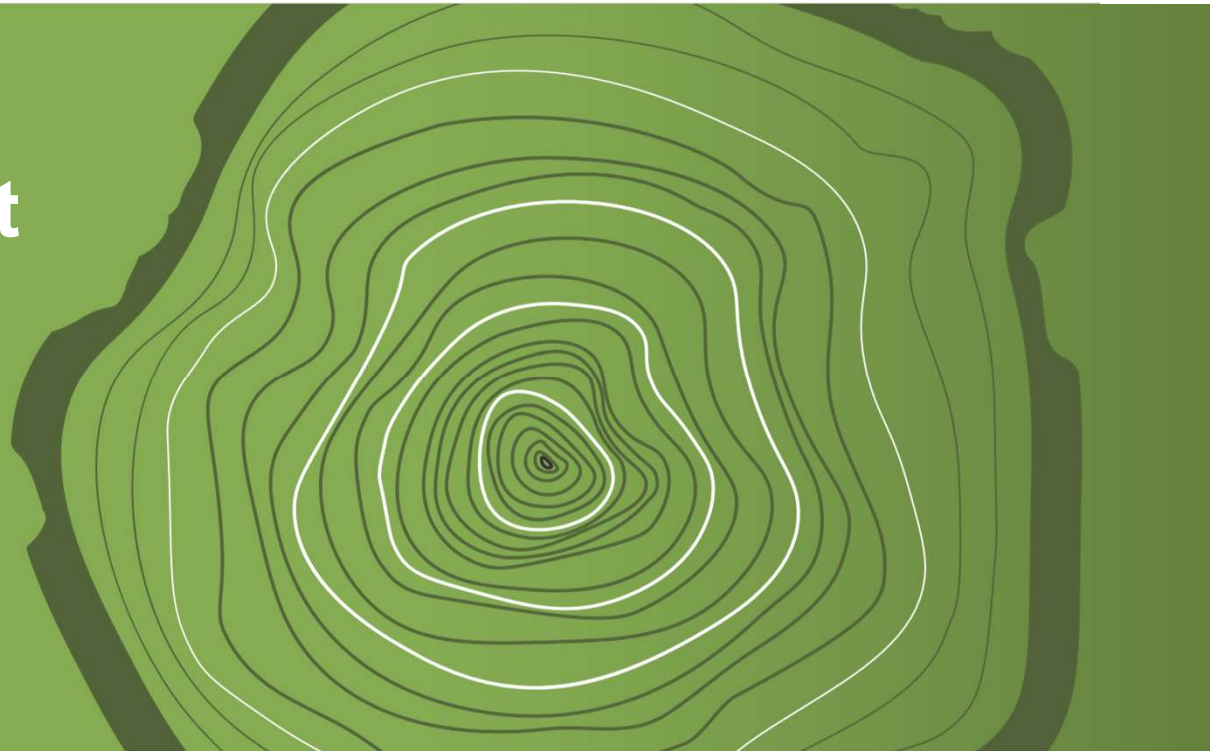
Orchard therapeutics™

Barclays GT Summit

November 16, 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 may include, 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 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; (VI) the timing and likelihood of approval of such product candidates by the applicable regulatory authorities; (VII) the adequacy of the Company’s manufacturing capacity and plans for future investment and commercialization; (VIII) execution of the Company’s vision and growth strategy, including with respect to global growth; (IX) the size and value of potential markets for the Company’s product candidates; and (X) projected financial performance and financial condition. 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 include, without limitation, the severity of the impact of the COVID-19 pandemic on the Company’s business, including on preclinical and clinical development and commercial programs, 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 quarterly report on Form 10-Q filed with the SEC on November 3, 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.

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Dedicated to **transforming** the lives of people with rare diseases.

