

協和キリン-Orchard Therapeutics社 IR説明会

2024年4月8日

協和キリン株式会社



本日のアジェンダ

- ◆ Orchard Therapeutics社獲得の背景
 - 代表取締役社長 CEO 宮本 昌志
- ◆ Orchard Therapeutics社とHSC-GT*について
 - The CEO of Orchard Therapeutics plc, Bobby Gaspar, M.D., Ph.D.
- ◆ HSC-GTに関する今後の計画
 - 代表取締役社長 CEO 宮本 昌志

*造血幹細胞遺伝子治療

2030年に向けたビジョン

2030年に向けたビジョン

協和キリンは、イノベーションへの情熱と
多様な個性が輝くチームの力で、
日本発のグローバル・スペシャリティファーマとして
病気と向き合う人々に笑顔をもたらす
Life-changingな価値*の
継続的な創出を実現します。

UMNを満たす 医薬品の提供

抗体技術の進化へ挑戦を続ける
ことに加え、多様なモダリティを駆
使し協和キリンの強みを生かした
創薬により、有効な治療法のない
病気の治療に取り組んでいきます。

社会からの信頼獲得

常に信頼され、成長が期待される
企業であり続けるため、世界トップ
クラスの製品品質とオペレーショナ
ルエクセレンスを追求し続けます。

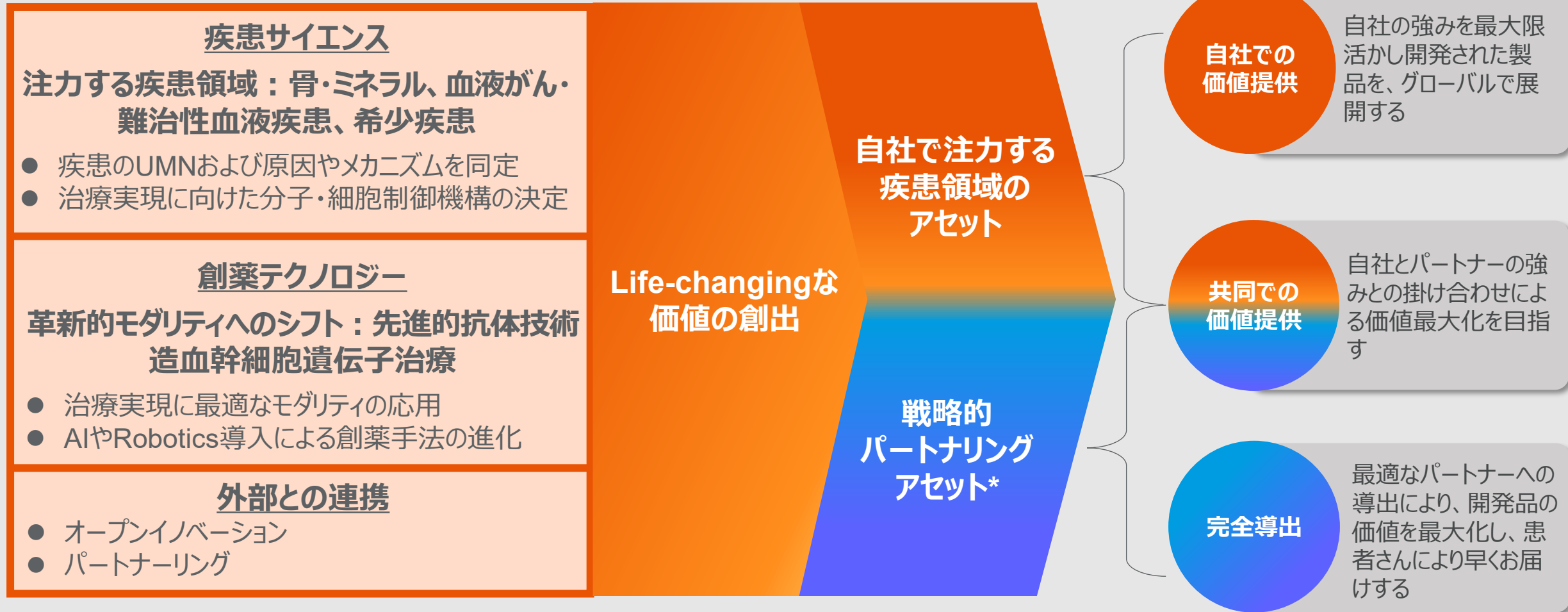
患者さんを中心においた 医療ニーズへの対応

医薬品事業で培った疾患に関する
知見と最先端の科学・技術の応用
に努め、医薬品にとどまらない社会
の医療ニーズに応えていきます。

* 病気と向き合う人々の満たされていない医療ニーズを見出し、その課題を解決するための新たな薬やサービスを創造し、提供することで、患者さんが「生活が劇的に良くなった」と感じ笑顔になること



