Orchard therapeutics™

Dedicated to Transforming the Lives of Patients Through Innovative Gene Therapies

March 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) the likelihood and timing of construction of an in-house manufacturing facility; (VIII) execution of the Company’s vision and growth strategy, including with respect to global growth; and (IX) projected financial performance and financial condition, including the sufficiency of the Company’s cash, cash equivalents and investments 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 results 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 10-K filed with the SEC on February 27, 2020, 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.

Orchard therapeutics

Global gene therapy company

Dedicated to transforming the lives of patients with rare diseases

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

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THE ORCHARD THERAPEUTICS STORY

Strong Momentum – Transformative Year Ahead

1 **Strong Fundamentals**

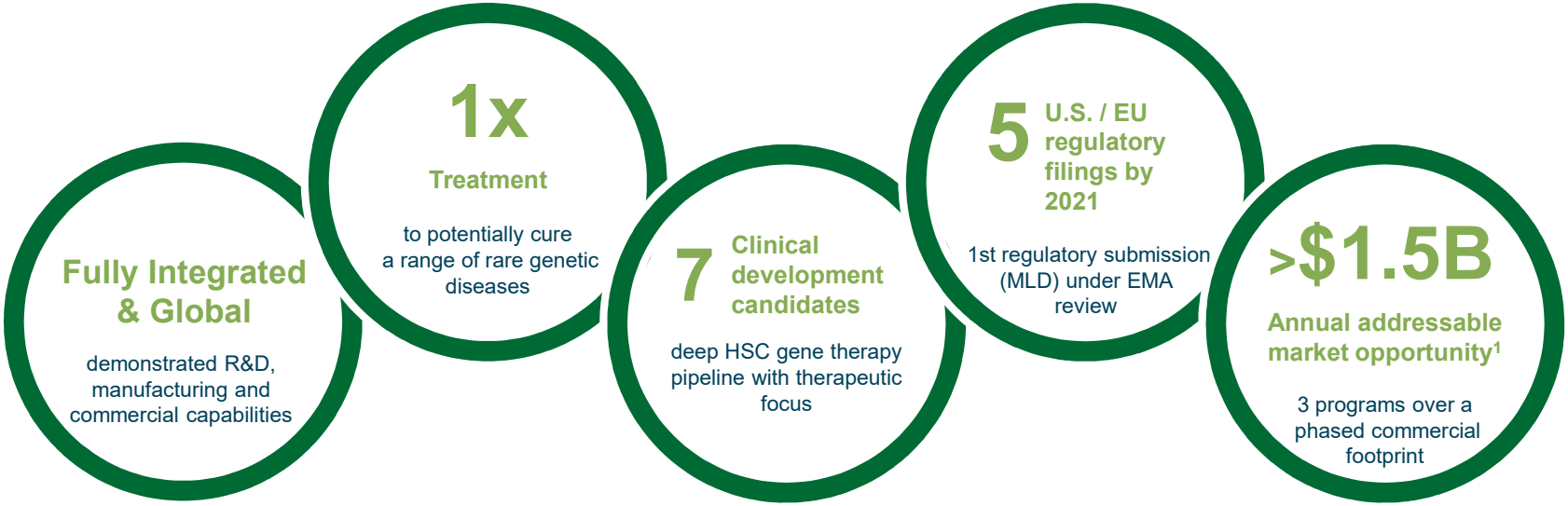
2 Powerful Platform Approach

3 Commercial Ready

4 Our Future

Orchard therapeutics

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

[1]Based on target label and pricing of recent gene therapy analogs, see slide 7-8 for additional detail

