Corporate presentation

November 2025



Advancing promising therapies for rare diseases With purpose, partnership and performance

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Our vision

We are working toward a future where people and families living with rare diseases, especially those with few or no treatment options, have access to therapies that can transform their lives.





Strategic principles guide our journey

- Acquire and develop programs in rare diseases with high prevalence – partner of choice for in-licensing
- Focus on our core competencies and experience in rare diseases
- Develop pipeline of rare disease programs which have already received significant investment and retain global or regional rights where possible (initially in Europe)
- Partner our programs where it makes strategic sense and target monetization of royalty streams for non-core programs





Two pivotal rare disease programs and a capital efficient model

Achievements and fundamentals

- > Two rare disease programs in-licensed and progressed to pivotal stage:
 - **Setrusumab** for Osteogenesis Imperfecta (OI) poised to deliver Phase 3 results around the end of 2025, powered by partnership with rare disease leader, Ultragenyx
 - **Alvelestat** for Alpha-1 Antitrypsin Deficiency-associated Lung Disease (AATD-LD) activities to support initiation of the Phase 3 ongoing, following agreement in principle of the primary endpoints
- > Maintained European commercial rights to an early-stage rare bone disease program
 - Vantictumab for osteopetrosis out-licensed to āshibio IND planned H2 2026
- > Financial discipline delivers cash runway into 2027 through key inflection points
 - \$48.7 million of cash and cash equivalents as of September 30, 2025
 - Balance FTE headcount with outsourcing through key data milestones
- > Management team with a proven track record in corporate development



Track record of value-creating partnerships

Potential to provide future milestone payments and royalties

- Setrusumab:
 - Acquired from Novartis
 - Partnered with Ultragenyx
 - Mereo retains European rights
- Alvelestat:
 - Acquired from AstraZeneca
- Vantictumab:
 - Licensed to āshibio Mereo has retained European commercial rights
- Non-core programs a potential to provide milestones and royalties
 - Leflutrozole licensed to ReproNovo
 - Navicixizumab licensed to Feng Biosciences









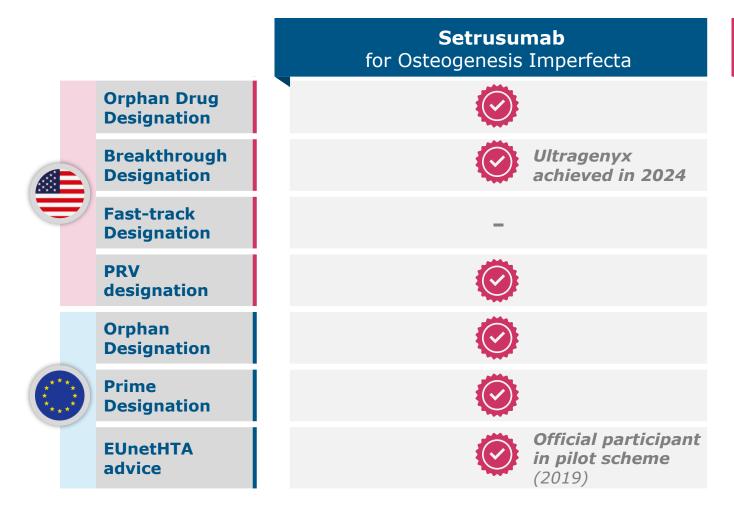
Addressing patient populations with high unmet needs and significant market opportunities of >\$1Bn¹