Life-changingな価値を創出・提供するための戦略



*：注力する疾患領域以外のアセットを戦略的パートナーリングアセットとし、パートナーとの連携で価値最大化を実現する

なぜOrchard Therapeutics社を獲得したのか？

内部変化

- 骨・ミネラル、血液がん・難治性血液疾患、希少疾患が強みのある疾患領域に
- Rocatinlimabの価値最大化、いくつかのパイプラインの開発中止などによりポートフォリオが変化
- グローバル体制の進展と共に、多様なスキルや仕組みを取り込み成長できる組織へ

外部変化

- 有効な治療法が存在しない疾患への解決策
- 個別化医療
- 根本治療
の実現に向けた社会的要請が増大している

創薬研究における課題

- 従来の抗体・低分子などの創薬ターゲットが枯渇
- 遺伝性疾患・希少疾患はターゲットが存在するがアクセス方法が限定的

Orchard Therapeutics社の技術・パイプラインに着目

- 造血幹細胞遺伝子治療（HSC-GT）による遺伝性疾患・希少疾患へのアクセス向上
- Libmeldy®/Lenmeldy™ — 治療法が存在しない疾患の根本治療に向けた挑戦
- 協和キリンの研究開発との融合による新たな価値創造への期待

Bobby Gaspar – the CEO of Orchard Therapeutics plc



■ Bobby Gaspar, M.D., Ph.D.

- Co-founder and chief executive officer of Orchard Therapeutics
- Studied medicine and surgery at Kings College in London
- Completed Ph.D. at the UCL Great Ormond Street Institute of Child Health



Imagine Limitless Possibilities

8 April 2024

Bobby Gaspar, M.D., Ph.D.





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

Orchard Therapeutics: A global gene therapy leader

Our Mission

Dedicated to ending the devastation caused by severe genetic diseases through the curative potential of hematopoietic stem cell (HSC) gene therapy



Our Approach

Our approach harnesses the unique power of a patient's own genetically modified HSCs, **to potentially correct the underlying cause of a genetic disease permanently** with a one-time treatment.



Our Focus

We are focused on treating severe genetic disorders **where the disease burden on children, families and caregivers is immense** and current treatment options are limited or do not exist.



U.S. headquarters
Boston



101 Seaport Blvd
U.S. headquarters



Global headquarters
London



245 Hammersmith Road
Office, laboratories and global HQ

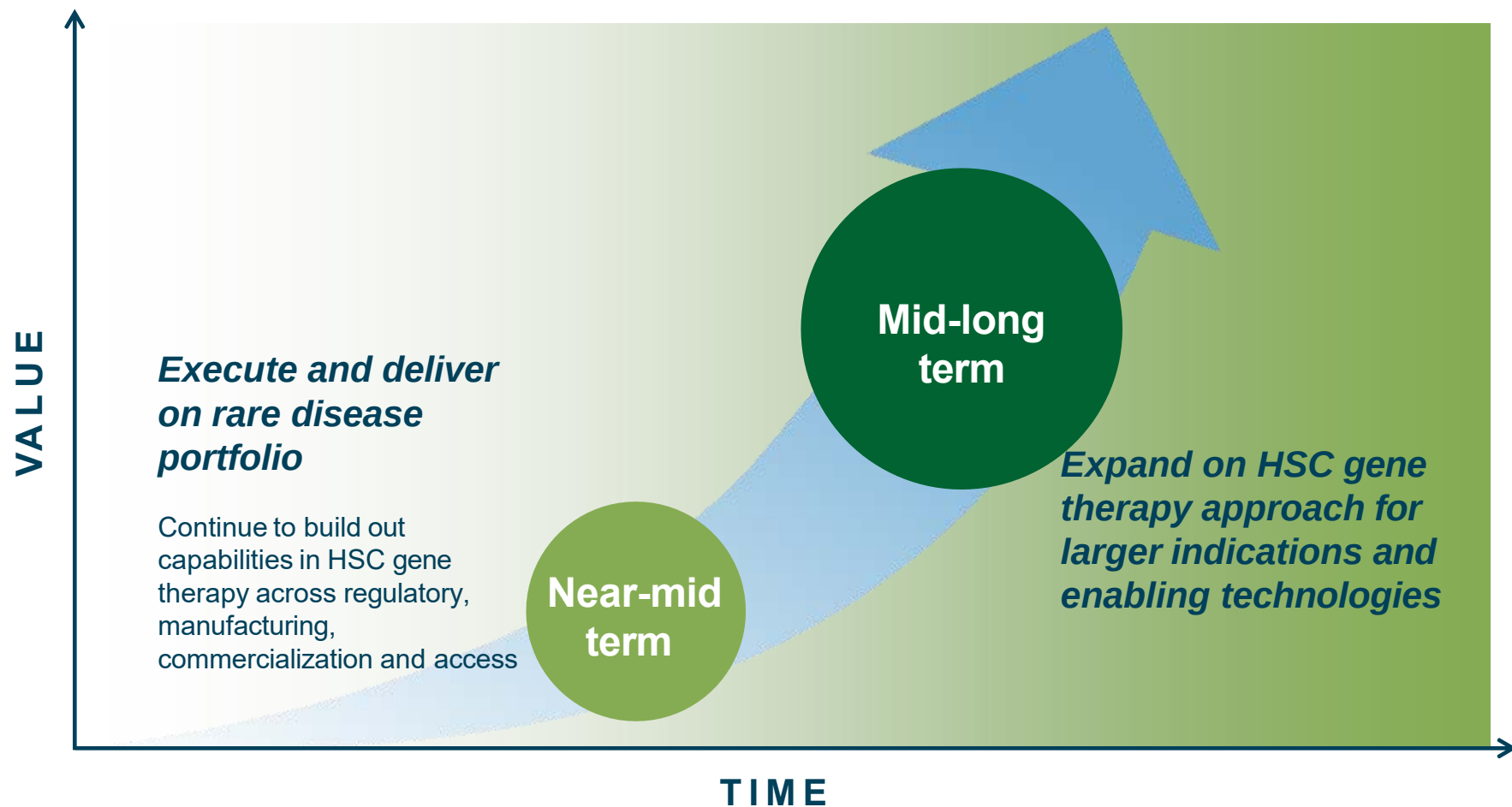
Global footprint:

~170
Employees

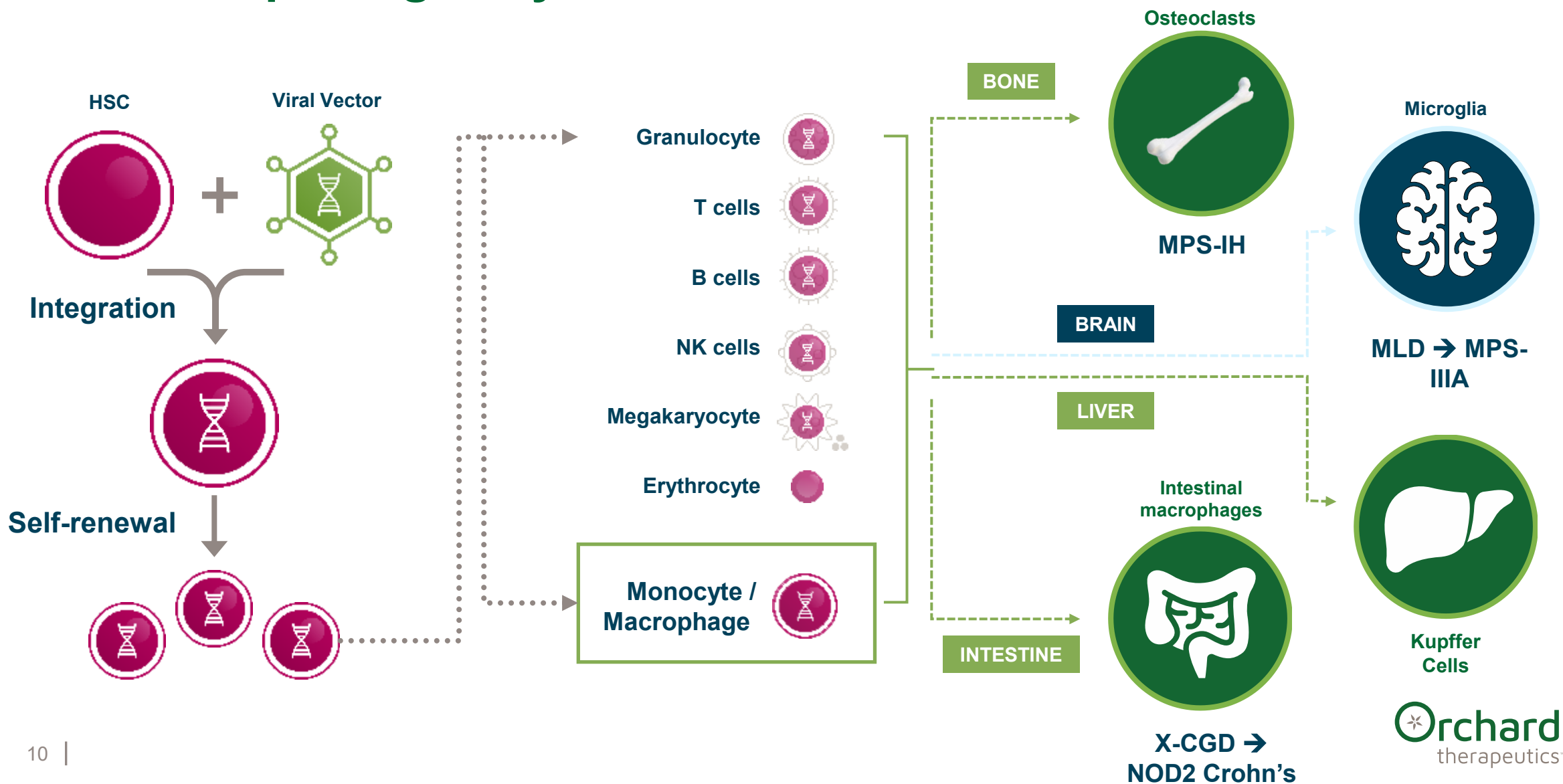
Established presence in:

- France
- Germany
- Italy
- Netherlands
- Sweden
- Switzerland

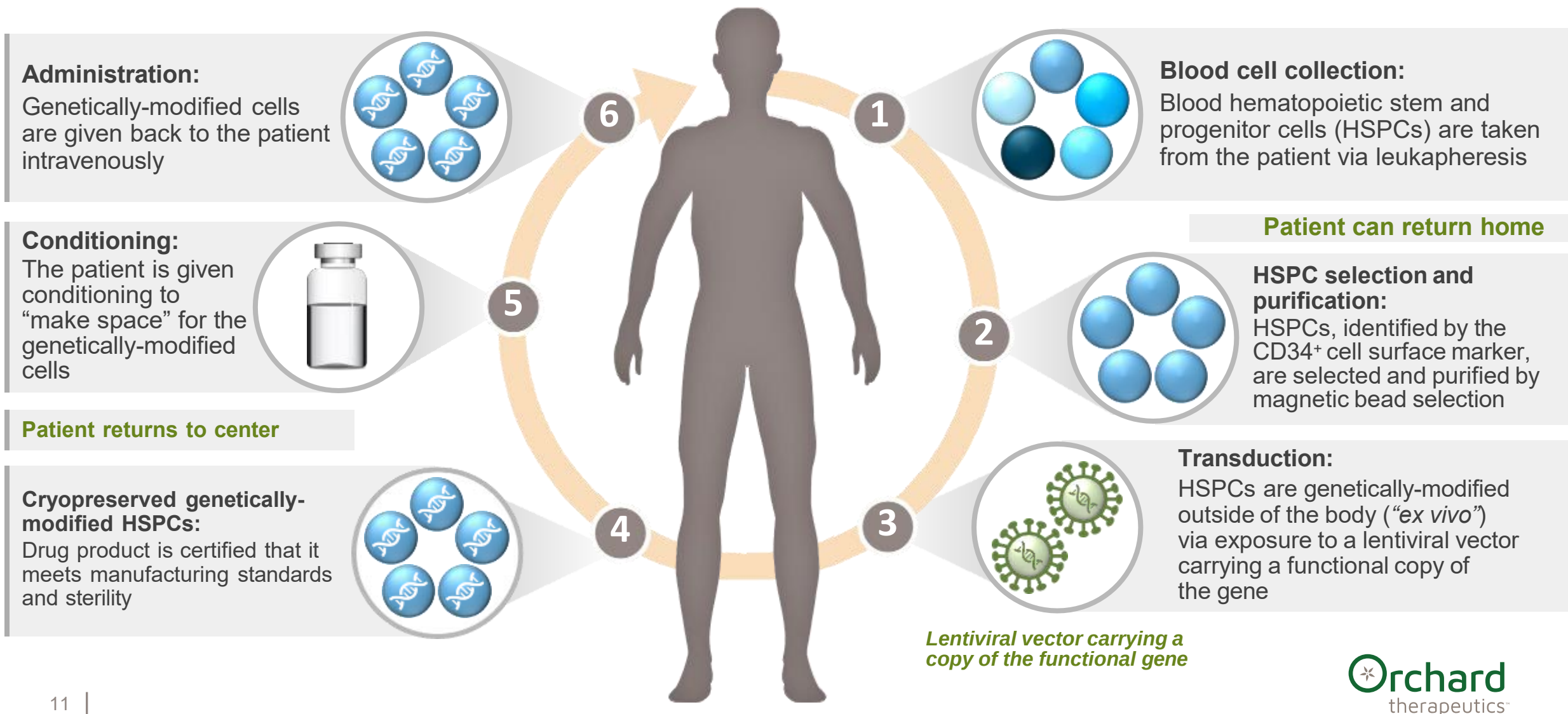
Strategic long-term growth and value creation with expansion into larger indications



