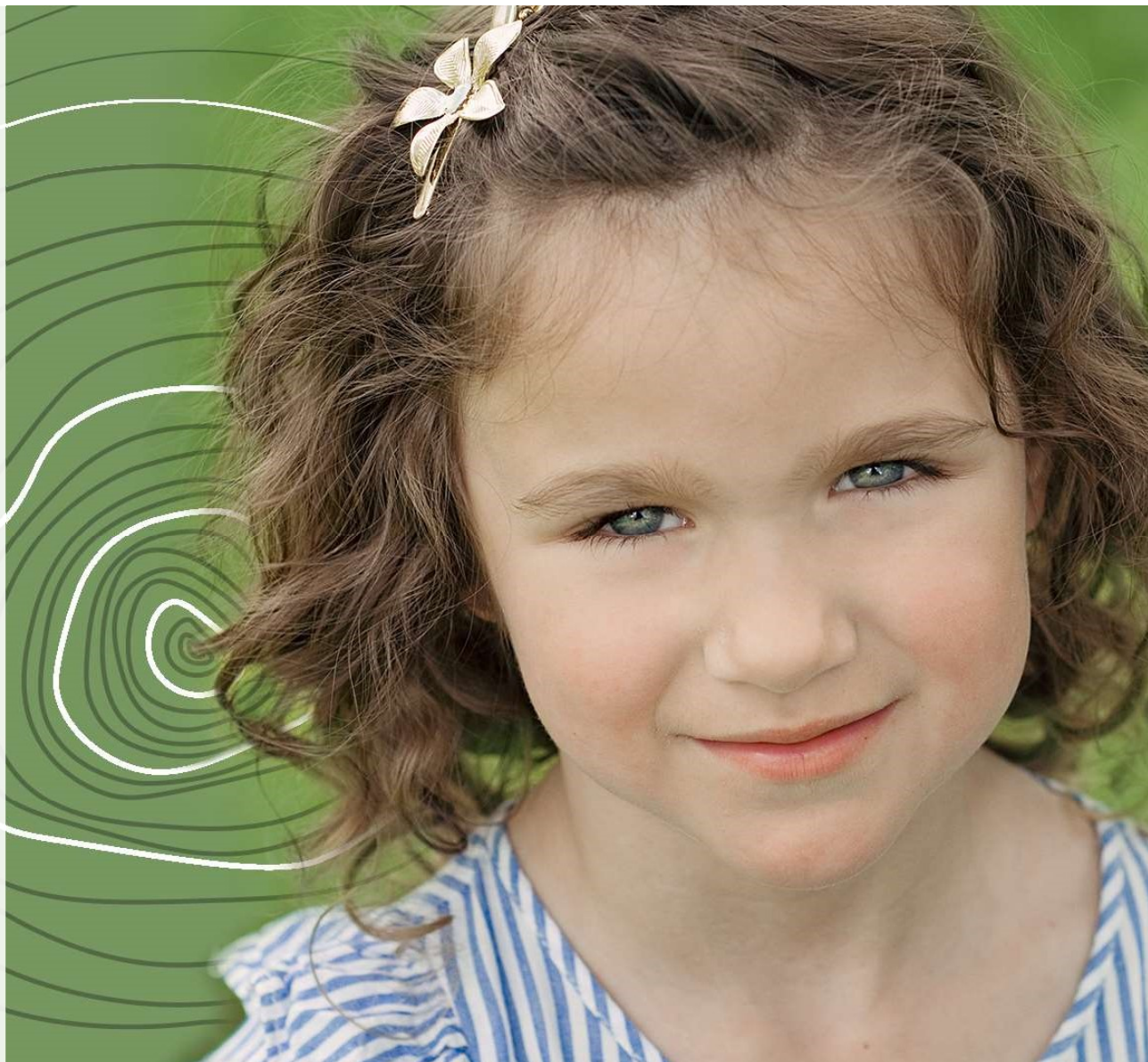




**Dedicated to  
Transforming the  
Lives of Patients  
Through Innovative  
Gene Therapies**

January 13 - 15, 2020





# Forward Looking Statements

Certain information set forth in this presentation and in statements made orally during this presentation contains “forward-looking statements”. Except for statements of historical fact, information contained herein constitutes forward-looking statements and includes, but is not limited to, the Company’s expectations regarding: (I) the safety and efficacy of its product candidates; (II) the expected development of the Company’s business and product candidates; (III) the timing of regulatory submissions for approval of its product candidates; (IV) the timing of interactions with regulators and regulatory submissions related to ongoing and new clinical trials for its product candidates; (V) the timing of announcement of clinical data for its product candidates and the likelihood that such data will be positive and support further clinical development and regulatory approval of these product candidates; (VI) the likelihood of approval of such product candidates by the applicable regulatory authorities; (VII) execution of the Company’s vision and growth strategy, including with respect to global growth; and (VIII) projected financial performance and financial condition, including the sufficiency of the Company’s cash and cash equivalents to fund operations in future periods and future liquidity, working capital and capital requirements. 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, which may cause actual performance and financial results in future periods to differ materially from any projections of future performance or result expressed or implied by such forward-looking statements. You are cautioned not to place undue reliance on forward-looking statements. These statements are subject to a variety of 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. For additional disclosure regarding these and other risks faced by the Company, see the disclosure contained in the Company’s public filings with the U.S. Securities and Exchange Commission (the “SEC”), including in the Company’s annual report on Form 20-F filed with the SEC on March 22, 2019, 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.