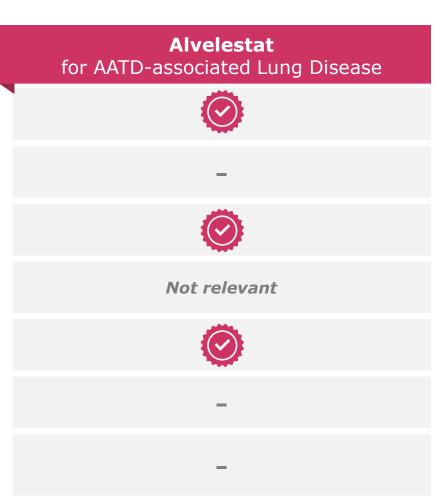
| | Osteogenesis Imperfecta | Alpha-1 Antitrypsin Deficiency | Osteopetrosis |
|-------------------------------|--|--|--|
| Disease Background | Rare genetic bone condition leading to problems including frequent fractures and skeletal deformities | Rare genetic progressive lung disease characterized by unregulated NE-driven lung destruction | Rare genetic bone disease characterized by dense, brittle bones leading to multiple fractures and significant morbidity |
| Epidemiology | ~60,000 patients across the US & Europe ² | Severe deficiency patient estimates: ~50,000 in North America and ~60,000 in Europe ³ | 1 in 20,000 incidence in North America and Europe with onset typically in late childhood ⁴ |
| Unmet Need | No FDA/EMA approved therapy. SoC (bisphosphonates) has not been shown to consistently reduce fractures | Augmentation therapy lacks clarity on efficacy and isn't reimbursed across all markets | No FDA/EMA approved therapy |
| Mereo's Unique Approach | Setrusumab A sclerostin-targeting antibody | Alvelestat An oral neutrophil elastase inhibitor | Vantictumab An anti-FZD antibody |



^{1.} Based on Cantor Fitzgerald estimates of Net Peak Sales in the US and EU5, Global Data and internal modelling; 2. Based on internal forecast; 3. Blanco I et al. 2017. alpha-1 antitrypsin Pi*Z gene frequency and Pi*ZZ genotype numbers worldwide: an update. Int J COPD: 12 561-569; 4. Wu CC, Econs MJ, DiMeglio LA, et al. Diagnosis and management of osteopetrosis: consensus guidelines from the Osteopetrosis Working Group. J Clin Endocrinol Metab. 2017 Sep 1;102(9):3111-3123.

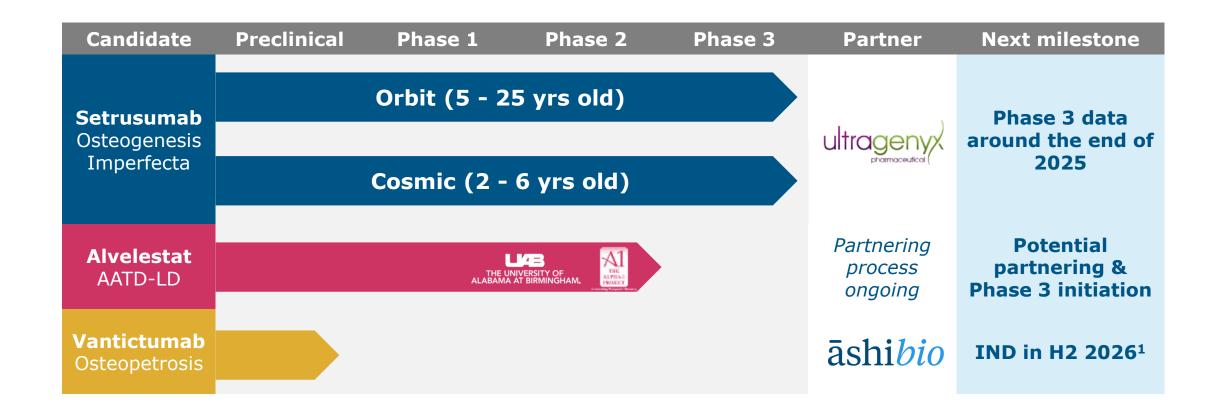
We have achieved key designations available for rare diseases







Late-stage pipeline poised to deliver first Phase 3 results





1. Per āshibio's website



"It's always a pleasure to come and speak with people who are actually making a difference on the ground and making a difference for people like myself and for others in the community.

Because it is what you do that helps us to live the lives that we want and that we deserve."

Thines Ganeshamoorthy, Trustee at the Brittle Bone Society, speaking at an event to mark Rare Disease Day 2023 at Mereo BioPharma.