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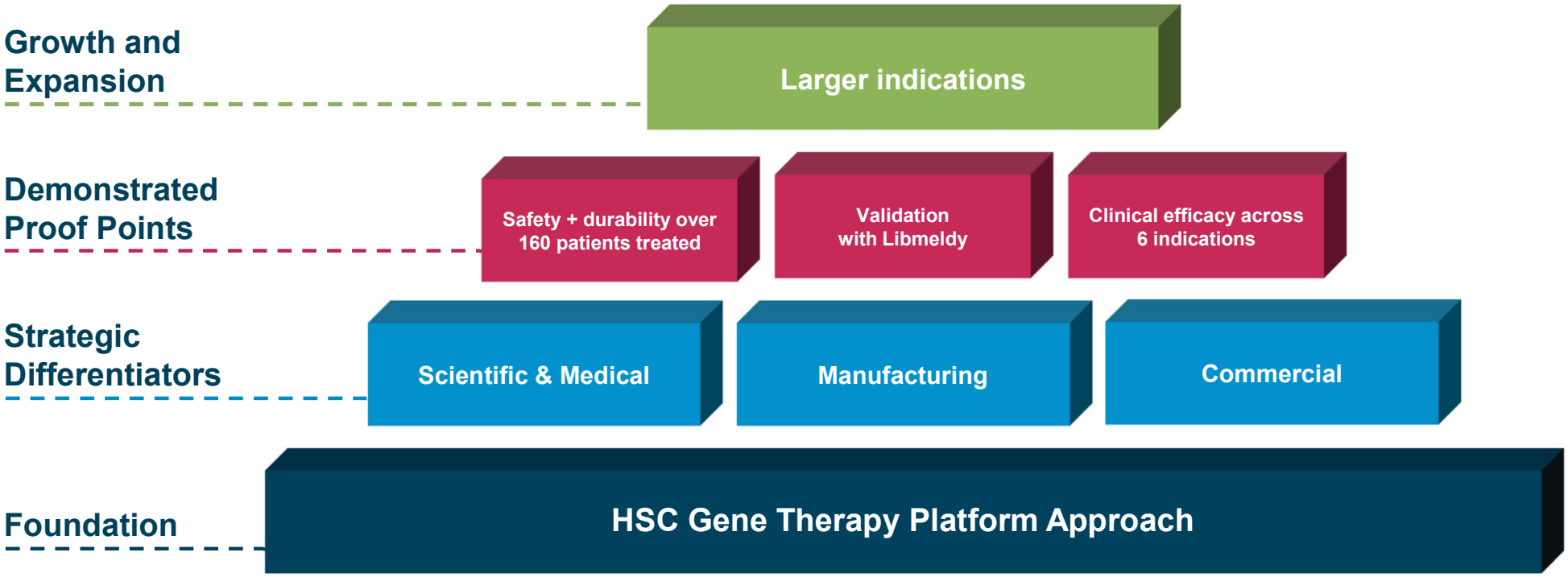
Delivering Now; Building for the Future



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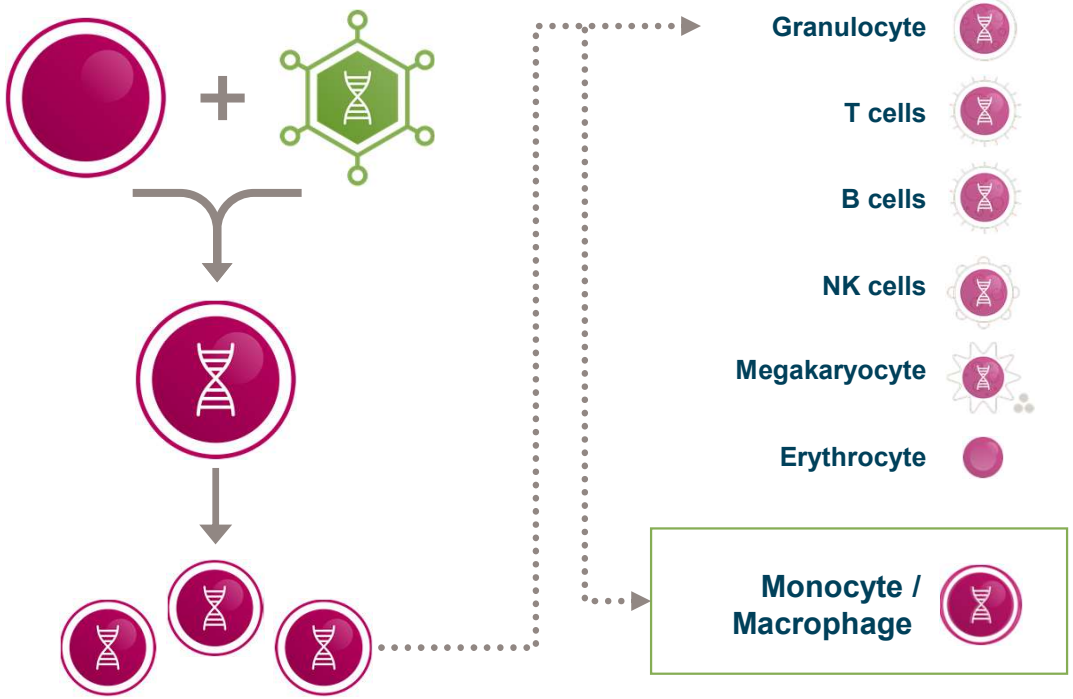
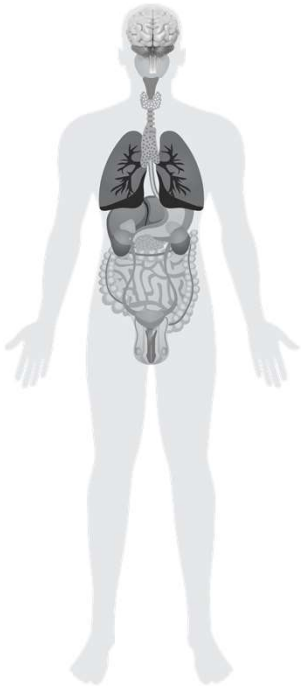
Gene-corrected HSCs Can Address Multiple Organ Systems