**Global gene therapy  
company**

**Dedicated to  
transforming the lives  
of patients with rare  
diseases**

**Focused today on  
ex-vivo autologous HSC  
gene therapy**

 **Orchard**  
therapeutics™

THE ORCHARD THERAPEUTICS STORY

# Strong Momentum – Transformative Year Ahead

**1**

**Strong  
Fundamentals**

**2**

**Powerful Platform  
Approach**

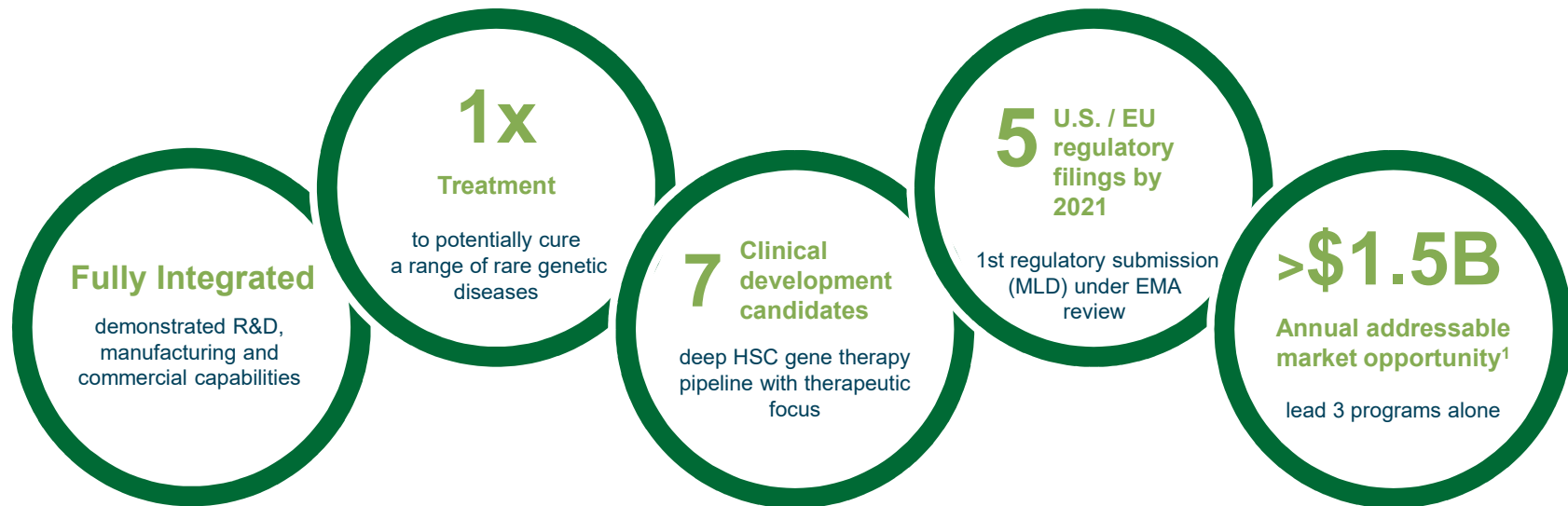
**3**

**Commercial  
Ready**

**4**

**Our  
Future**

# Compelling Fundamentals Driving Near and Long-term Growth



***Highly leverageable platform approach to gene therapy;  
potential to address numerous rare diseases***

**Strong balance sheet (~\$325M as of YE 2019) to fund the business into the second half of 2021**

# One of the Deepest Pipelines in Gene Therapy

	Preclinical	Clinical proof of concept	Registrational trial	Commercialization	Next expected milestone	Designations
<b>Neurometabolic disorders</b>						
OTL-200	MLD				MAA decision BLA late 2020 / early 2021	RPD
OTL-203	MPS-I				Interim POC data - 2020	
OTL-201	MPS-IIIA				Interim POC data - 2020	RPD
OTL-202	MPS-IIIB					
<b>Primary immune deficiencies</b>						
Strimvelis®	ADA-SCID					RPD
OTL-101	ADA-SCID				Initiate rolling BLA 1H 2020	RPD, BKT
OTL-103	WAS				MAA & BLA submissions 2021	RPD, RMAT
OTL-102	X-CGD					
<b>Blood disorders</b>						
OTL-300	TDT					PRIME

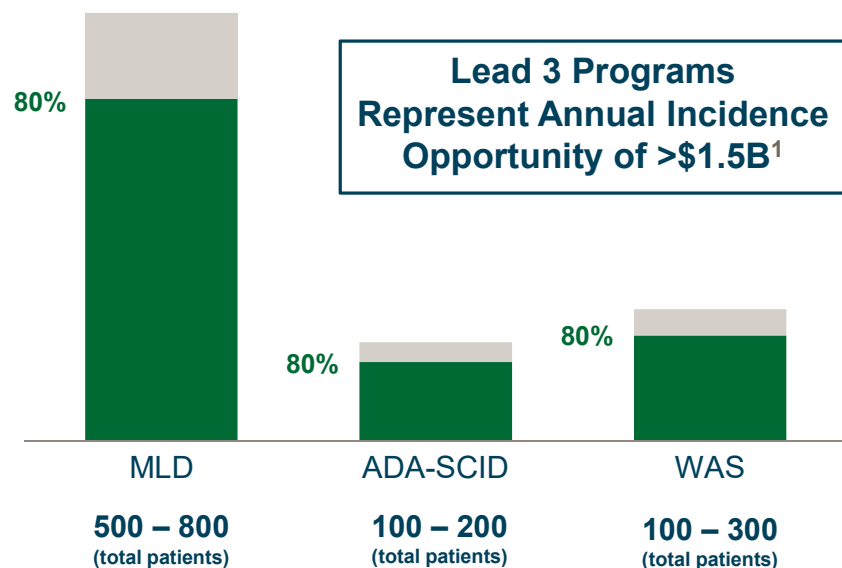
Several additional research and preclinical programs under development

RPD Program with Rare Pediatric Disease Designation; eligible for a Priority Review Voucher | BKT Breakthrough Therapy Designation  
PRIME Priority Medicine (PRIME) Designation | RMAT Regenerative Medicine Advanced Therapy

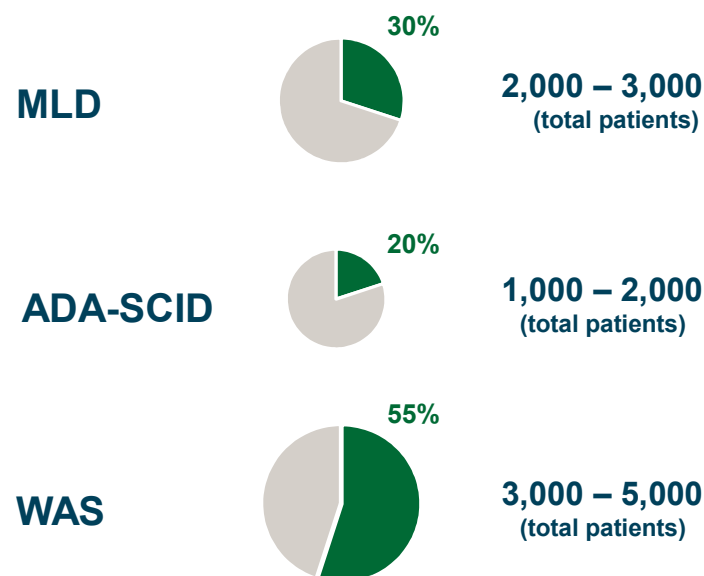
# Building a Scalable Business in Rare Diseases

■ Ineligible  
■ Eligible

## Annual Incidence



## Prevalence



<sup>1</sup>Based on target label and pricing of recent gene therapy analogs

Incidence / prevalence figure estimates based on available literature, population data and in-house estimates, in countries where rare disease therapies are typically reimbursed.

Higher incidence rates have been observed in certain populations with higher rates of consanguinity.

Epidemiology incidence references: MLD: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5027970/>; SEG: <https://ghr.nlm.nih.gov/condition/metachromatic-leukodystrophy>

