Confirmed cases of MLD following screening of **~150k** newborns

- ✓ 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



# 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<sup>3</sup>

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.



# Steady Libmeldy Revenue Growth Since Launch



Patients from 6 different countries treated commercially at 4 of 5 qualified centers



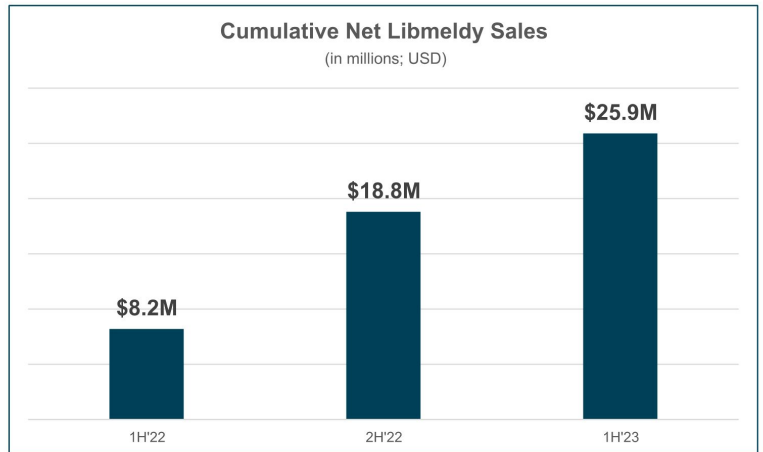
Reimbursement via access agreements, cross-border and named patient pathways



Average vein-to-vein time of 55 days with 100% success in production



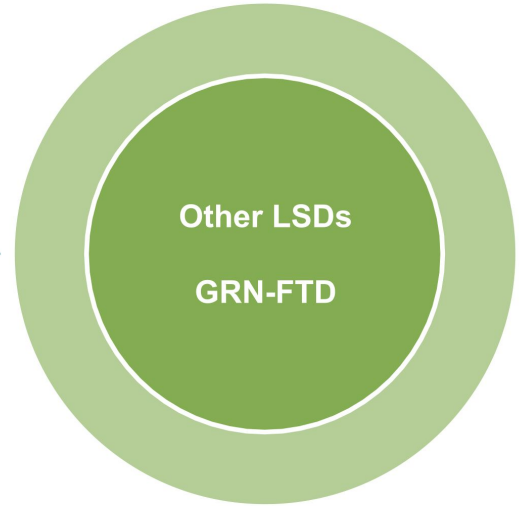
Company on track for year-over-year revenue growth