HSC gene therapy enables delivery of gene-corrected cells to multiple organ systems



Autologous ex vivo gene therapy approach



Advancing a pipeline to address serious genetic diseases

Preclinical		Clinical proof of concept	Registrational trial	Commercialization
Neurometabolic/Neurodegenerative Disorders				
Lenmeldy™ / Libmeldy® (atidarsagene autotemcel)	Early-onset MLD		Approved in the U.S. and EU*	
OTL-203	MPS-I			
OTL-201	MPS-IIIA			
OTL-204	FTD			
Immunological Disorders				
OTL-104	CROHN'S			

*Lenmeldy™ is approved in the U.S. for the treatment of children with pre-symptomatic late infantile, pre-symptomatic early juvenile, or early symptomatic early juvenile metachromatic leukodystrophy (MLD). Libmeldy® is approved in the European Union, UK, Iceland, Switzerland, Liechtenstein and Norway.

Strong operational execution already in 2024

BLA approval by
FDA for
Lenmeldy in
early-onset MLD

Built U.S. field
team to set the
stage for
successful
execution of the
launch

MLD patients
identified for
treatment driving
significant
revenue growth

Beneluxa
reimbursement
agreement
expanded
Libmeldy market
in Europe

Randomized first
patients in OTL-
203 pivotal study

Lenmeldy™ / Libmeldy® (MLD): Potential significant clinical benefit for a devastating genetic disease



Age 5, pre-diagnosis



Age 9, advanced disease

Disease Snapshot

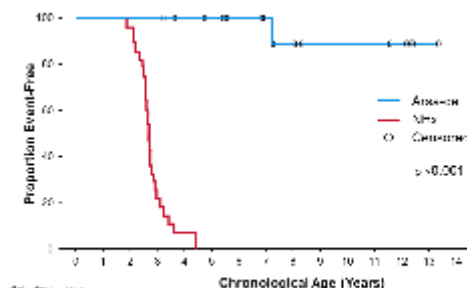
- Fatal genetic CNS disorder
- Rapid and irreversible loss of motor and cognitive function
- In its most severe form, most children pass away within five years of symptom onset¹

Severe Motor Impairment Free Survival (sMFS)

Interval from birth to first occurrence GMFC-MLD ≥ 5
(no locomotion and unable to sit) or death

Treatment with OTL-200 resulted in statistically significant and clinically meaningful improvement in sMFS in the PSLI ($p < 0.001$), PSEJ ($p = 0.042$) and ESEJ ($p < 0.001$) MLD subgroups compared to disease natural history.

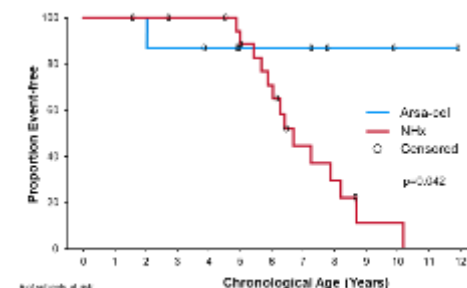
Pre-Symptomatic Late Infantile (PSLI)



OTL-200 100%

NHx 0%

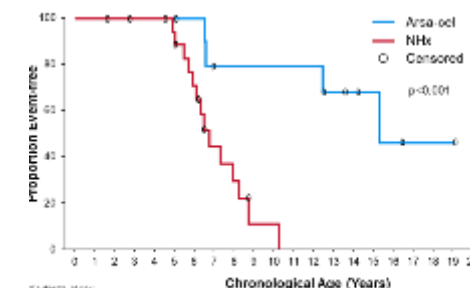
Pre-Symptomatic Early Juvenile (PSEJ)



87.5%

11.2%

Early-Symptomatic Early Juvenile (ESEJ)



80%

11.2%

Data presented at the at the Society for the Study of Inborn Errors of Metabolism (SSIEM) Annual Symposium 2023, August 2023

All 7 surviving PSEJ patients maintained the ability to walk with normal performance for age (GMFC-MLD Level 0)

Untreated NHx sibling



GMFC-MLD Level 6
3 years post-onset
8 years of age

Treated Child



GMFC-MLD Level 0
8 years post-GT
12 years of age

Pioneering Commercial Operations Leading to Sustainability

Access



Patients treated across all six qualified treatment centers in Europe

Reimbursement

Secured for all eligible MLD children



Landmark agreements secured in a dozen European countries for all eligible MLD children