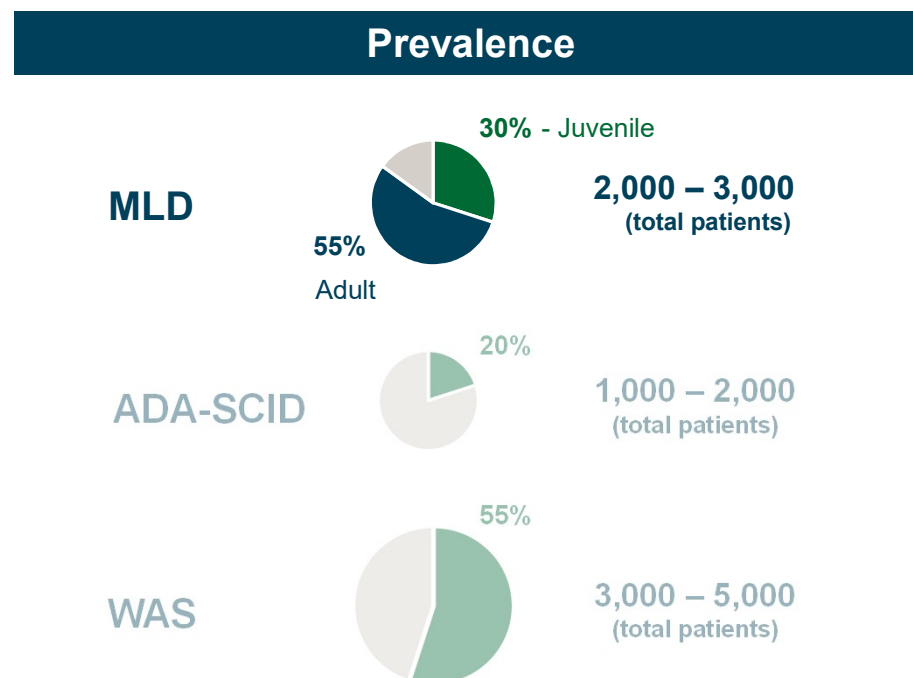
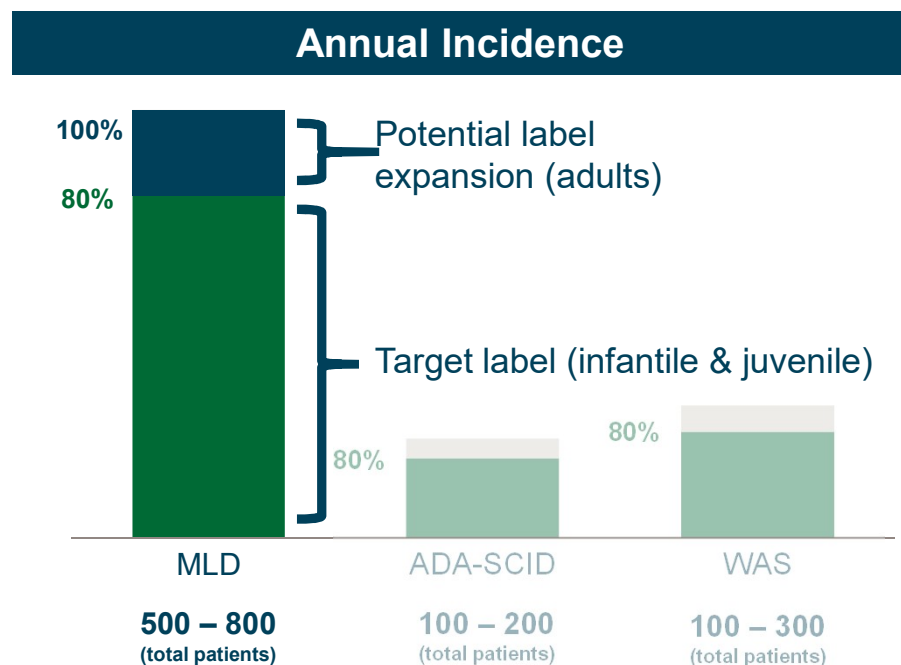
ADA-SCID; <https://ghr.nlm.nih.gov/condition/adenosine-deaminase-deficiency#statistics> SEG: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5911483/>;

WAS: ASM. Annals of Saudi Medicine. Wiskott-Aldrich Syndrome; NIH Genetics Home Reference <https://ghr.nlm.nih.gov/condition/wiskott-aldrich-syndrome>.

# Initial Target Label Focusing on Pediatric MLD

## Potential label expansion opportunity in adult MLD

■ Ineligible  
■ Eligible



<sup>1</sup>Based on target label and pricing of recent gene therapy analogs

Incidence / prevalence figure estimates based on available literature, population data and in-house estimates, in countries where rare disease therapies are typically reimbursed.

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ADA-SCID; <https://ghr.nlm.nih.gov/condition/adenosine-deaminase-deficiency#statistics> SEG: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5911483/>;

WAS: ASM. Annals of Saudi Medicine. Wiskott-Aldrich Syndrome; NIH Genetics Home Reference <https://ghr.nlm.nih.gov/condition/wiskott-aldrich-syndrome>.