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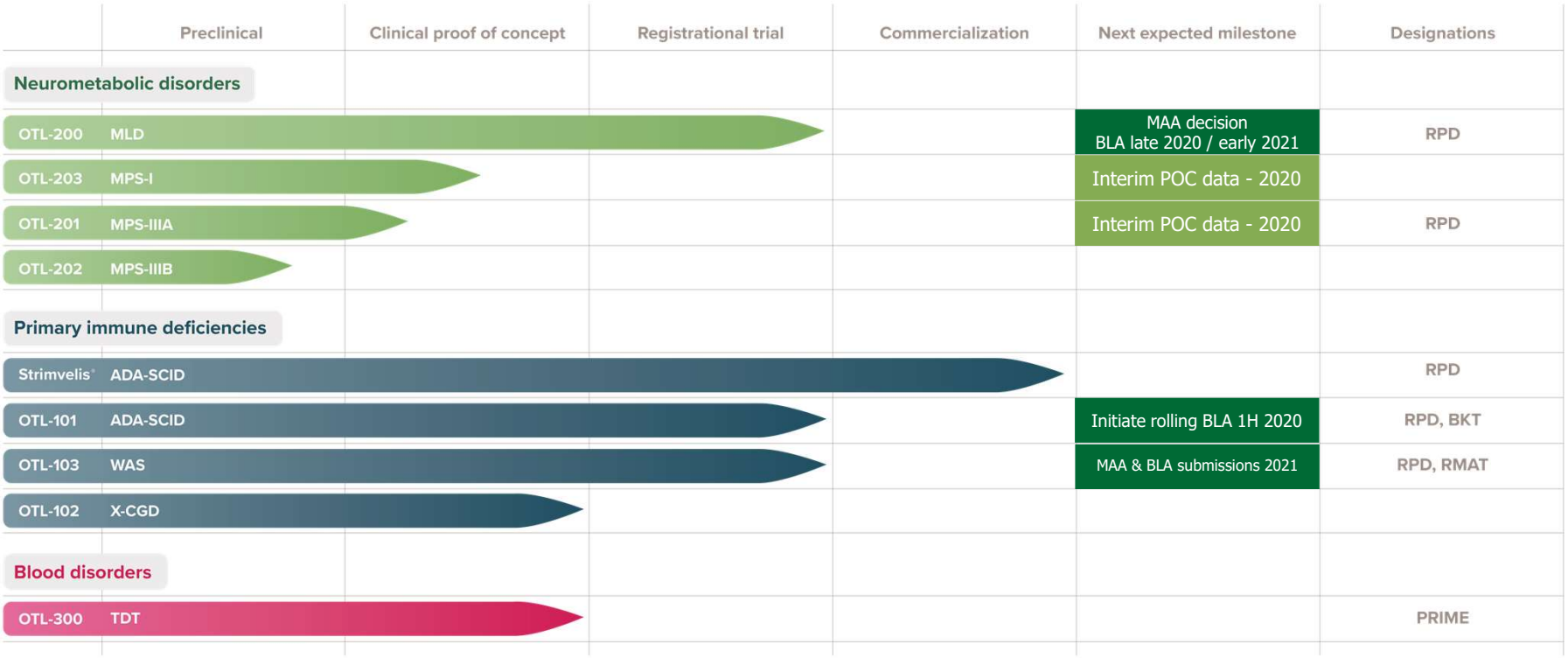
One of the Deepest Pipelines in Gene Therapy



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

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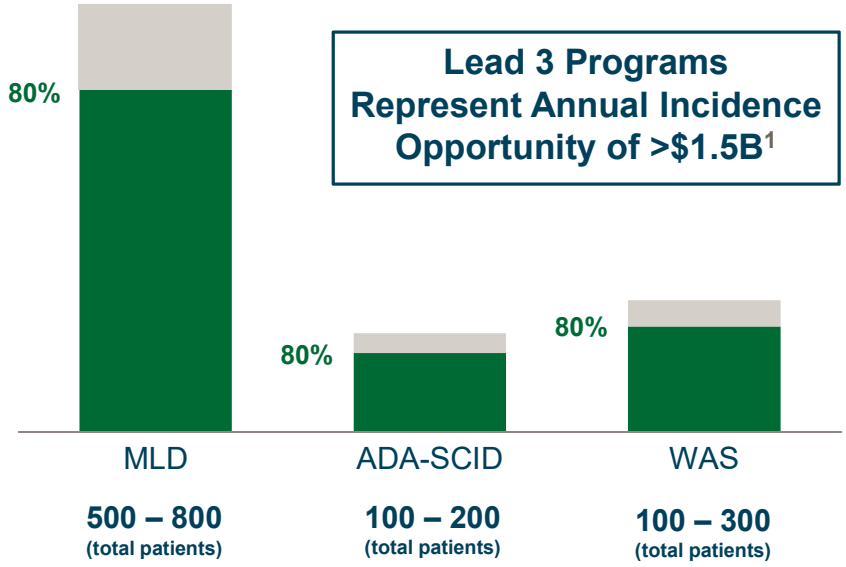
Building a Scalable Business in Rare Diseases

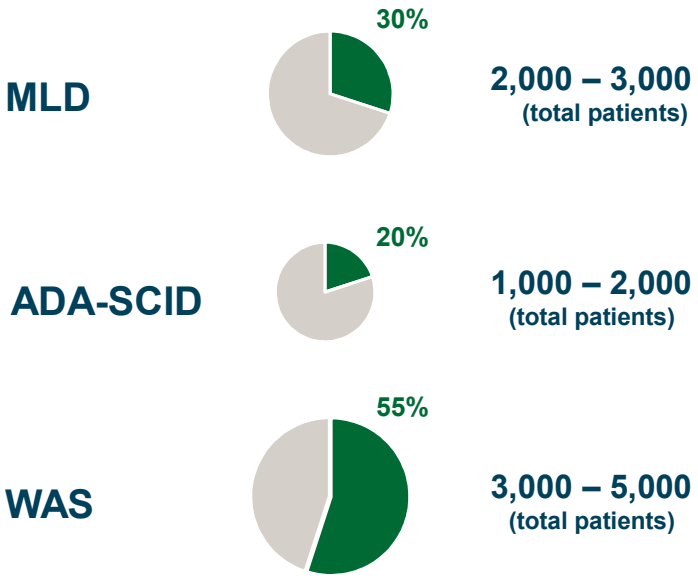
Ineligible
Eligible

Annual Incidence



Lead 3 Programs Represent Annual Incidence Opportunity of >$1.5B[1]

Prevalence



[1]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.