Early access program: AP2 granted and renewed (France)

Treatment abroad: Named patient program in the Middle East established (Saudi Arabia)

Cross border: European pathway (S2) leveraged in multiple CEE countries

Alternative pathways for reimbursement successfully utilized

Treatment



Europe & Middle East	2022	2023 (1H)	Total
Leads	98	54	152
Confirmed MLD	73	40	113
LI or EJ MLD	57	31	88

Focus on lead generation, disease awareness and diagnosis

OTL-203 (MPS-IH): Disease background & *NEJM* interim proof-of-concept results

Disease snapshot

- **Multisystemic neurometabolic condition affecting cognition, growth and skeletal function**
- **Current standard of care: HSCT and/or ERT as a bridging or chronic therapy**
- **~1:100,000 live births; NBS established in some geographies, including U.S.**

Next steps

Pivotal trial initiated

- Randomized controlled trial vs. HSCT (standard of care)
- 40 patients
- 2-year primary analysis
- Composite endpoint
- Initial six sites to be activated globally

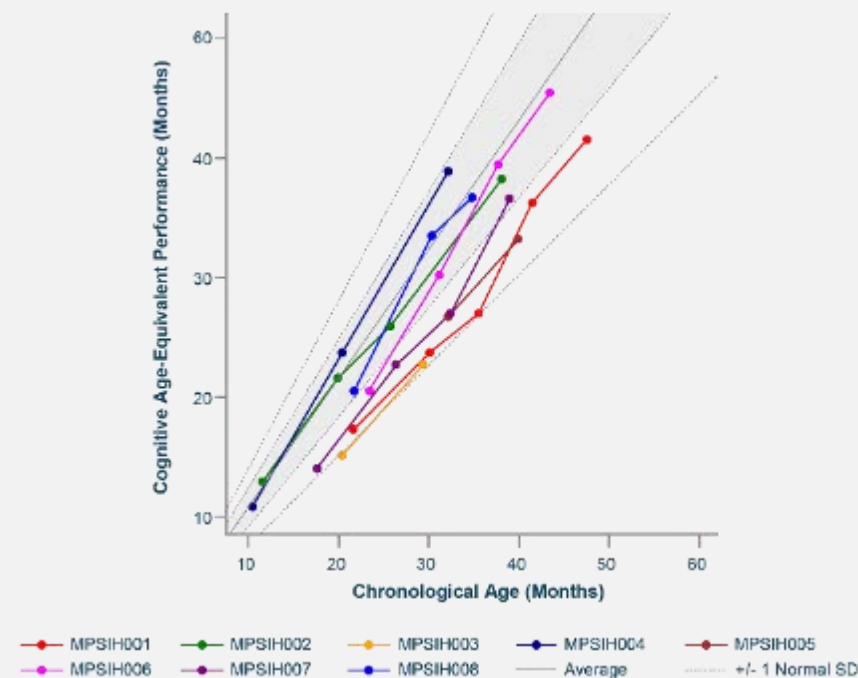
Before gene therapy



1.5 yrs. after gene therapy



Neuropsychological Tests over Time Cognitive Age-Equivalent Score (Overall)



Interim Proof-of-Concept (PoC) Study Results Published in *NEJM*

OTL-201 (MPS-IIIA): A progressive and devastating disease with no approved treatment options

Disease snapshot

- Sanfilippo syndrome type A; pathogenic variants in *SGSH* gene
- Accumulation of substrate heparan sulfate leading to severe CNS degeneration w/ somatic manifestations
- Severe phenotype development slows from 3 years of age, followed by cognitive decline, behavioural disturbances, loss of skills and eventual death
- No successful treatment options
- Incidence: ~1 in 100,000 live births

Early Neurocognitive Outcomes

- Change in cognitive function (age equivalent scores) against natural history of MPSIIIA
- Change in patient behavior, patient QoL and daily living
- Early follow-up in trial patients:
 - Gain of skills in line with development of normal children in 4 out of 5 pts.
 - Developmental gains not seen in untreated MPS-IIIA, e.g. acquisition of speech, continence and complex play
 - Longer follow up ongoing to assess safety and efficacy outcomes