THE ORCHARD THERAPEUTICS STORY

# Strong Momentum – Transformative Year Ahead

**1**

Strong  
Fundamentals

**2**

Powerful Platform  
Approach

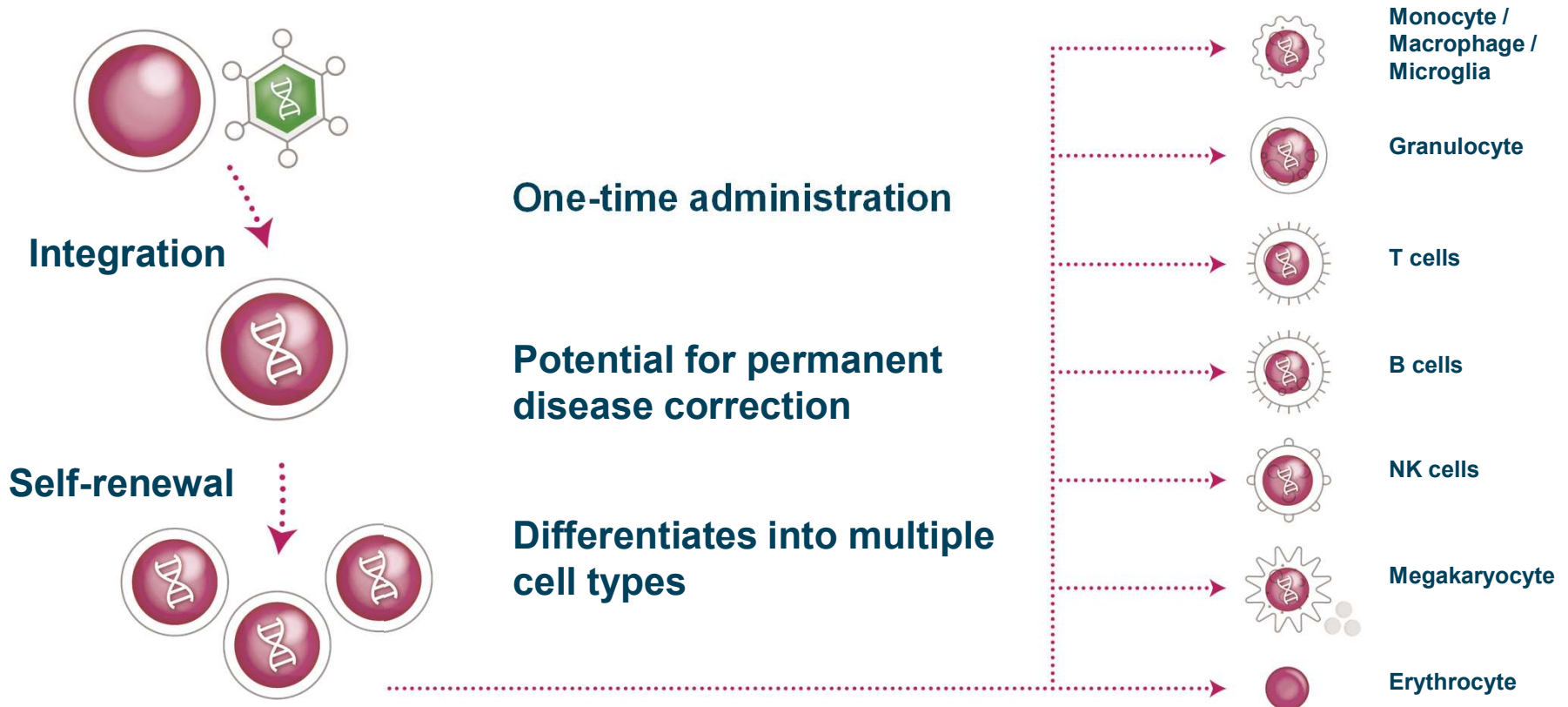
**3**

Commercial  
Ready

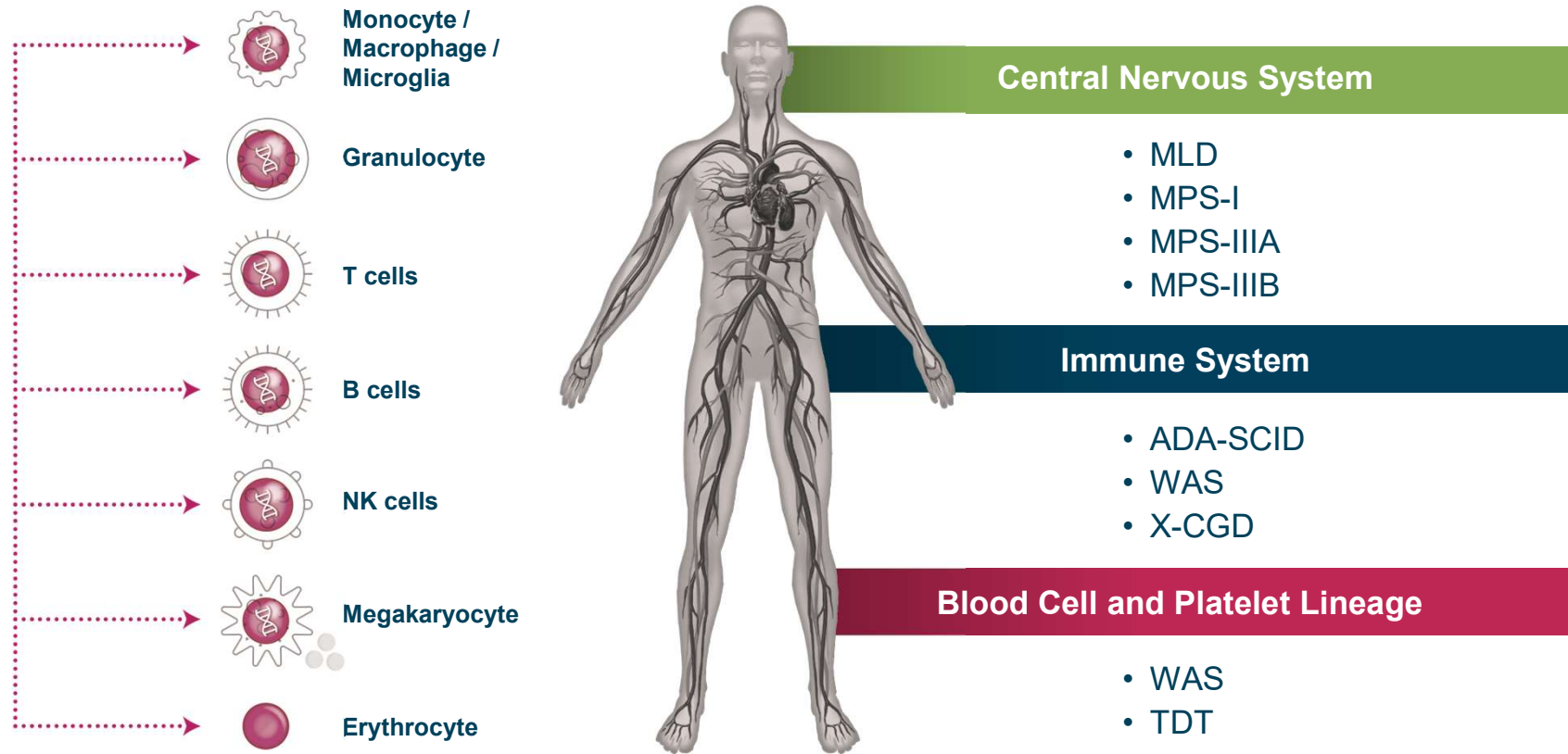
**4**

Our  
Future

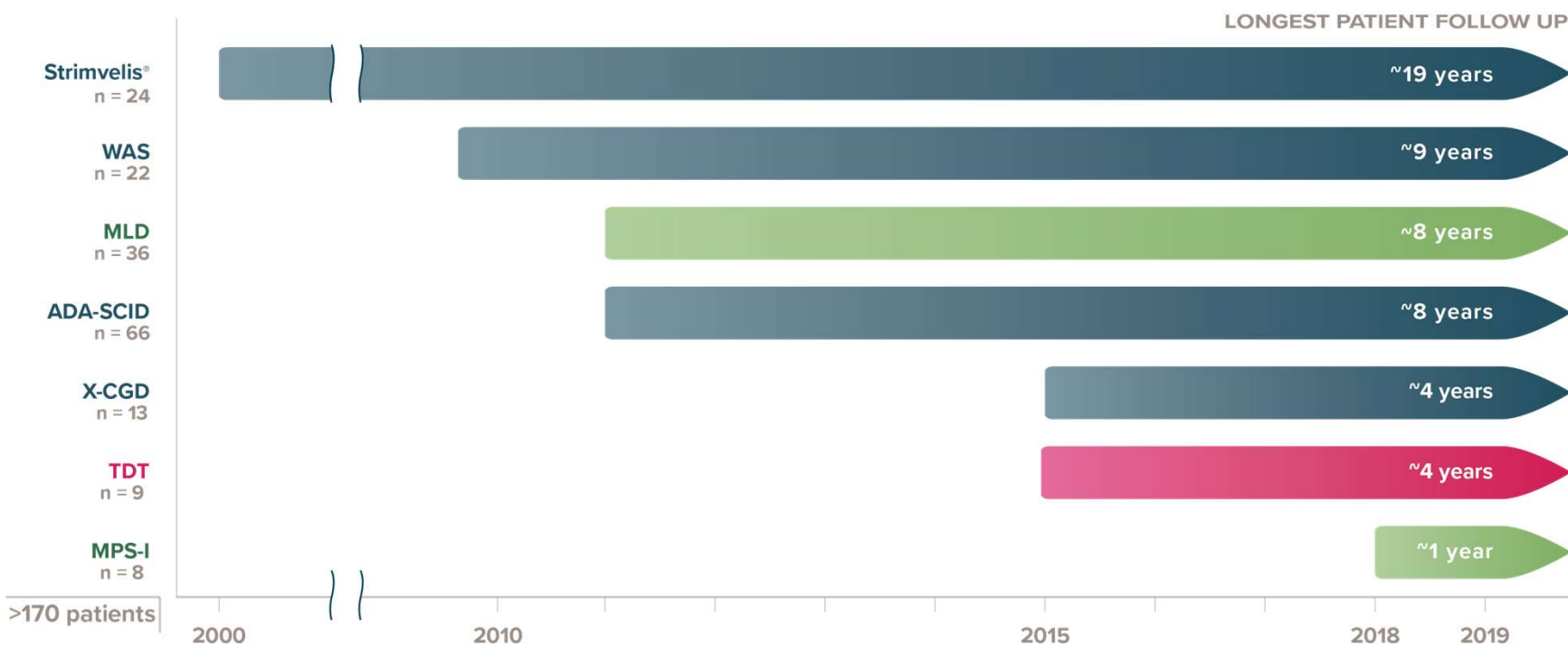
# HSC Gene Therapy Offers a Highly Differentiated Approach



# Potential to Correct Multiple Cell Types Addresses Many Rare Diseases



## Durability of Response Out to 18+ Years with > 170 Patients Treated



Patients treated in the development phase, including in clinical trials and under pre-approval access (defined as any form of pre-approval treatment outside of a company-sponsored clinical trial, including, but not limited to, compassionate use, early access, hospital exemption or special license).