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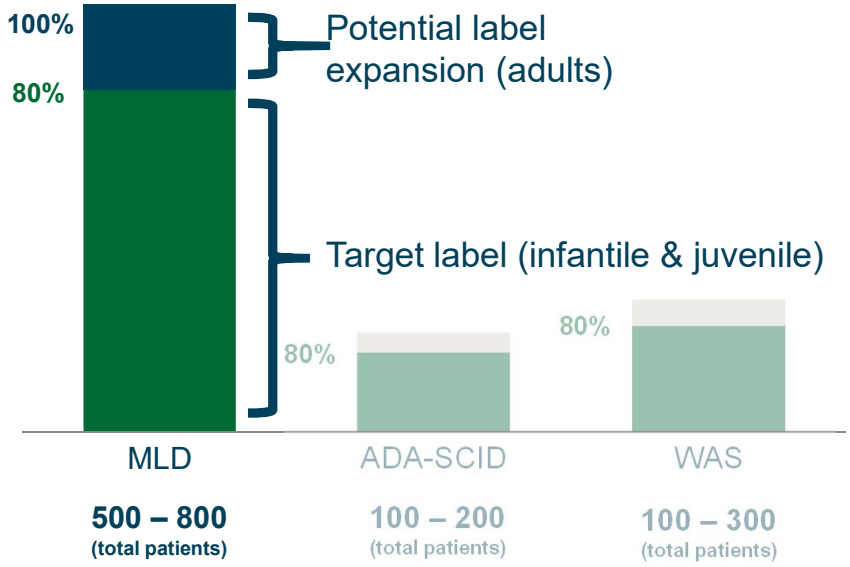
Initial Target Label Focusing on Pediatric MLD

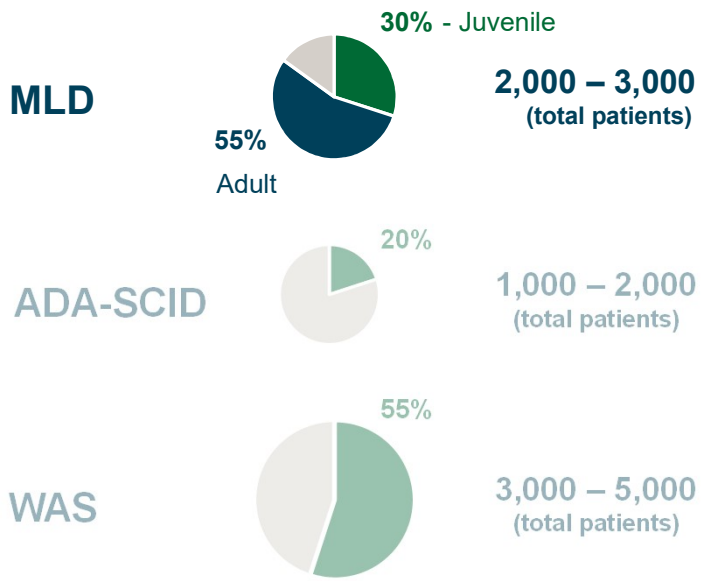
Potential label expansion opportunity in adult MLD

Ineligible
Eligible

Annual Incidence



Prevalence



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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.

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THE ORCHARD THERAPEUTICS STORY

Strong Momentum – Transformative Year Ahead

1 Strong Fundamentals

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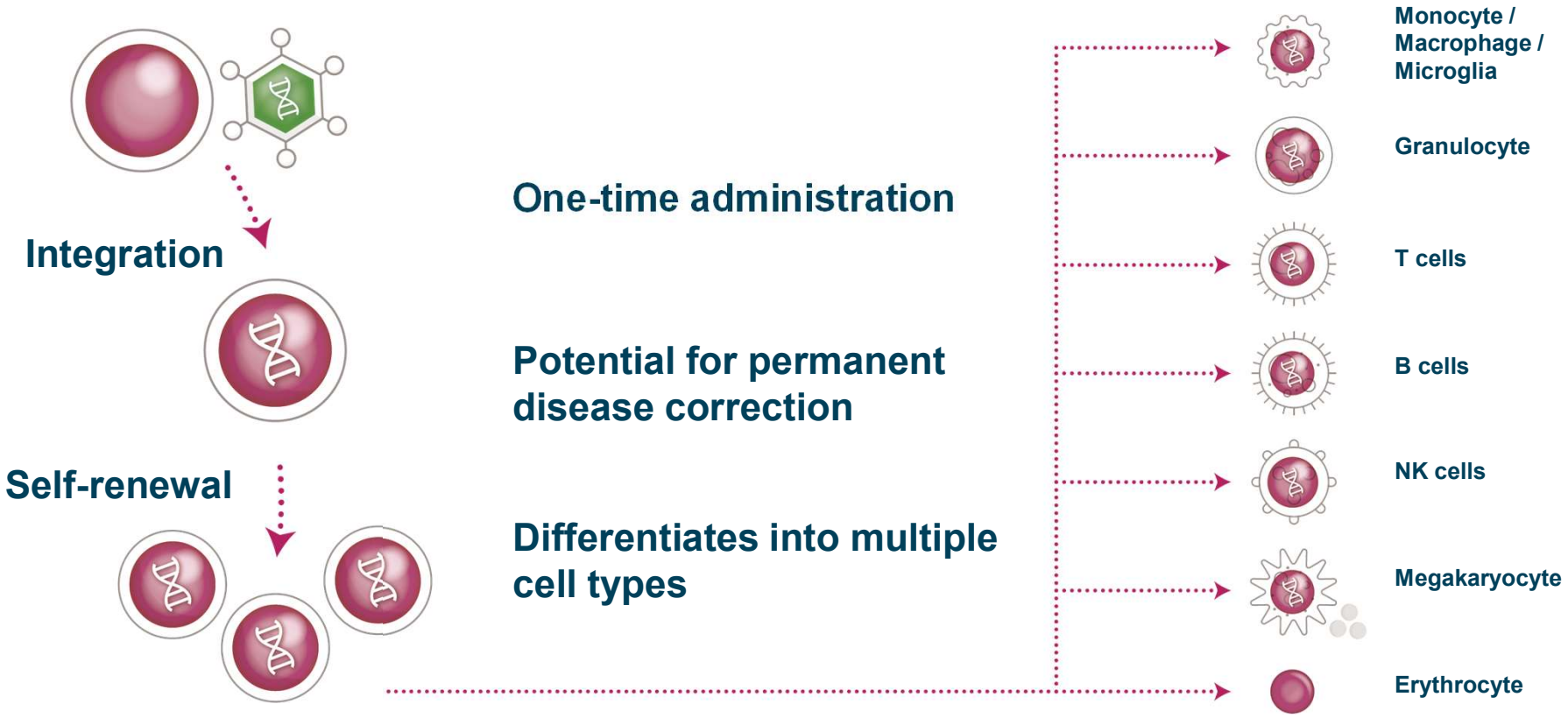
HSC Gene Therapy Offers a Highly Differentiated Approach