Brain
GI

High area of focus

Other Organ Systems

Areas for potential future expansion

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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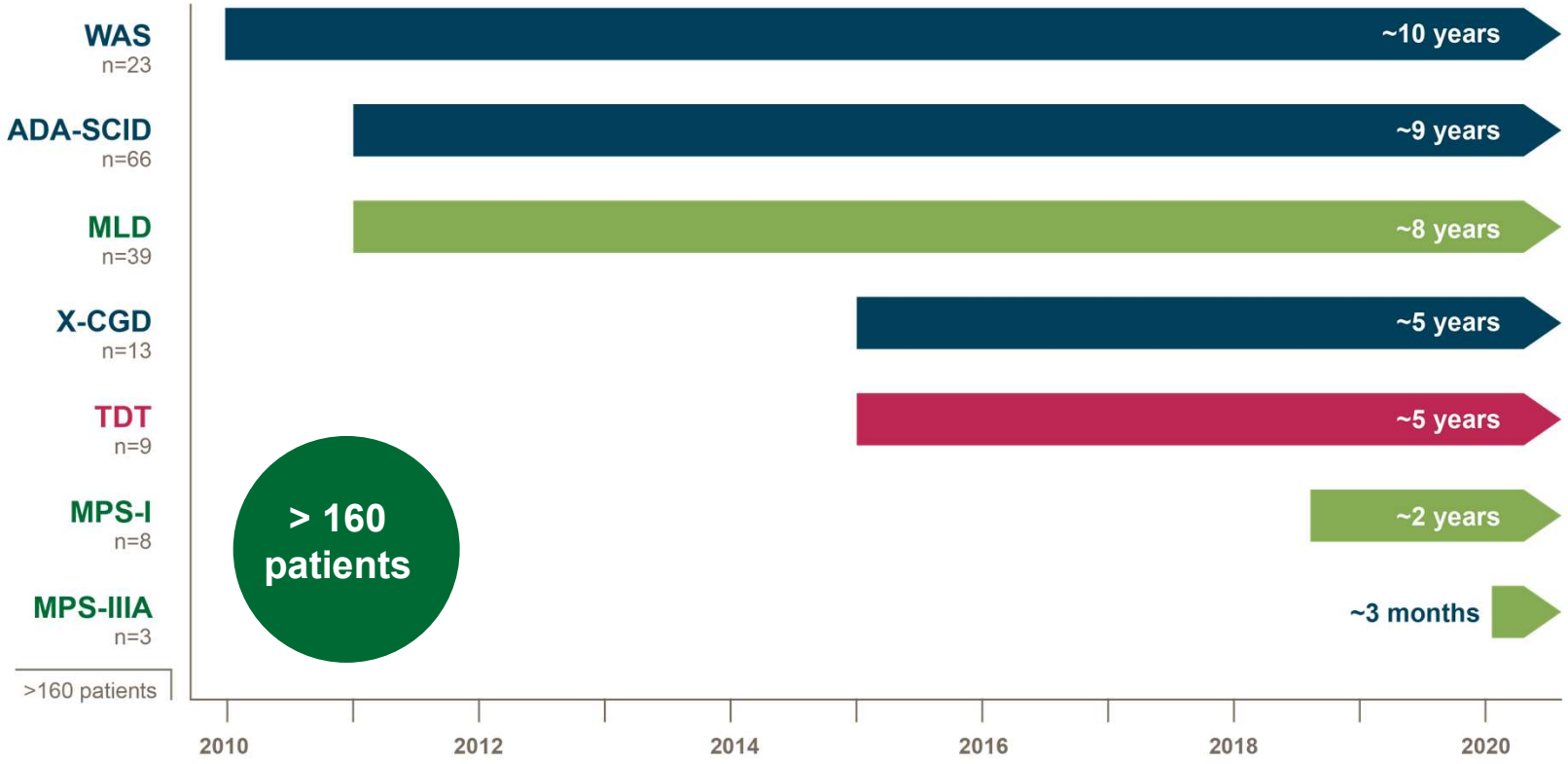
Durability of Response with Lentiviral HSC Gene Therapy Demonstrated via Longest Patient Follow-up