Patient with longest Strimvelis® follow-up enrolled in registry study, with data available up to 19 years.

Data based on in-house data as of December 2019.

Data include all patients treated with CD34+ hematopoietic stem cells transduced ex vivo with vector of interest.



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# Metachromatic Leukodystrophy is a Devastating, Rapidly Progressive Disease

## Disease Snapshot



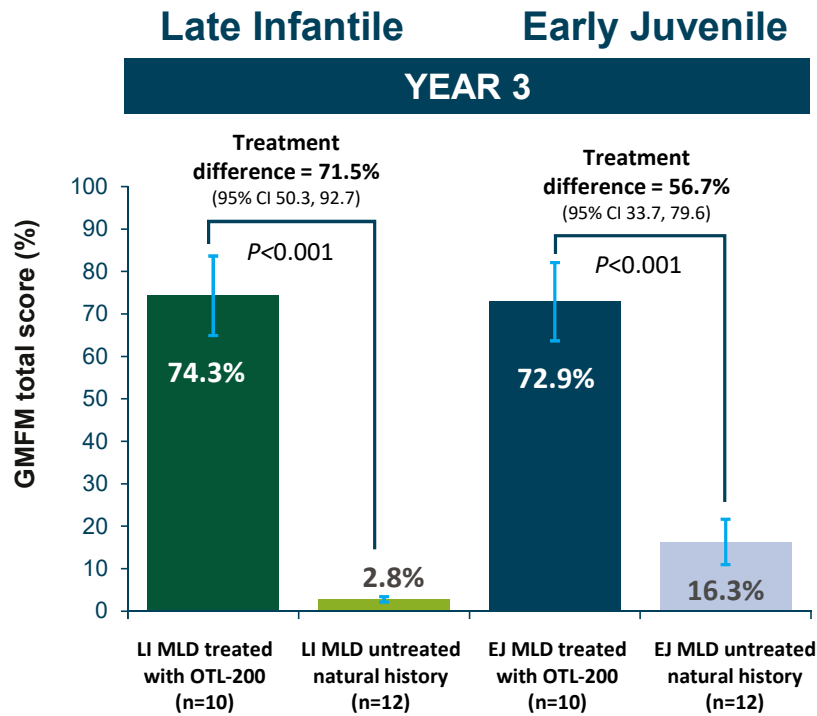
Age 5, pre-diagnosis



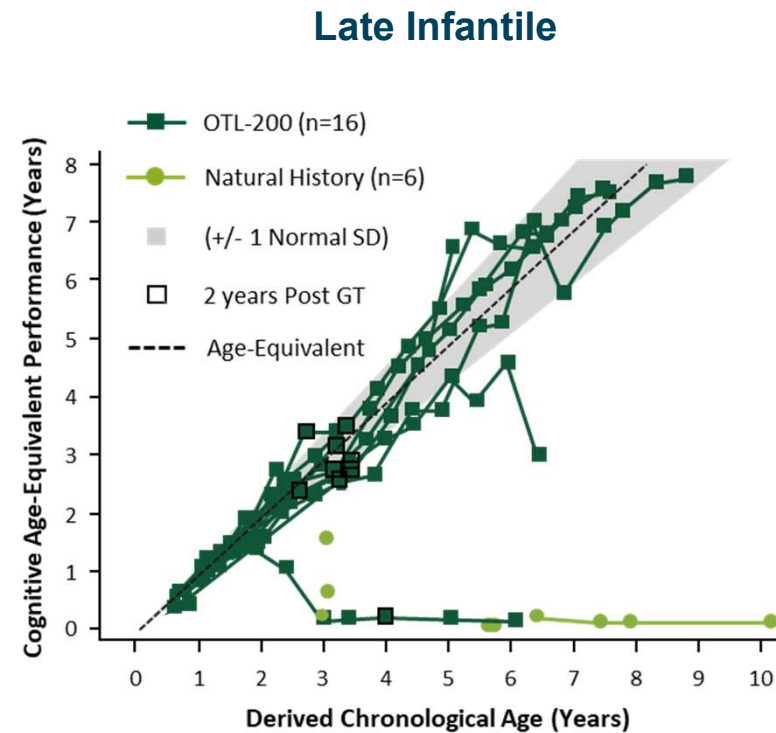
Age 9, advanced disease

- Fatal genetic CNS disorder
- Relentless loss of physical and cognitive function
- Presents on a spectrum with different ages of onset

# Significantly Superior Motor and Cognitive Function Demonstrated vs. Natural History



Both LI and EJ patients achieved a statistically significant difference on the co-primary endpoint of improvement of >10% of the total GMFM score in treated subjects when compared to the Natural History cohort at Year 2, and these were maintained through Year 3. Note: vertical error bars are SE of the adjusted mean; P-values are from a two-sided 5% hypothesis test with null hypothesis of  $\leq 10\%$  difference; CI, confidence interval; EJ, early juvenile; GMFM, gross motor function measurement; LI, late infantile; MLD, metachromatic leukodystrophy.



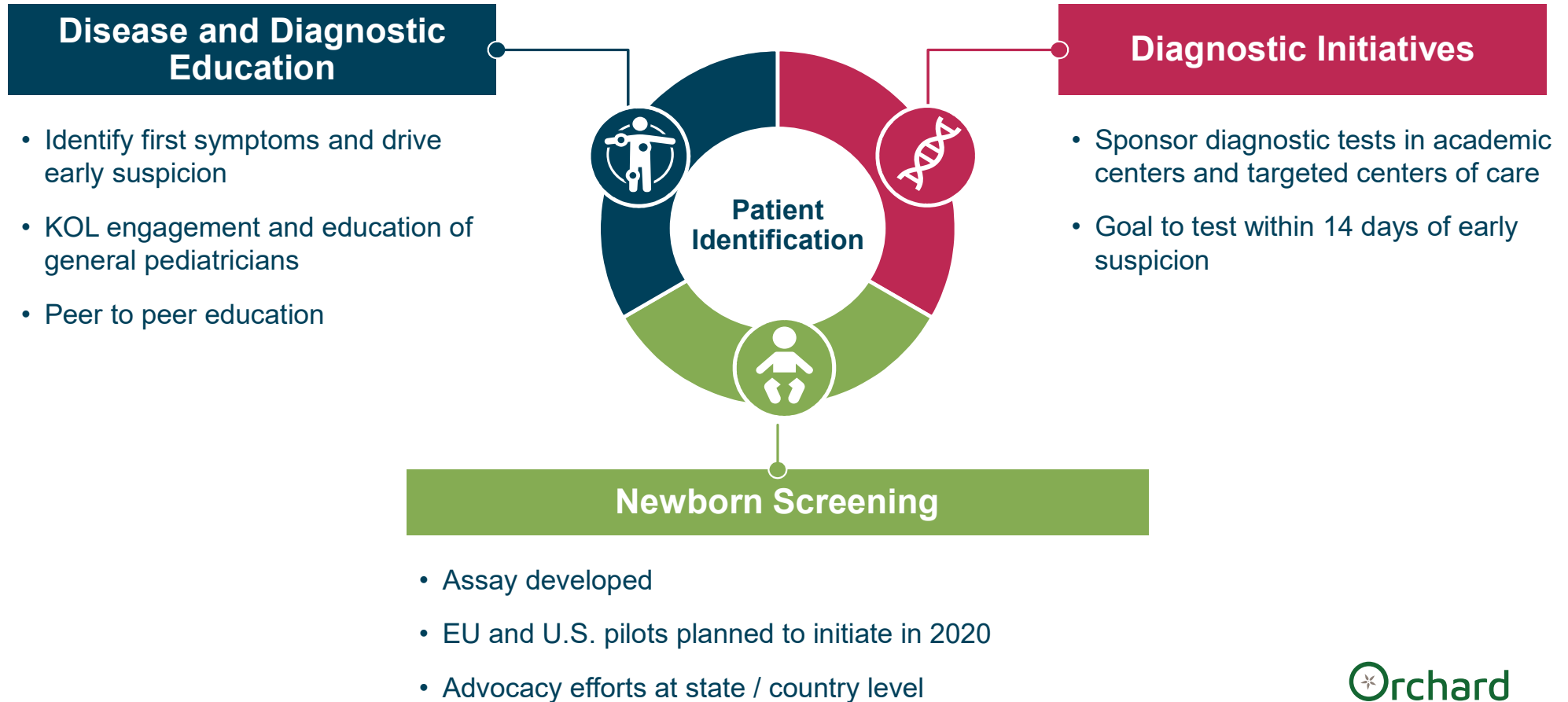
Cognitive Age-Equivalent at each visit has been derived as follows: For WPPSI and WISC: (DQp x Chronological Age)/100. For Bayley III: Cognitive Raw Scores have been compared to the tabulated values in the Bayley III manual to calculate Cognitive Age-Equivalent. For Bayley II: Cognitive Age-Equivalent is based on Mental Development Age as reported on the CRF. The Psychological Corporation. 2006. Bayley N. Bayley scales of infant and Toddler Development. Third Edition. San Antonio.