Setrusumab (UGX143)

Osteogenesis Imperfecta: a rare genetic bone condition with no FDA or EMA approved therapy



Setrusumab: a >\$1Bn market opportunity in OI





(

A serious, but not mysterious condition

- 80-90% linked to a mutation in Type I collagen^{2,3} (Type I, III and IV)
- Frequent bone fractures, skeletal deformities, pain, respiratory and gastric problems
- Affects approximately 60,000 individuals³ (pediatrics and adults) in the US and Europe

Established community

- Well-established
 Community groups
 (OIFE + national members and OIF)* are a key source of support and valued resource
- OI is a progressive condition, without clear care pathways, especially for adult patients

Clear need for treatment options

- No FDA / EMA approved therapy
- Current standard of care (bisphosphonates) has not been shown to reduce fractures

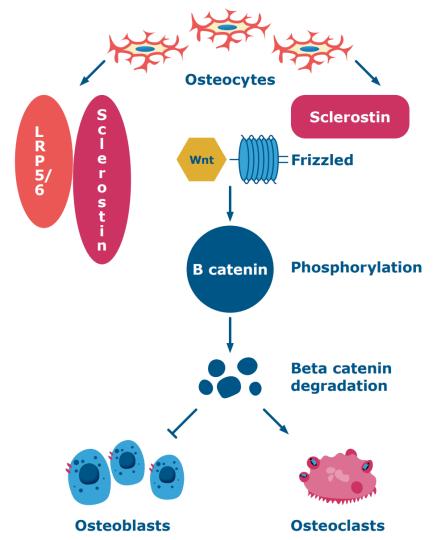


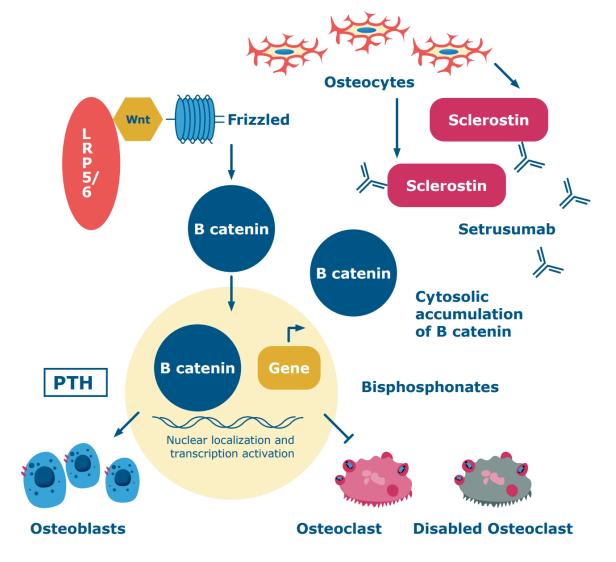
^{1.} Based on Cantor Fitzgerald estimates of Net Peak Sales in the US and EU5; 2. Based on Osteogenesis Imperfecta Foundation estimates;

^{3.} Based on Orphanet estimates; 3. Internal BD forecast;

^{*}OIFE: Osteogenesis Imperfecta Federation Europe; OIF: Osteogenesis Imperfecta Foundation

Setrusumab - a well-defined Mechanism of Action

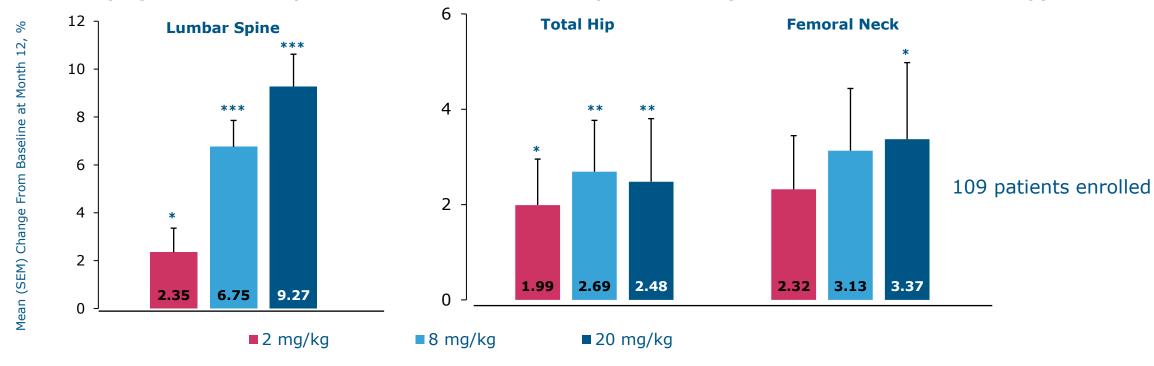






Phase 2b ASTEROID study demonstrated increased BMD in adults with OI Type I, III and IV