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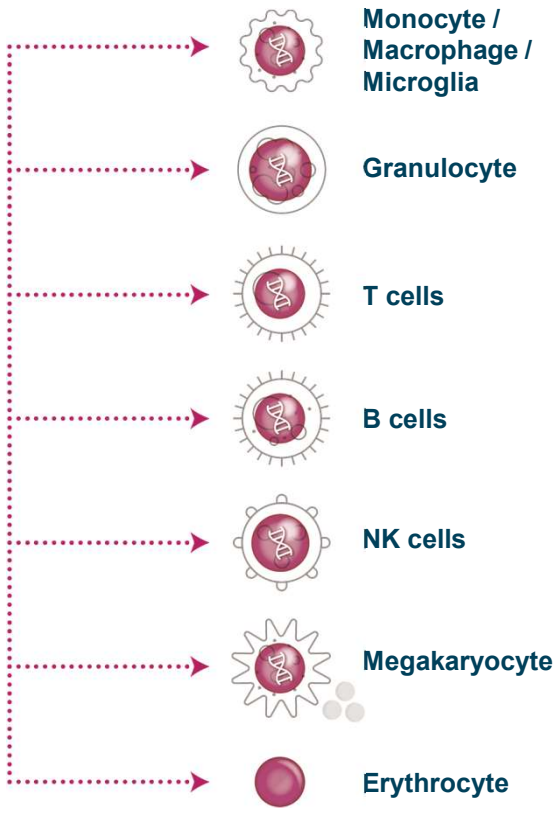
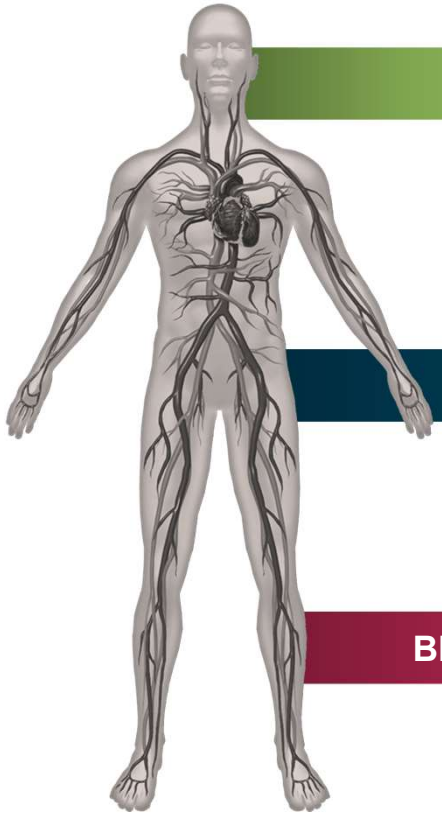
Potential to Correct Multiple Cell Types Addresses Many Rare Diseases