# Implementing Commercial Strategy to Launch OTL-200 Globally

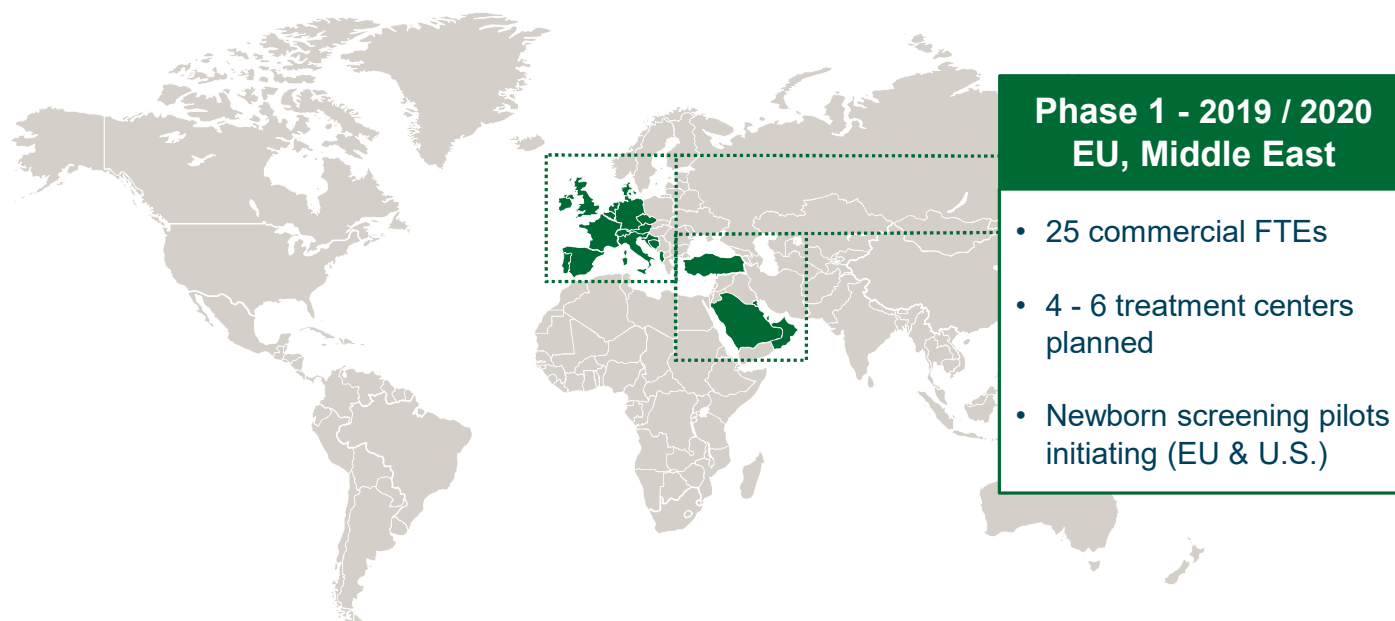




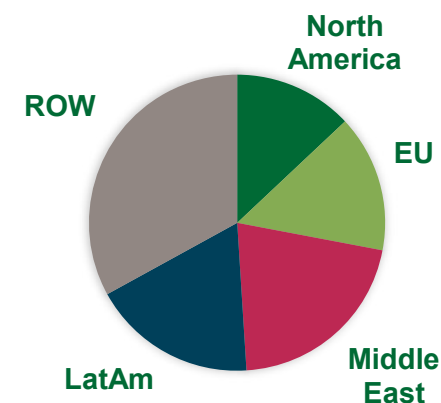
# Multi-Pronged Approach to Identifying MLD Patients