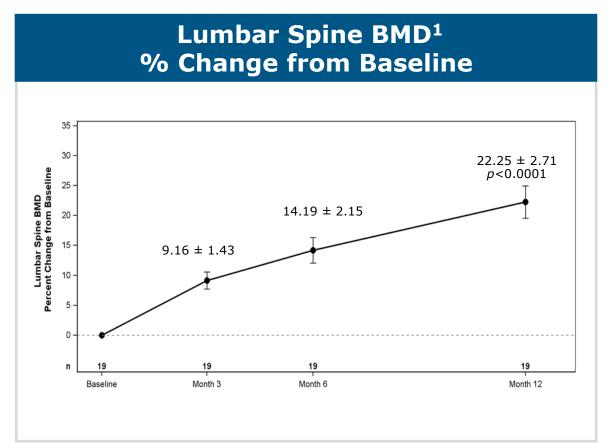
Statistically significant dose-dependent increases in areal BMD by DXA following 12 months of setrusumab therapy

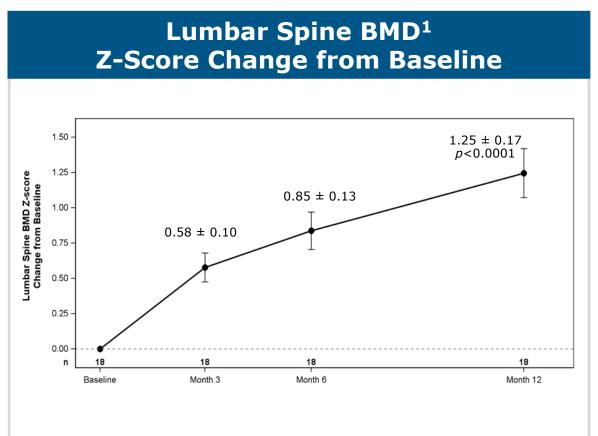


*p<0.05, **p<0.01, ***p<0.001 vs baseline based on an ANCOVA model with baseline values, treatment group and OI type as covariates. ANCOVA, analysis of covariance; BMD, bone mineral density; DXA, dual-energy X-ray absorptiometry; OI, osteogenesis imperfecta; SEM, standard error of the mean. At the 20 mg/kg dose - increase in failure load (p=0.037) and stiffness at the radius (p=0.022) as measured by finite element analysis (FEA). Increase in trabecular bone score (TBS) - 3D bone architecture, helps predict fracture (p<0.001 at 8mg/kg and 20mg/kg).



Phase 2 Orbit showed increased BMD and Z-score increases¹ Improvements consistent across all OI Types studied



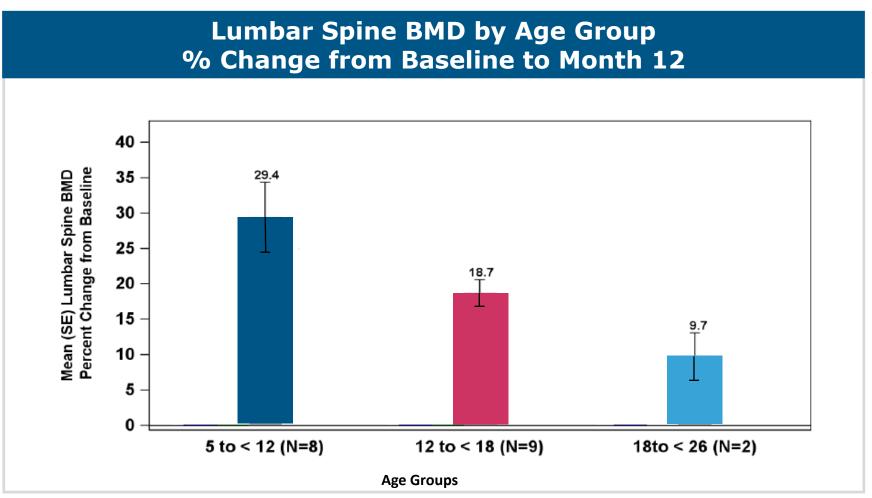


Change in lumbar spine BMD from baseline at 12 months = 22% (p<0.0001, n=19) (14% at 6 months) Change in baseline lumbar spine BMD Z-score at 12 months = +1.25 (p<0.0001, n=18) (+0.85 at 6 months)