Central Nervous System

- MLD
- MPS-I
- MPS-IIIA
- MPS-IIIB

Immune System

- ADA-SCID
- WAS
- X-CGD

Blood Cell and Platelet Lineage

- WAS
- TDT

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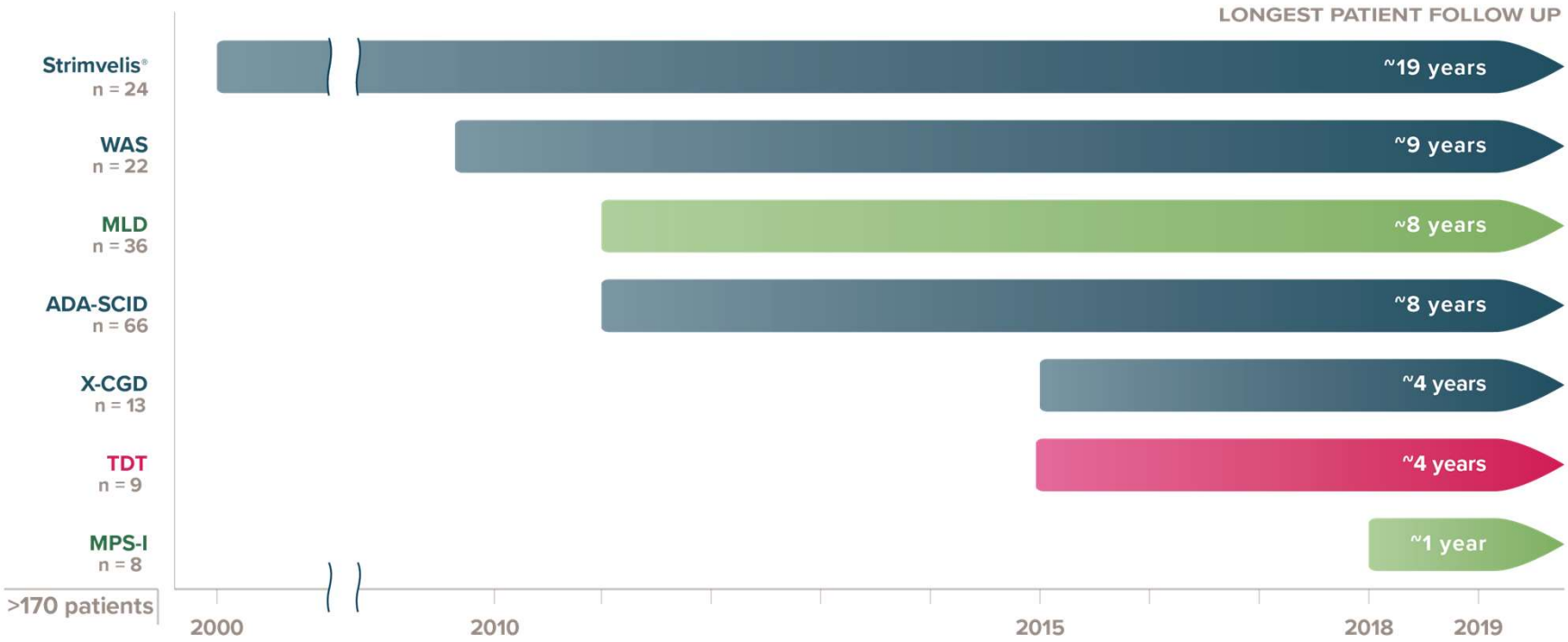
Durability of Response Out to 18+ Years with > 170 Patients Treated



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

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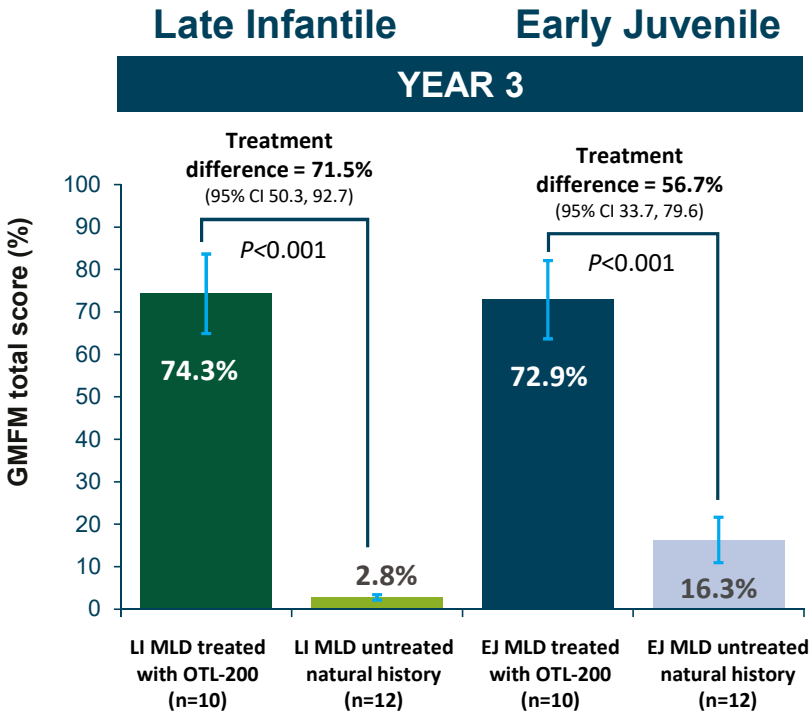
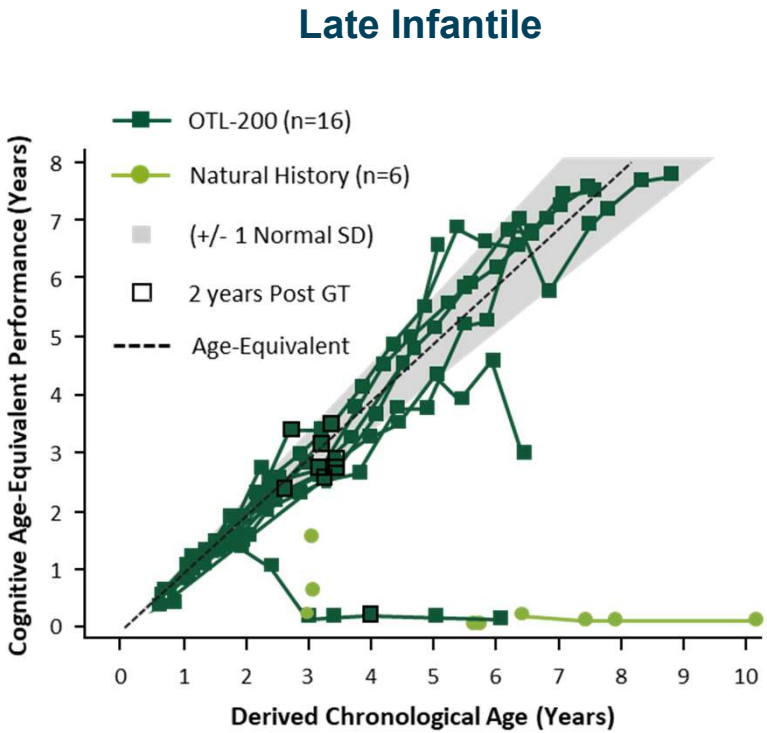
Significantly Superior Motor and Cognitive Function Demonstrated vs. Natural History