# Establish Commercial and Operational Model: Building Teams and Infrastructure to Serve Patients Worldwide

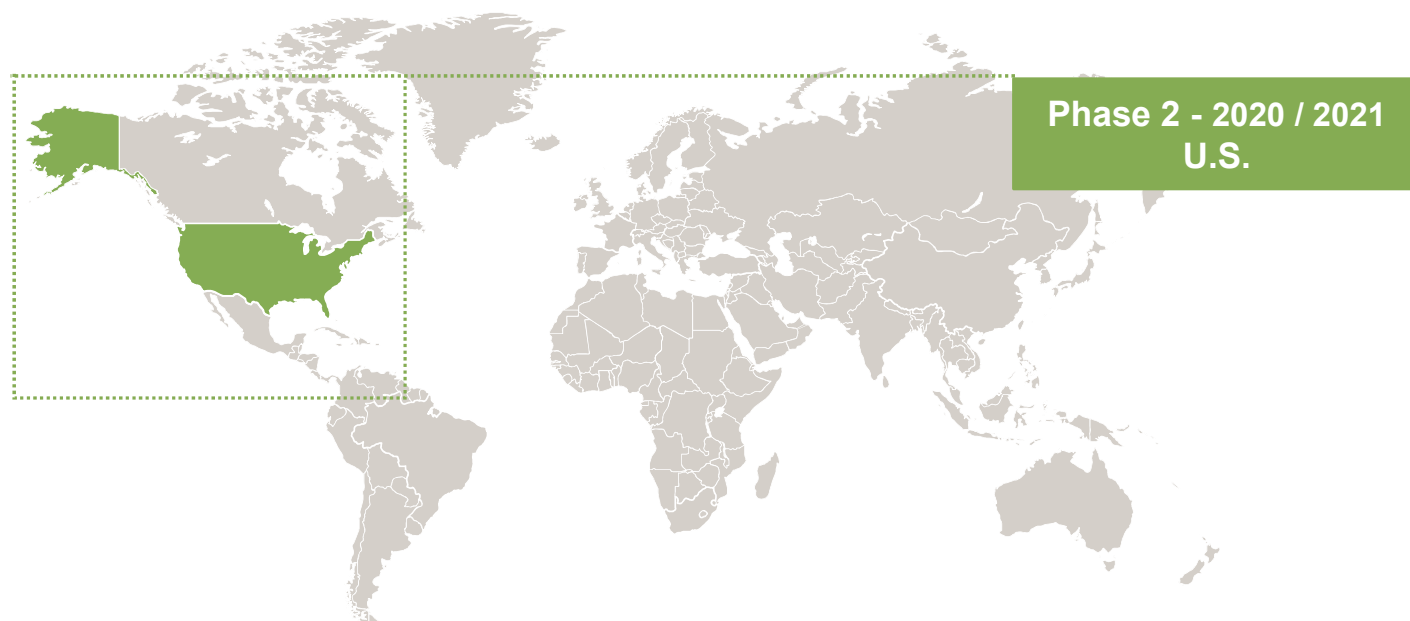


**GEOGRAPHIC MLD PATIENT  
DISTRIBUTION (ESTIMATED)  
2,000 – 3,000 PATIENTS**

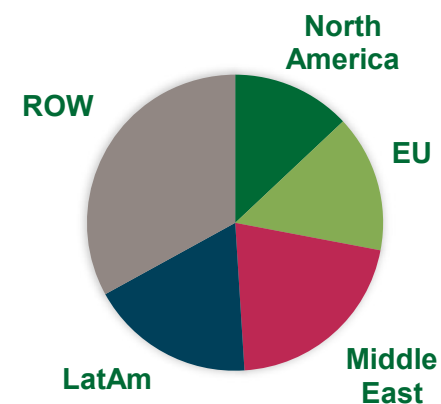


**Penetration and reimbursement varies by market**

## Establish Commercial and Operational Model: Building Teams and Infrastructure to Serve Patients Worldwide

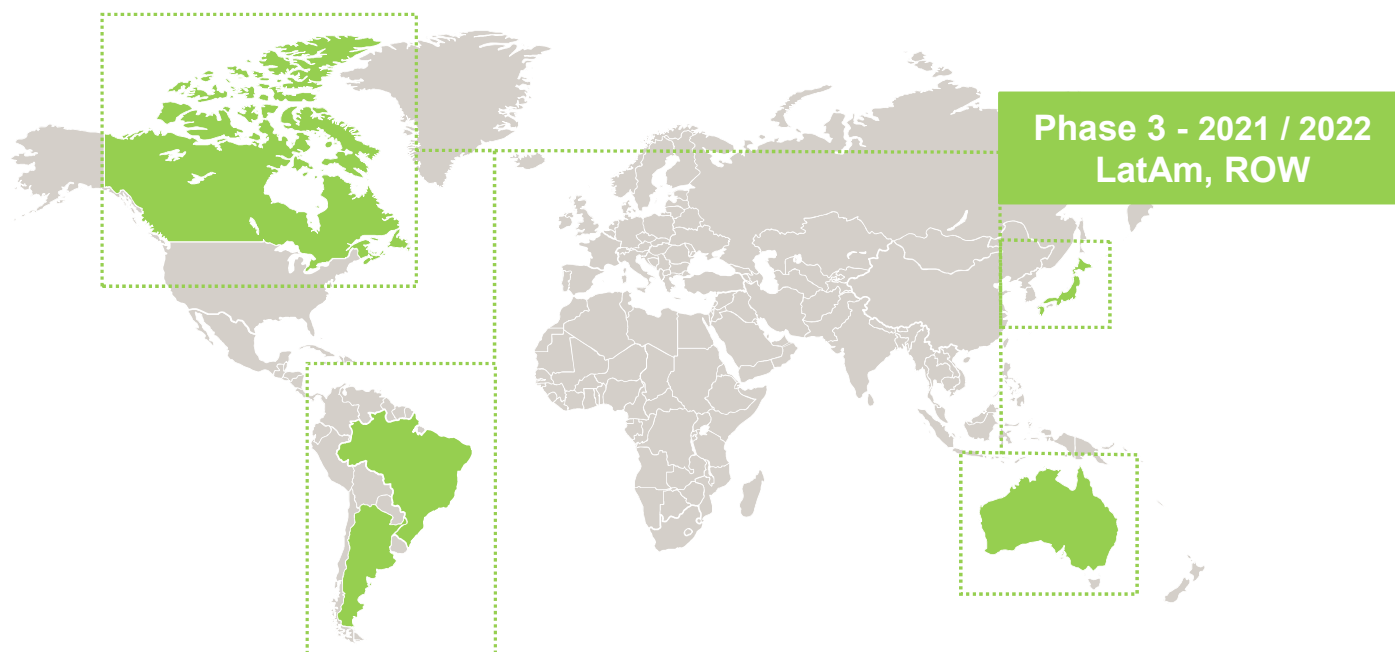


GEOGRAPHIC MLD PATIENT DISTRIBUTION (ESTIMATED)  
2,000 – 3,000 PATIENTS

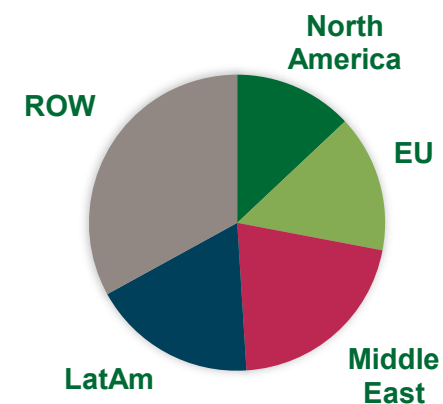


Penetration and reimbursement varies by market

# Establish Commercial and Operational Model: Building Teams and Infrastructure to Serve Patients Worldwide



GEOGRAPHIC MLD PATIENT DISTRIBUTION (ESTIMATED)  
2,000 – 3,000 PATIENTS



Penetration and reimbursement varies by market



# Manufacturing in Place to Support Commercialization

## NEAR TERM

CMO Infrastructure  
Established for Initial  
MLD Launch

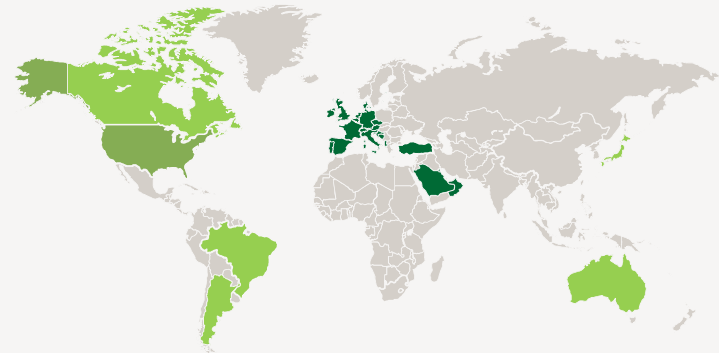
- MolMed producing drug product and vector
- Sufficient inventory being produced to meet expected launch demand
- Leveraging commercial process experience from Strimvelis



## MID - LONG TERM

Invest in Own  
Manufacturing  
Facilities

- Continue partnerships with CMOs
- Orchard facility in Fremont, CA
  - Design complete
  - Construction planned to initiate in 2020
  - Goal to be operational by 2021