Mereo BioPharma 1. Data as of June 2024

Orbit Phase 2 – increase in BMD observed in all age groups, 1,2

Younger patients showed a 29% increase in BMD at Month 12



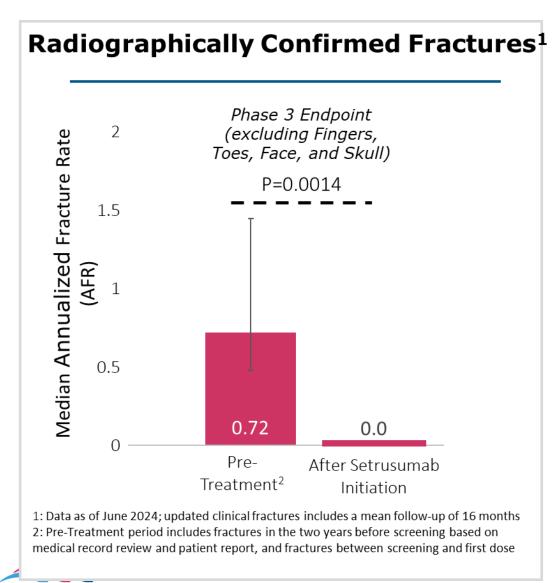
Data consistent with ASTEROID Phase 2 data in adults²

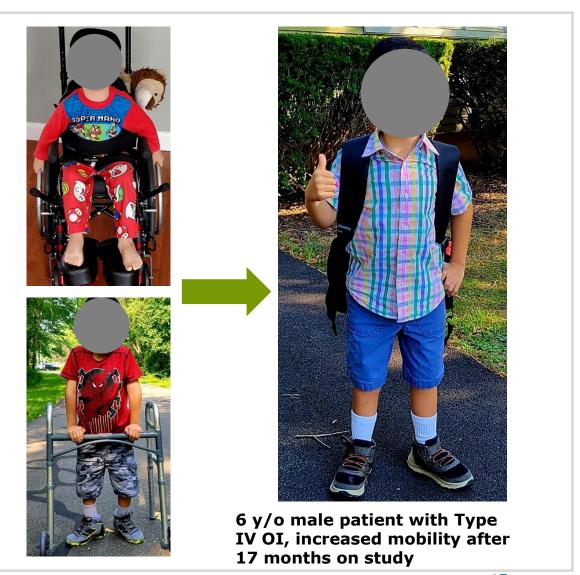


^{1.} Data as of June 2024; 2. Lewiecki EM *et al.* Evaluating Setrusumab for the Treatment of Osteogenesis Imperfecta: Phase 2 Data from the Phase 2/3 Orbit Study. Presented at the American Society for Bone and Mineral Research; October 13–16, 2023; Vancouver, BC, Canada. Abstract/Poster LB SAT-650 16

2. Setrusumab for the Treatment of Osteogenesis Imperfecta: 12-Month Results from the Phase 2b Asteroid Study, Journal of Bone and Mineral research, July 2024

Treatment with setrusumab (mean duration of 16 months) resulted in a 67% reduction in annualized fracture rate (AFR) compared to pre-treatment AFR





Safety evaluation at 14 months shows setrusumab is well tolerated

No treatment-related SAEs

No unexpected adverse events or safety concerns

No subject discontinued treatment for any adverse event

No drug-related hypersensitivity reactions

Most common adverse events (AEs) reported at 6 months*1

| Adverse Event at 6 months | Phase 2 Patients (N=24) | |
|-------------------------------------|-------------------------|--|
| Infusion-related events (low grade) | 7 (29%) | |
| Headache | 3 (13%) | |
| Abdominal discomfort | 1 (4%) | |
| Infusion site pain | 1 (4%) | |
| Bone pain | 1 (4%) | |
| Upper respiratory tract infection | 1 (4%) | |

^{*}All related adverse events were mild to moderate in severity



Orbit* & Cosmic** - Phase 3 studies are fully enrolled







Objective



Enrollment



Inclusion Criteria



Primary Endpoint Setrusumab vs. placebo 2:1 randomization
Double blind

158 subjects ages 5 to 25 years with OI Types I, III, or IV

≥1 fracture in prior 12 months or ≥2 or ≥1 long bone in prior 24 months

Annualized clinical fracture rate (excluding fingers, toes, face and skull)