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).
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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Our Work in Neurometabolic Disorders

Metachromatic Leukodystrophy (MLD) 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

"The positive CHMP opinion for marketing authorization of Libmeldy is a remarkable achievement that we share with the MLD community, as it brings us closer to delivering a one-time, potentially transformative therapy for eligible children suffering from this devastating disease"

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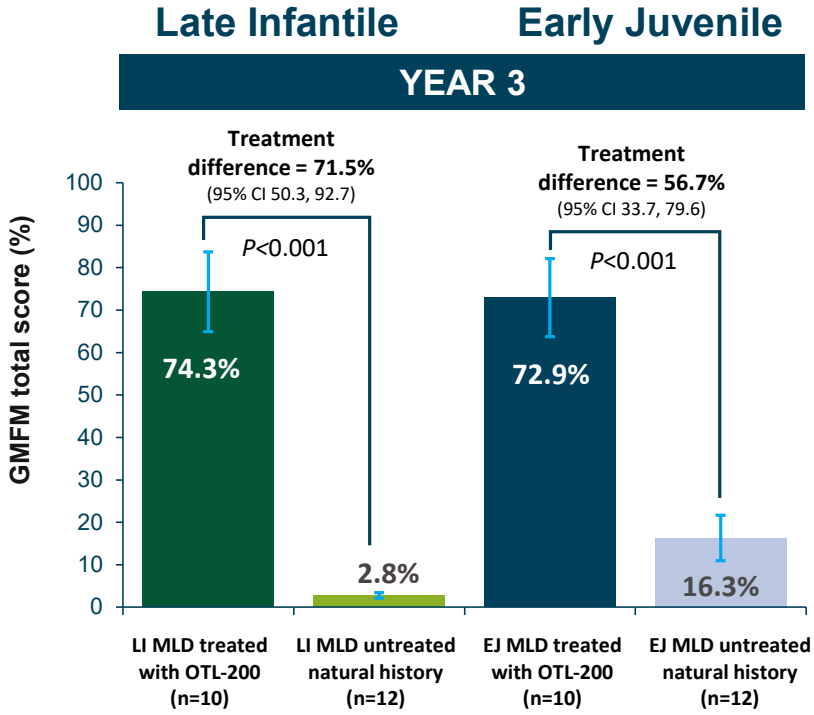
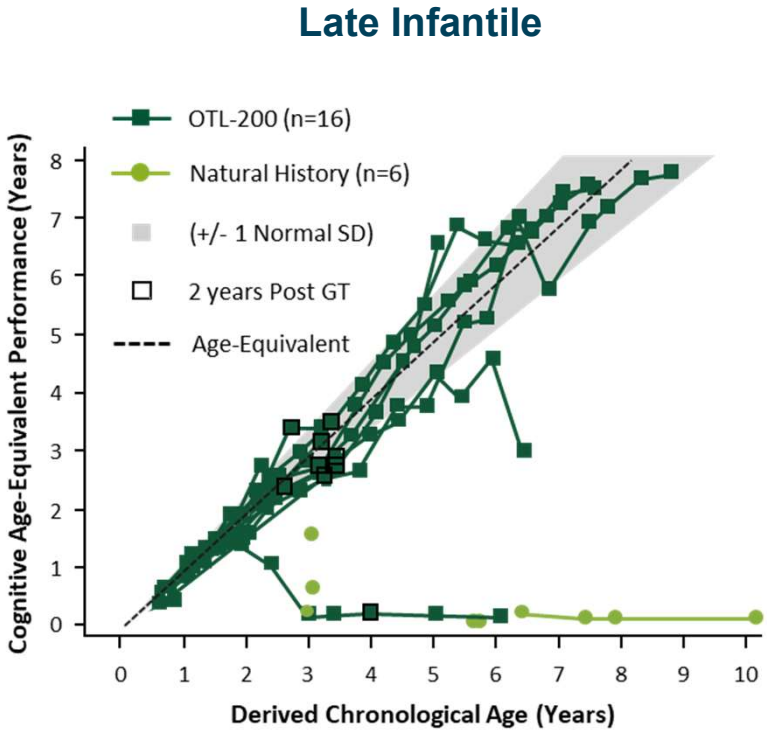
Libmeldy™ (OTL-200) for MLD: Significantly Superior Motor and Cognitive Function Demonstrated vs. Natural History