## Drive Global Access: Our Pricing Commitments

<b>Shared value</b>	Ensure patients, society and industry share in human and economic benefits of innovation – now and in the future
<b>Shared risk</b>	Stand behind therapeutic outcomes and be willing to tie payment to outcomes
<b>Informed pricing</b>	Use demonstrable, objective measures of value and the best available evidence to inform price
<b>System-wide evolution</b>	Support healthcare system to adapt to emergence of one-time, potential cures

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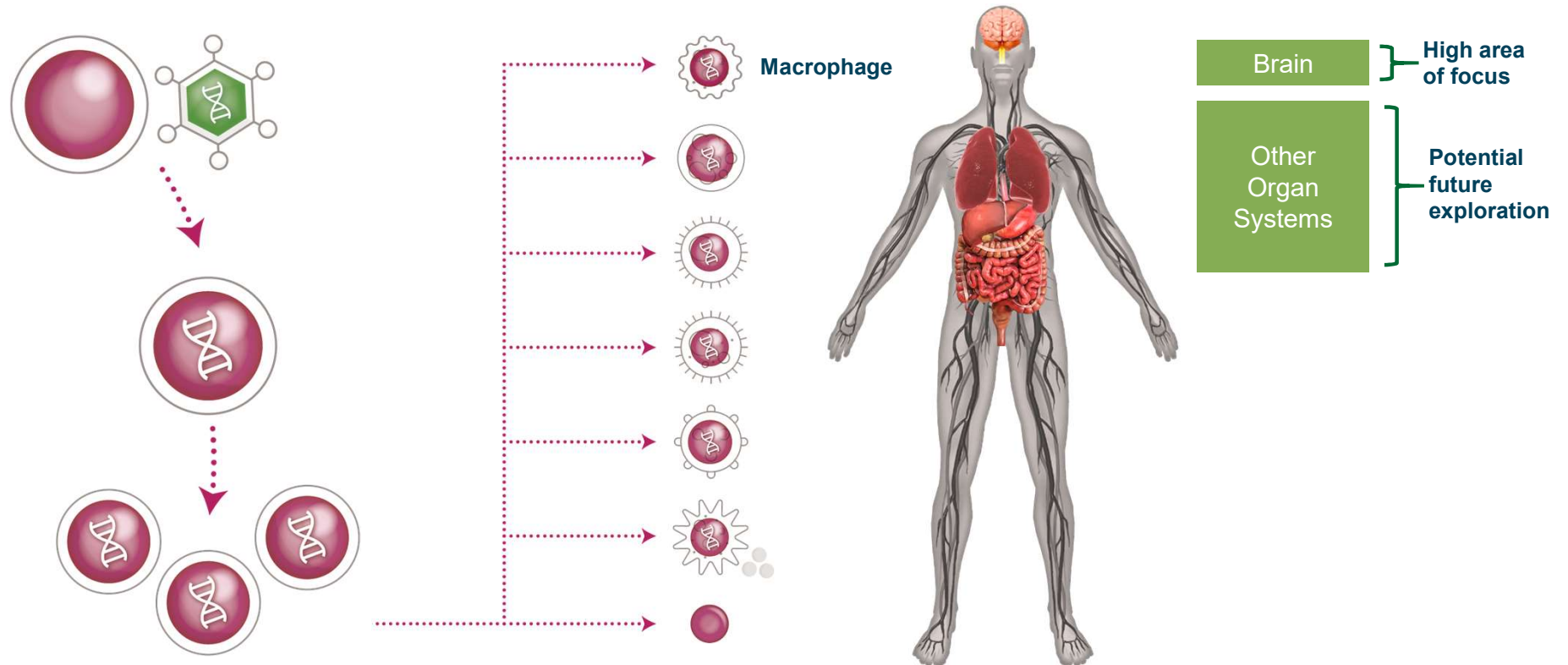
**4**

Our  
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## Investment to Scale and Innovate Across Our Business

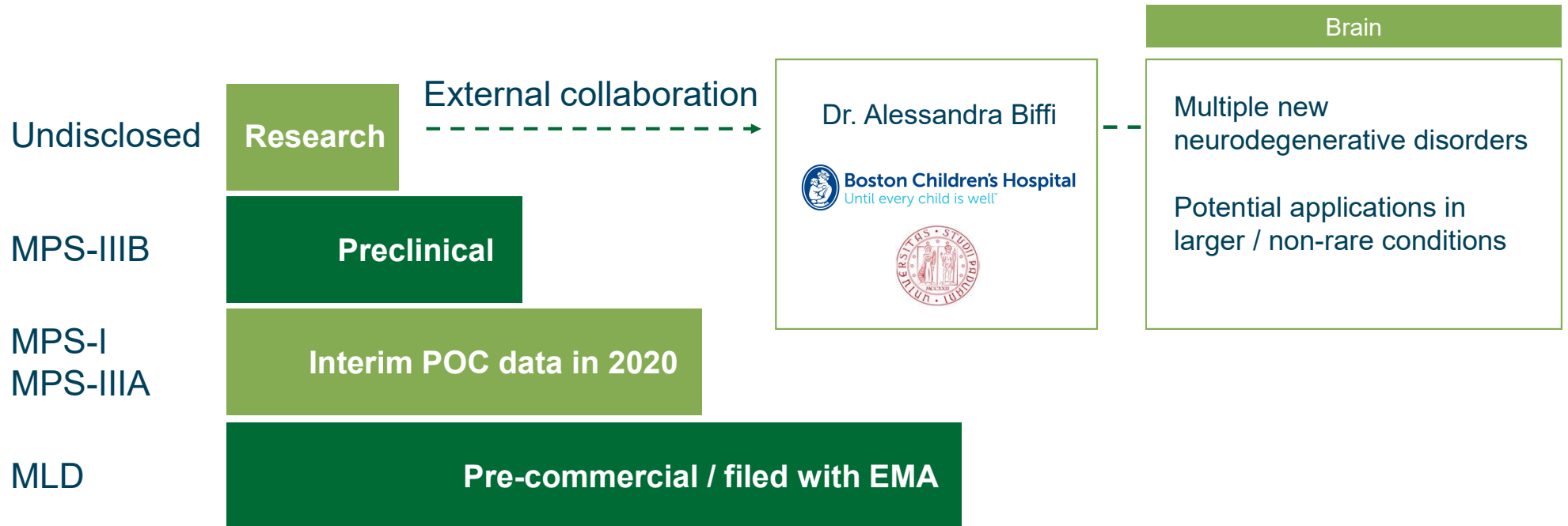
Technology innovations 		In-house capabilities 
PRODUCT	PROCESS	
Transduction enhancers	Stable cell line	Manufacturing facility (expected operational in 2021)
Non-toxic conditioning	Closed automated systems	Research and discovery for new indications in 2020
HSC subsets		

## Gene-corrected HSCs and Macrophage Progeny Can Address Brain and Other Organ System Disorders



Other rare indications • Potential non-rare (longer-term)

## Building on our Strength in Neurometabolic Disorders



## Corporate Priorities & Expected Key Milestones

<b>MLD</b>	Obtain approval and launch OTL-200 for MLD in Europe in 2H 2020 Submit a BLA filing in late 2020 or early 2021
<b>ADA-SCID</b>	Initiate a rolling BLA in the U.S. for OTL-101 in 1H 2020 with completion within 12 months
<b>WAS</b>	Submit BLA and MAA filings for OTL-103 in 2021
<b>MPS-I</b>	Release interim data from POC study in 2020
<b>MPS-IIIA</b>	Enroll 5 patients in POC study, release interim data in 2020
<b>Manufacturing</b>	Initiate construction of in-house manufacturing facility in 2020