Setrusumab vs. bisphosphonates 1:1 randomization
Open label

69 subjects ages **2 to 6 years** with OI Types **I, III, or IV**

≥1 fracture in prior 12 months or ≥2 or ≥1 long bone in prior 24 months

Annualized clinical fracture rate (including morphometric fractures)

Final analysis at 18 months: around the end of 2025 (Orbit p<0.039, Cosmic p<0.05)



Laying the foundation for a successful setrusumab launch in Europe

Targeted resourcing with rare disease expertise

Capturing & articulating value to healthcare systems

Partnering with physician community to be delivery-ready

Maximizing readiness for patients & caregivers

- Long-established OI patient community
- High-level of readiness for new treatments and to advocate
- Mereo engagement since Day 1 (2017)

- Connected physician community – small number of expert OI centers
- High enthusiasm for new, effective therapies (BP's limitations)
- High diagnosis rate

- Early engagement with HTAs and payors (2018)
- AFR "hard" primary endpoint – highly valued
- Quantified high level of unmet medical need
- HTA and economic value tools and postapproval data generation program ready

- Defined number of expert centers – peak 65-70 field force
- Initial flexible footprint established 2022
- High-value, firstlaunch countries priority
- Maximize first-mover advantage



Building a foundation for commercial success in Europe

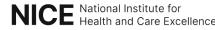


Setting the baseline: Impact /
Burden of Disease in OI in Adult
and Pediatric patients across
Mereo European territory markets

Largest ever burden of disease survey on the impact of OI on patients, physicians and caregivers. Successful collaboration between OIFE, OIF and Mereo. Made possible by the generous contribution of the OI community.







Regulatory scientific advice & HTA & Payor advice

Scientific advice from GBA & NICE in 2024 – sets our **base framework**



Validated "library" of data sources to answer authorities' questions: at time of MAA submission and to support ongoing reimbursement

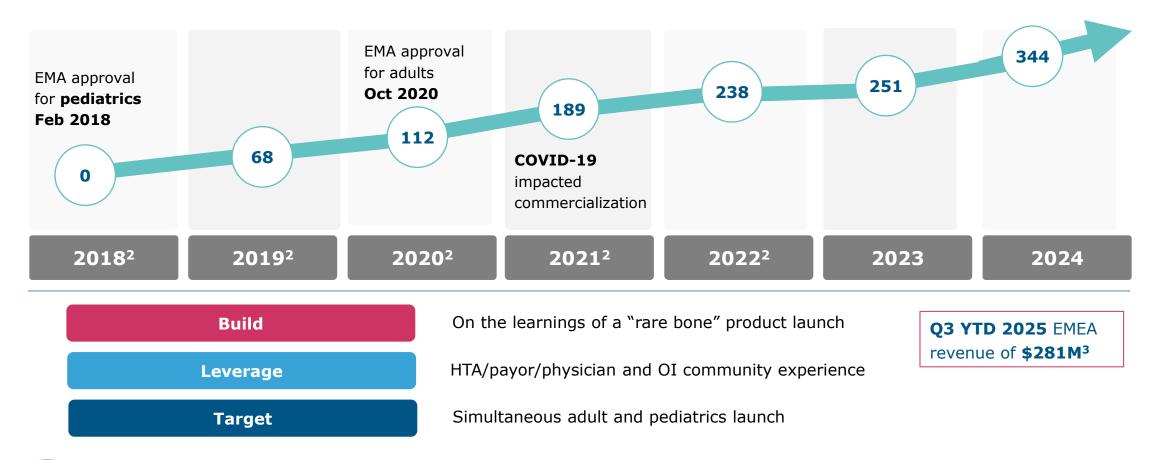
Using existing data sets to provide coordinated data across multiple European treatment centers for OI