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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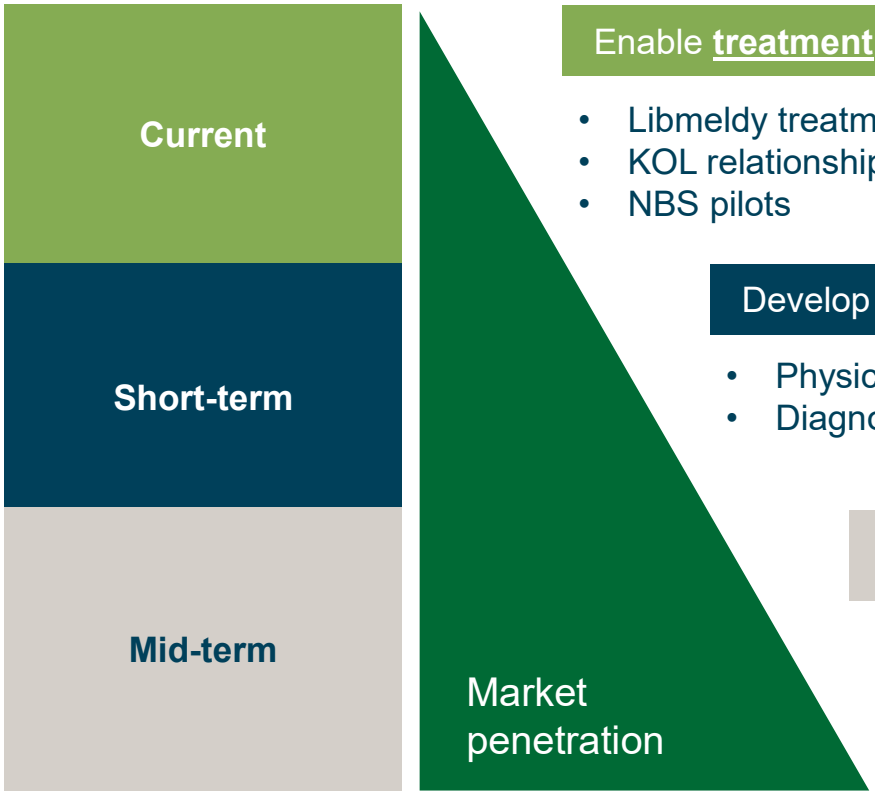
Staged Investment in EU Commercial Infrastructure for Libmeldy

Leverage this infrastructure for future launches



Enable treatment

- Libmeldy treatment centers
- KOL relationship building
- NBS pilots

Develop urgency to diagnose and refer

- Physician awareness
- Diagnostic capabilities and availability

Implement newborn screening

- NBS on the national level

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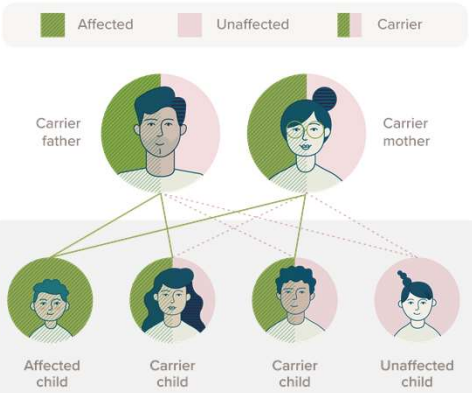
Accelerating MLD Diagnosis from EU Launch of Libmeldy