Pre-treatment with GT



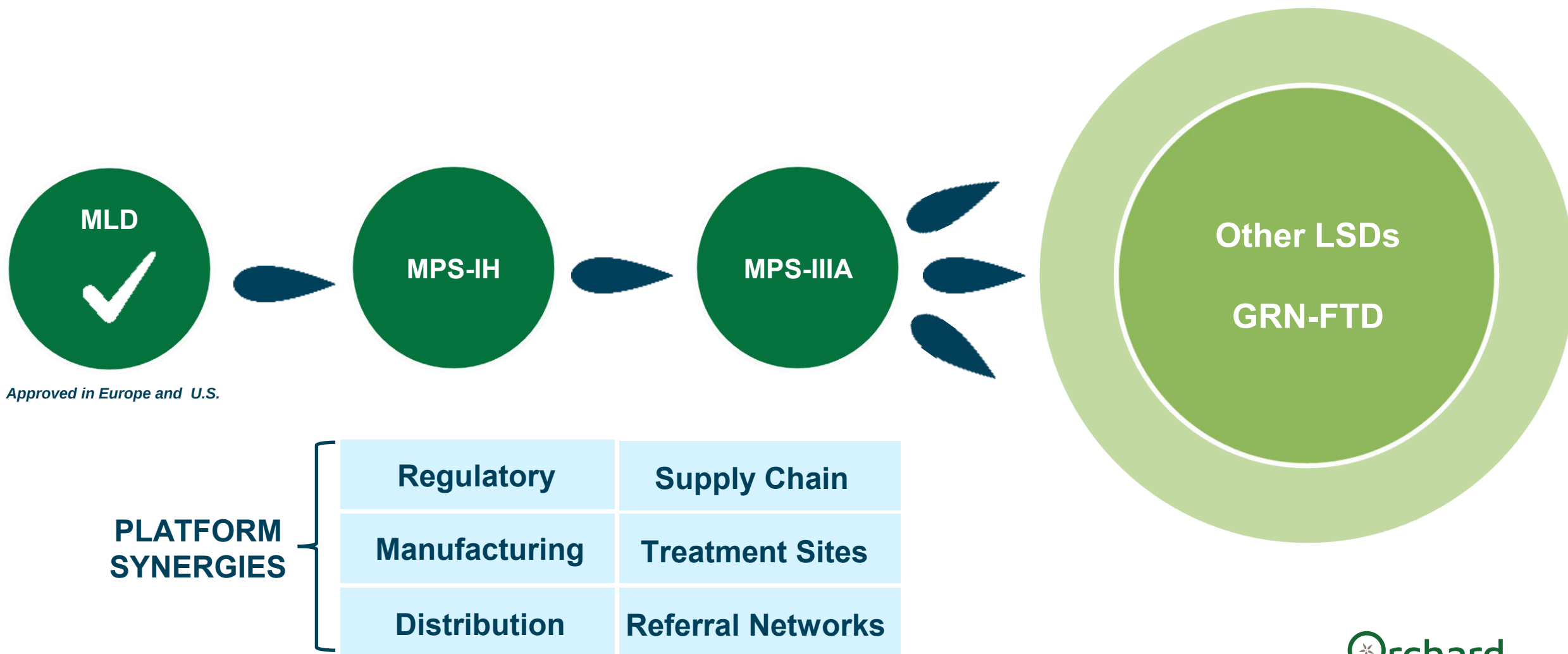
Post-GT Treatment



Post-GT Treatment



Success in MLD provides roadmap, common infrastructure for next-in-line neurometabolic and CNS programmes