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



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

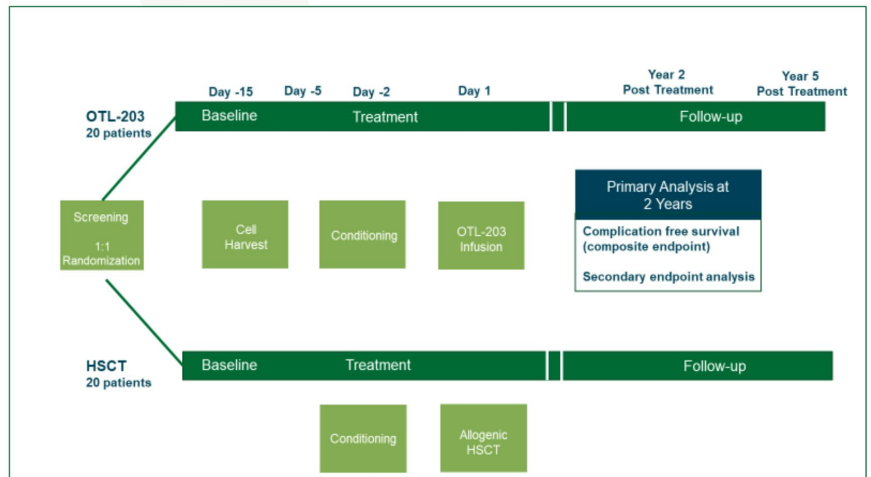


PLATFORM  
SYNERGIES

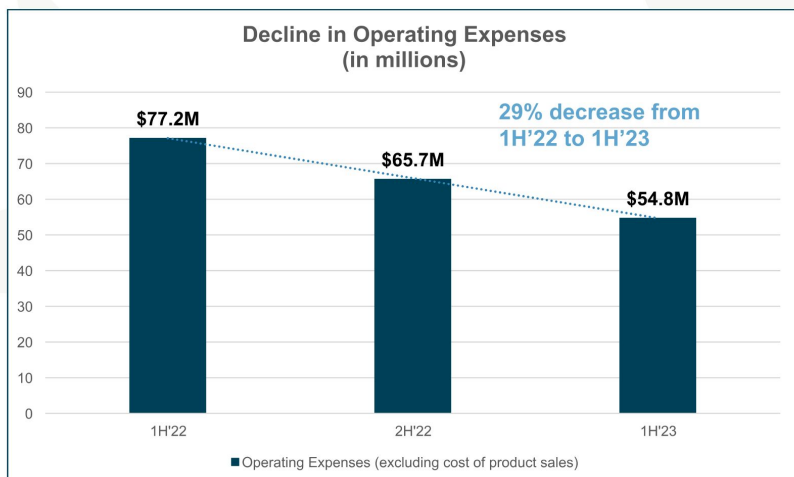
Regulatory	Supply Chain
Manufacturing	Treatment Sites
Distribution	Referral Networks

# 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



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



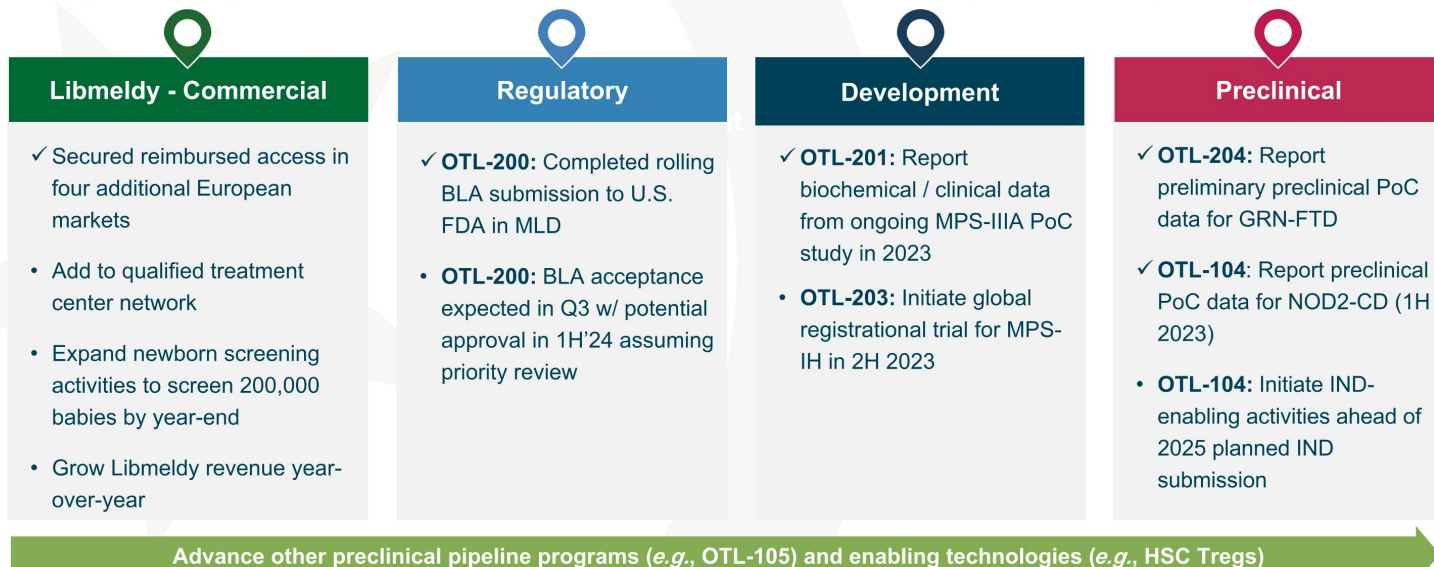
- Anticipated year-over-year increase in Libmeldy product sales
- Ongoing management of operating expenses
- Annual burn rate expected to continue declining in 2023 vs. 2022

## Summary of Q2'23 Financial Results

Statement of Operations:	Three Months Ended June 30		
	2023	2022	% Change
Libmeldy product sales	\$6.6M	\$3.2M	+111%
Strimvelis product sales	-	\$0.6M	-
Collaboration revenue	\$0.7M	\$0.6M	+13%
<b>Total revenues</b>	<b>\$7.3M</b>	<b>\$4.4M</b>	<b>+67%</b>
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%
<b>Total costs and operating expenses</b>	<b>\$29.9M</b>	<b>\$36.8M</b>	<b>-19%</b>
Loss from operations	\$22.6M	\$32.4M	-30%
<b>Balance Sheet:</b>			
Ending cash and investments	\$155.0M	\$175.2M	-12%
Ending ADS outstanding	22.7M	12.6M*	+80%

# Executing on Key Corporate Milestones

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



# Strategic Anchors Represent Breakout Opportunities for Orchard



All based on a HSC GT scientific and clinical platform