Successful European launch of Crysvita validates market outlook

Kyowa Kirin reported EMEA revenues for Crysvita¹, \$M, 2018-2024







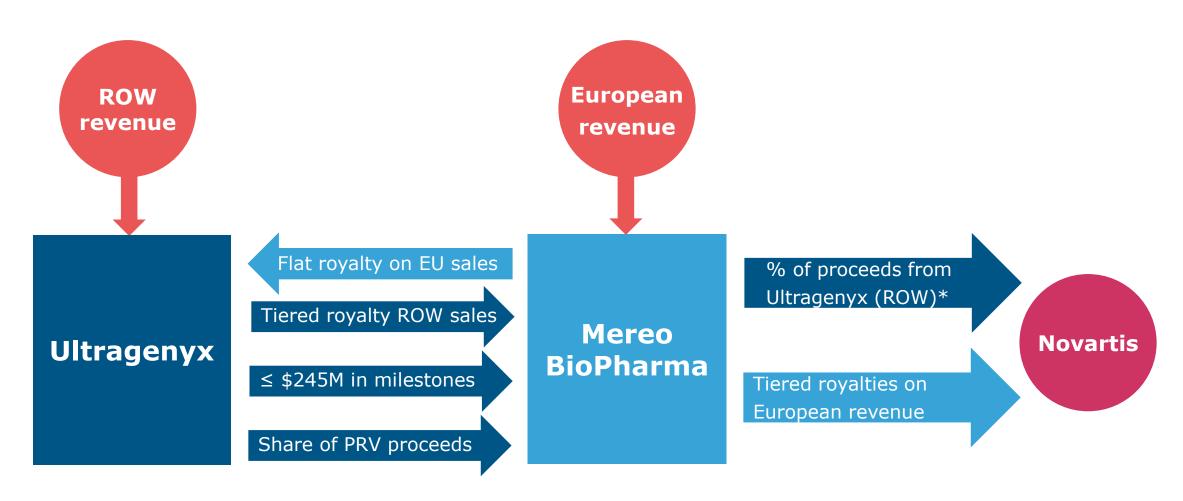
The Ultragenyx partnership, a highly effective collaboration

- Ultragenyx leads and funds the global development plan, including CMC (Dec 2020)
- Mereo retains European rights (including UK) and Ultragenyx has the USA and Rest of the World rights
- Mereo received \$50M upfront and a \$9m milestone with potential additional \$245M in clinical,
 regulatory and commercial milestones and shared potential PRV proceeds
- Ultragenyx pays Mereo tiered double digit % royalties on net sales in Ultragenyx territories
- Mereo pays Ultragenyx fixed double digit % royalty on net sales in Mereo territories

Combining the potential European revenue with focused Opex costs, and the cash inflows from milestones and royalties from Ultragenyx = a compelling business opportunity



The Ultragenyx partnership — potential attractive cash flows









Alvelestat (MPH966)

Alpha-1 Antitrypsin Deficiency-associated Lung Disease (AATD-LD): a rare progressive lung disease with high unmet need



Alvelestat: a potential >\$1bn market opportunity in AATD-LD









A rare progressive disease with high unmet need

- Presents age 20 to 50 with shortness of breath
- ~60-80% of severe patients develop lung disease¹
- Currently treated as COPD and only specific treatment is weekly IV – augmentation therapy
- No specific therapy to slow progression for early-stage lung disease

Alvelestat targets root cause of lung damage

- Lack of AAT → risk of progressive lung damage and early onset emphysema
- Potential to treat early stages of lung disease to delay progression
- Potential efficacy advantage due to sustained NE suppression

Two Phase 2 trials in AATD-LD

ASTRAEUS

- No augmentation
- Established disease
- Median baseline FEV₁:
 59%

ATALANTa

- ~50% on augmentation
- Earlier-stage patients
- Median baseline FEV₁: 81%

Total = 162 patients

Significant market opportunity

- Augmentation revenues \$>1Bn in 2023²
- AATD products forecast to reach \$3.2bn by 2031³ partially driven by increasing diagnosis rate
- Europe AAT augmentation not widely reimbursed
- Globally, many earlystage patients not treated



^{2.} Internal analysis

^{3.} GlobalData

Alvelestat's potential role in neutrophilic lung disease is supported by promising efficacy and safety data in Phase 2 studies

Bronchiectasis¹

N = 38

- Statistically significant (p=0.006) and Clinically Meaningful 100ml improvement FEV₁
- Numerical improvement patient reported outcome SGRQ of -5.64 over placebo