Compelling fundamentals driving near-term value creation and long-term growth



**Commercial
Model**

**Establish scalable
business and growth**



**Diagnostics and
Newborn Screening**

Develop markets



**Future Potential
Regulatory Approvals**

**Leverage success in
rare diseases**



**Manufacturing and
Distribution**

**Implement a sustainable
process**



**Other
Applications**

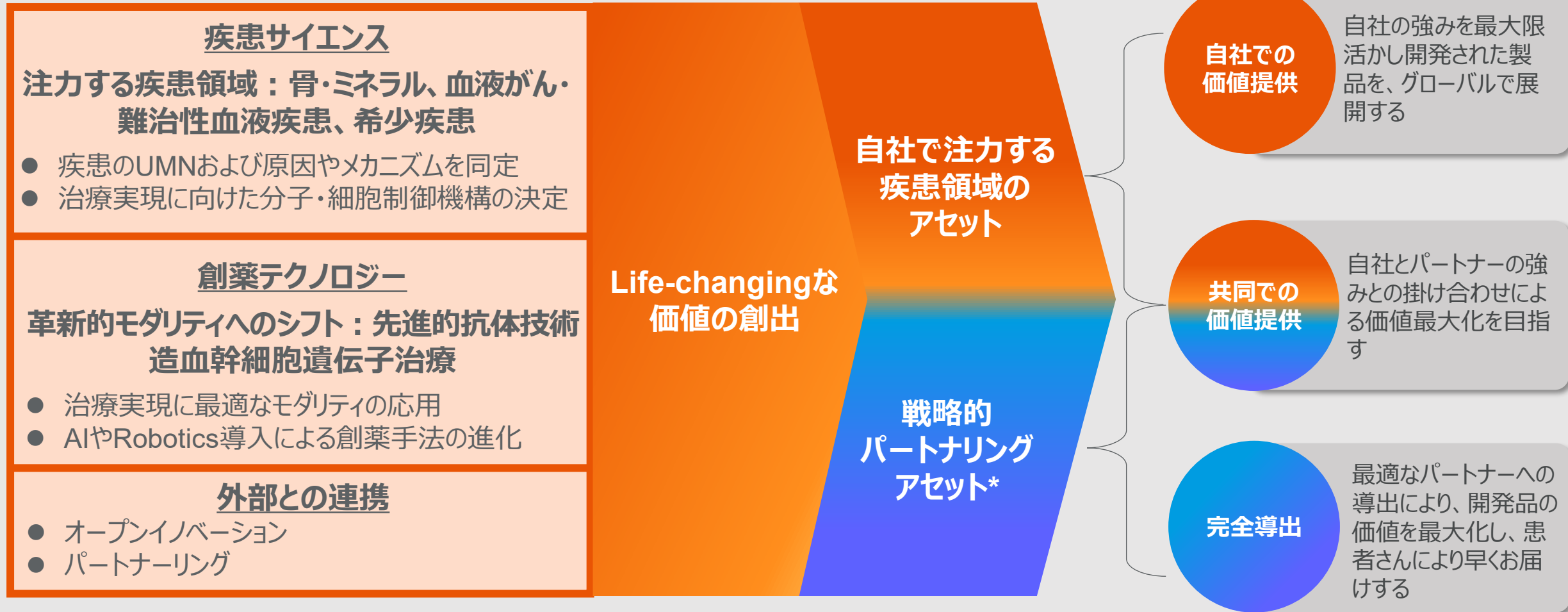
**Advance scientific
platform**

All based on a de-risked HSC GT scientific and clinical platform



The world's leading gene therapy company

Life-changingな価値を創出・提供するための戦略



*：注力する疾患領域以外のアセットを戦略的パートナーリングアセットとし、パートナーとの連携で価値最大化を実現する

HSC-GT 今後の計画

■ Libmeldy®/Lenmeldy™ 欧州・米国での使用拡大

- 2024年3月18日米国承認取得、発売
- 現在、米国・欧州・中東にて、MLDについて10本の前向きNBS*試験が進行中。2024年3月31日までに約27万5千人の新生児がスクリーニングされた
- 2024年度売上収益予想45億円

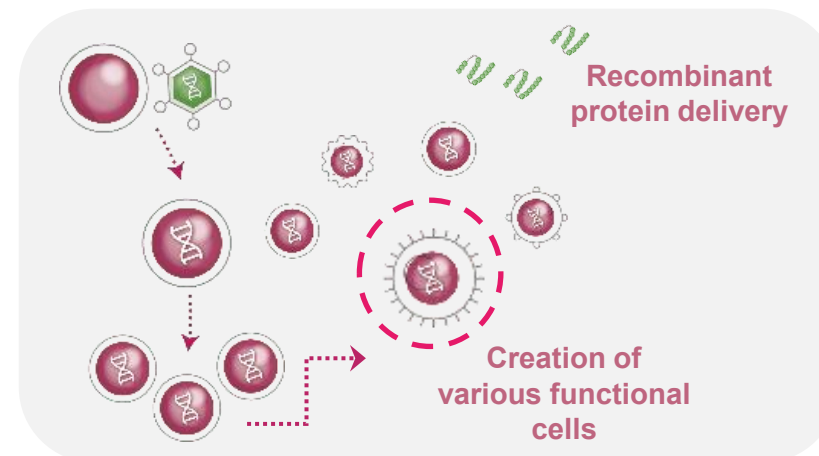
* Newborn screening, 新生児スクリーニング

■ 新たな創薬技術への展開（例）

- 当社の技術とHSC-GTの融合：通常では送達困難な部位への組換えタンパク質デリバリー
- HSCの多能性を利用した機能性細胞の創出

■ 現在の開発パイプラインの着実な進捗

開発コード	開発疾患	ステータス
OTL-203	ムコ多糖症I型 (Hurler症候群)	ピボタル試験進行中
OTL-201	ムコ多糖症IIIA型 (Sanfilippo症候群A型)	PoC試験進行中 ピボタル試験計画中



両社の強みの融合により、Life-changingな価値の継続的な創出を目指す



～本資料のお問合せ先～

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