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 ≤ 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.

Integrated analysis presented September 4 2019 at SSIEM annual meeting

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Implementing Commercial Strategy to Launch OTL-200 Globally

1 Patient ID and Diagnostics	• Disease awareness and diagnostic testing • Extensive newborn screening pilot testing efforts in EU and U.S.
2 Geographic Footprint	• Teams in place in key EU markets and U.S. • Expansion to Middle East, Turkey, LatAm and Asia over time • Qualifying leading centers with transplant and disease area experience
3 Global Supply Network	• Manufacturing hub to ship cryopreserved product globally • Inventory, capacity and logistics of supply for launch
4 Market Access	• Multi-stakeholder engagement • Gene therapy value determination • Option for flexible payment models

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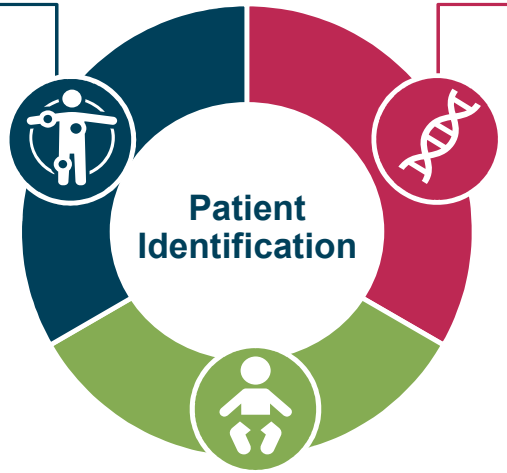
Multi-Pronged Approach to Identifying MLD Patients

Disease and Diagnostic Education

- Identify first symptoms and drive early suspicion
- KOL engagement and education of general pediatricians
- Peer to peer education



Diagnostic Initiatives

- Sponsor diagnostic tests in academic centers and targeted centers of care
- Goal to test within 14 days of early suspicion
- Sibling testing

Newborn Screening

- Assay developed
- EU and U.S. pilots planned to initiate in 2020
- Advocacy efforts at state / country level

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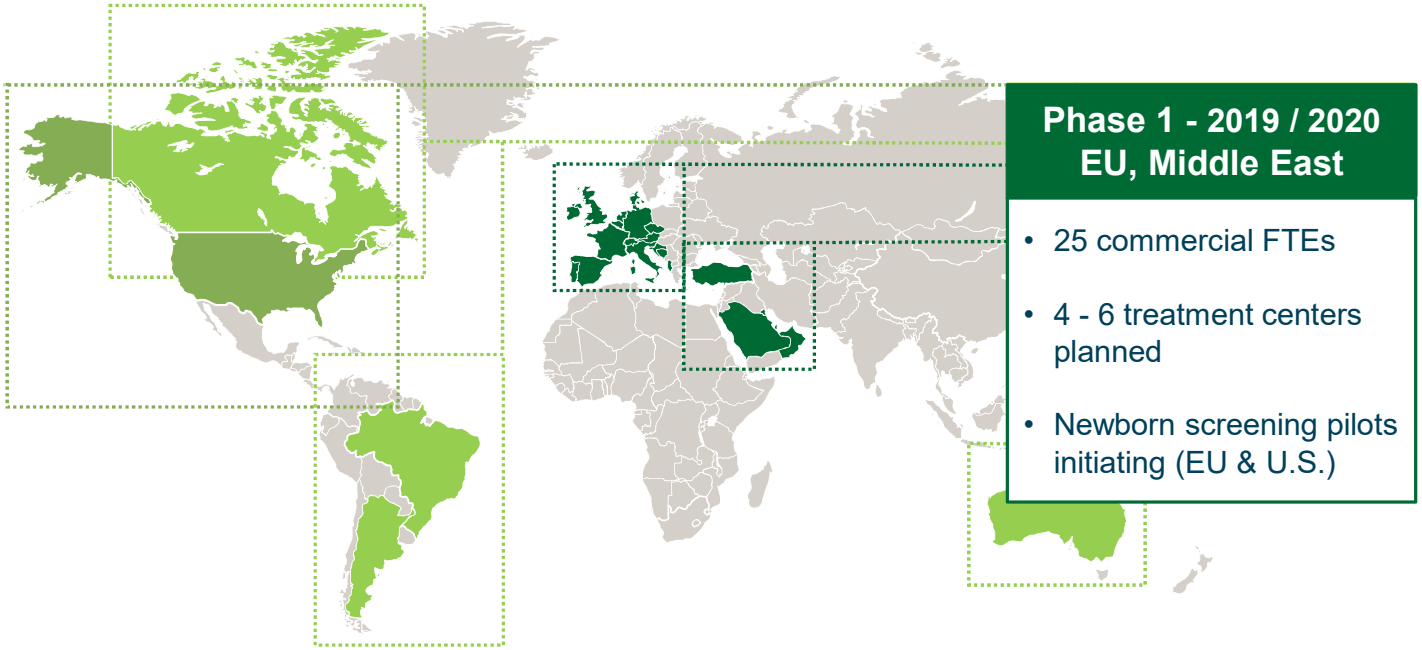
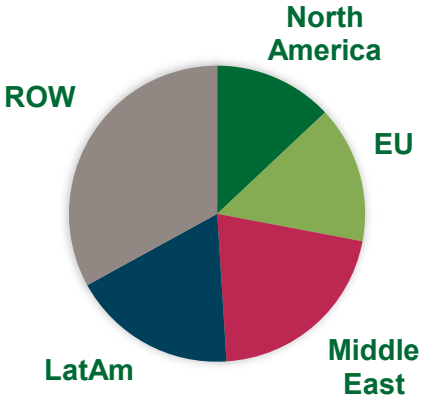
Establish Commercial and Operational Model: Building Teams and Infrastructure to Serve Patients Worldwide