Disease awareness

Provider education,
web, media

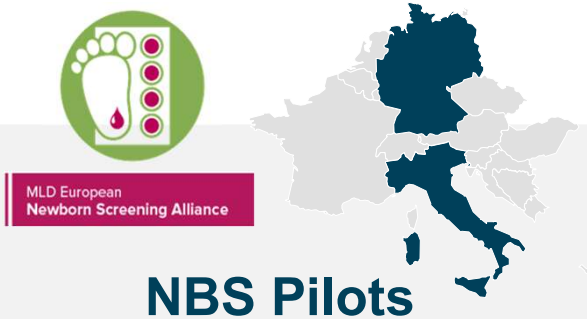
Educating physicians, caregivers and general public



Diagnostic initiatives

No-charge testing
& sibling screening

Facilitating biochemical and genetic testing



NBS Pilots

Universal NBS

Pilots underway/ready to start

Fostering a stakeholder network and generating data

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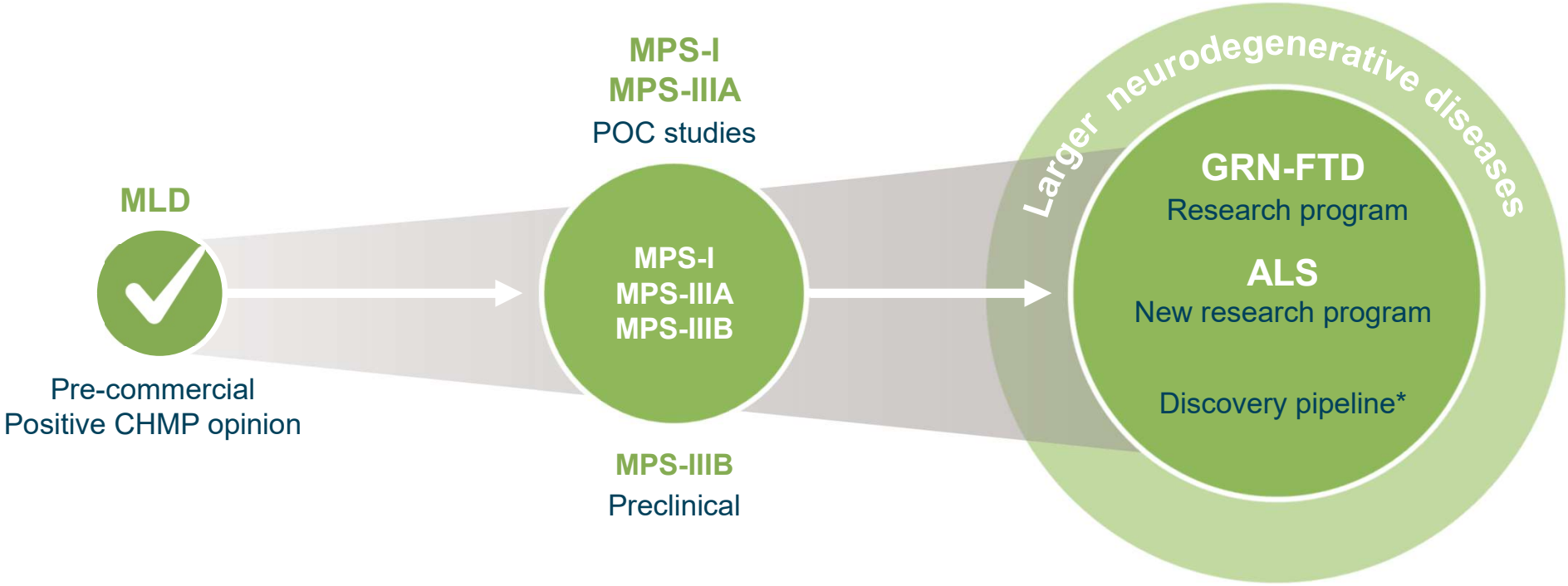
Clinical Validation in Rare Disorders Supports Application in Larger Populations such as GRN-FTD and ALS



*Other undisclosed development programs

Multiple Expected Milestones Over the Next 12 Months

MLD	☐	Obtain EC approval for Libmeldy™ in EU by YE 2020; launch in 1H 2021 Seek RMAT designation and file IND in U.S. by YE 2020
WAS	☐	Submit BLA and MAA filings for OTL-103 in 2021
MPS-I	☐	Report one-year follow-up results and initiate registrational study in 2021
MPS-IIIA	☐	Complete enrollment in OTL-201 POC study and release interim data in 2021
Research	☑	Provide detail on pre-clinical development in FTD and Crohn's disease programs at November R&D event

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