Phase 1 - 2019 / 2020
EU, Middle East

- 25 commercial FTEs
- 4 - 6 treatment centers planned
- Newborn screening pilots initiating (EU & U.S.)

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



Penetration and reimbursement varies by market

Middle East includes GCC countries and Israel

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Manufacturing in Place to Support Commercialization

NEAR TERM

CMO Infrastructure Established for Initial MLD Launch

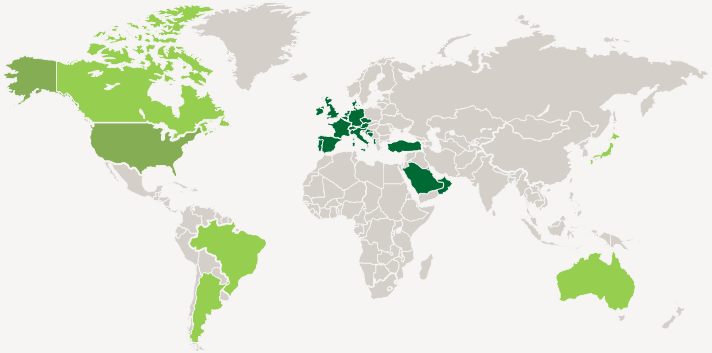
- MolMed producing drug product and vector
- Sufficient inventory being produced to meet expected launch demand
- Leveraging commercial process experience from Strimvelis

MOLMED

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



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Drive Global Access: Our Pricing Commitments

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

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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		

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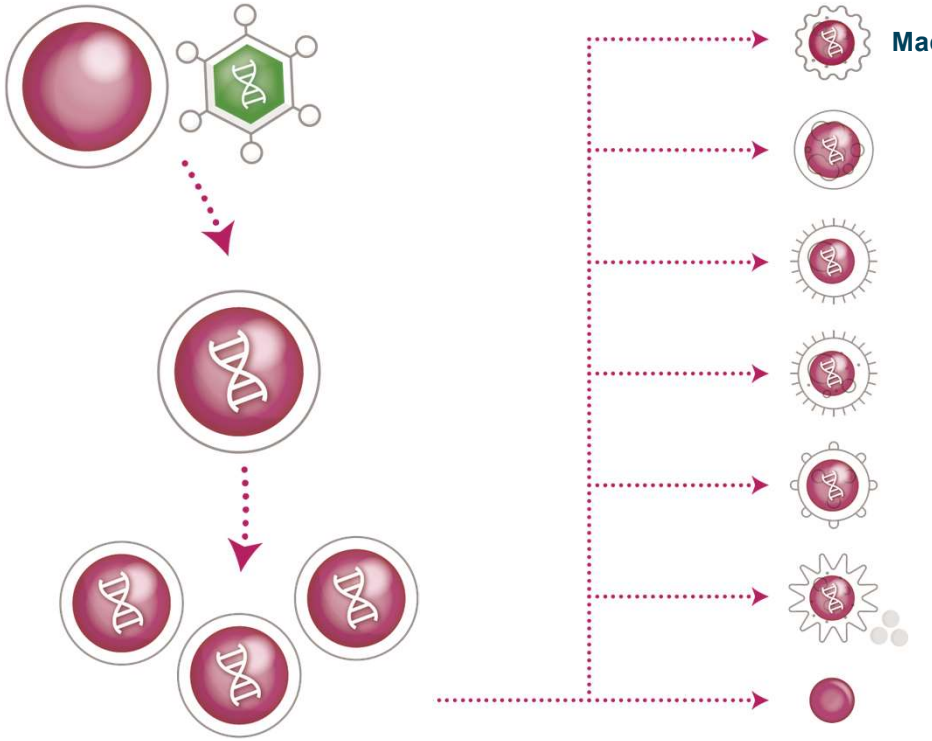
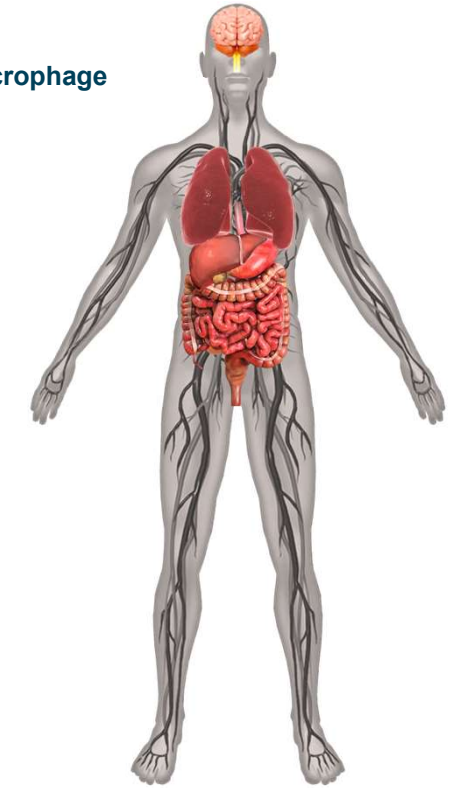
Gene-corrected HSCs and Macrophage Progeny Can Address Brain and Other Organ System Disorders



Macrophage



Brain — High area of focus

Other Organ Systems — Potential future exploration

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

Literature references: Alessia Capotondo, Rita Milazzo, Letterio Salvatore Politi, Angelo Quattrini, Alessio Palini, Tiziana Plati, Stefania Merella, Alessandro Nonis, Clelia di Serio, Eugenio Montini, Luigi Naldini, and Alessandra Biffi, PNAS September 11, 2012 109 (37) 15018-15023; https://doi.org/10.1073/pnas.1205858109; Tissue macrophages: heterogeneity and functions, Siamon Gordon and Annette Plüddemann, BMC Biology 2017 15:53, 29 June 2017

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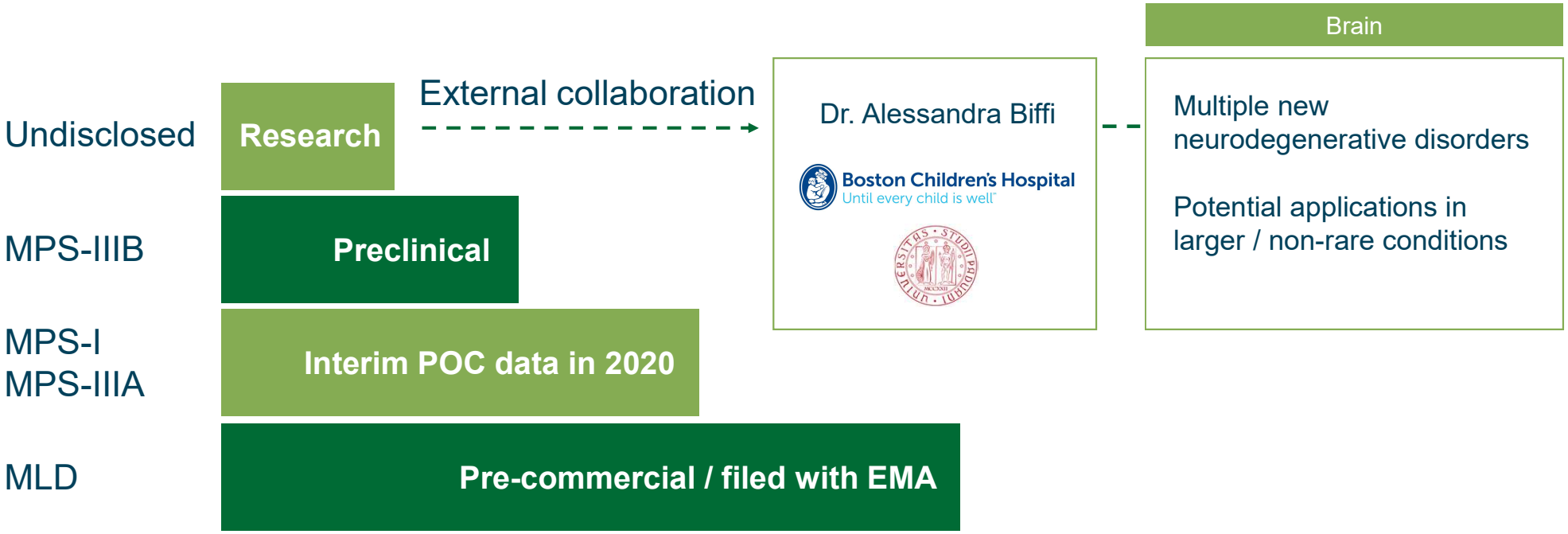
Building on our Strength in Neurometabolic Disorders



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Corporate Priorities & Expected Key Milestones

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

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