COPD²

- 2 studies ($N=\sim 1,500$) with effects in bronchitic subsets:
- Statistically significant and Clinically
 Meaningful >100 ml FEV₁ improvement in in
 one study (p<0.01) and trend to similar
 improvement observed in second study

Cystic Fibrosis³

N = 55

 Statistically significant reduction of biomarker of lung damage (desmosine) (p<0.05)



ASTRAEUS study Pi*ZZ

N=99. Statistically significant suppression relevant disease biomarkers:

- >90% suppression Elastase
- Reduction relevant biomarkers disease activity and connective tissue breakdown

ATALANTa study Pi*ZZ, Pi*SZ, Nulls N=63

- Significant suppression Elastase
- Statistically significant improvement in early-stage subgroup not receiving augmentation in SGRQ Activity Domain (-10.2, p=0.01) and trend in Total score (-4.7, p=0.1)

Data in >1,000 subjects



- 1. Stockley et al Resp Med 2013;107:524; 2. Kuna et al Resp. Med 2012; 106:531 supplement;
- 3. Elborn et al Eur Resp J 2012; 40:969;

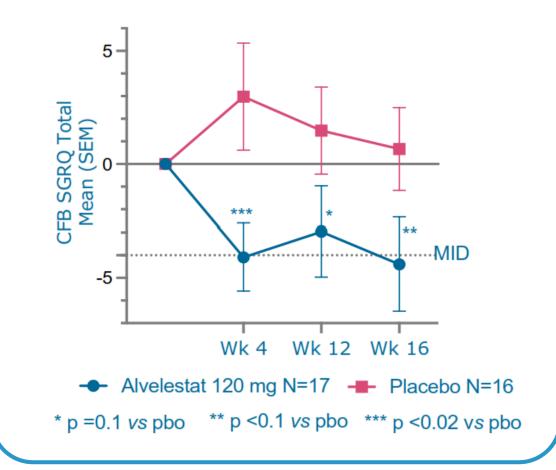
Symptomatic improvement (SGRQ) in AATD patients at early stages of respiratory disease supports Ph3 strategy for earlier intervention prior to FEV₁ decline

- ATALANTa study Non-augmentation subgroup (median FEV₁ 89.3%). Between group changes at week 12:
 - **SGRQ Total** = 4.7-point improvement (p=0.10)
 - **SGRQ Activity** = 10.0-point improvement (p=0.01)
- Post hoc analysis of ASTRAEUS earlier stage patients had greatest improvement in SGRQ Total

Qualitative validation study completed at several US sites to meet the initial requirements for SGRQ as a primary efficacy assessment in Phase 3.

"The SGRQ is fit for purpose, content valid measure for patients with AATD-LD and is suitable for use as a key COA endpoint"







Decreasing rate of elastin breakdown – Alvelestat is expected to be a long-term disease-modifying therapy going beyond augmentation therapy

Reduction in desmosine for 240 mg alvelestat at 12 weeks favourable to augmentation therapy

| | | Augmentation therapy ¹ | Alvelestat (240 mg, ASTRAEUS²) |
|--|-------------|--------------------------------------|--------------------------------|
| Desmosine | Month 3 | -0.013 ng/ml | -0.028 ng/ml |
| (absolute reduction from baseline, mean) | Month 48 | -0.074 ng/ml | Expect progressive improvement |

Long-term effect of alvelestat



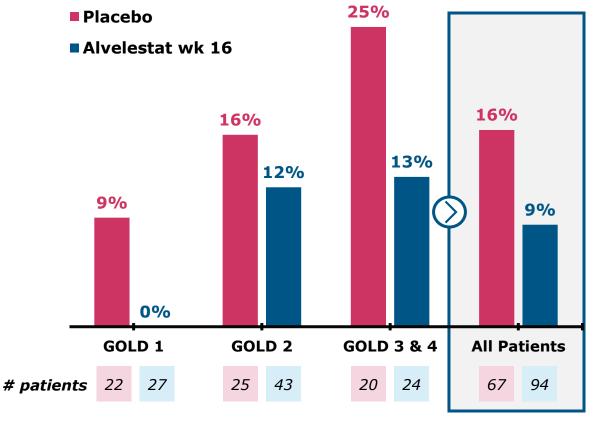
Desmosine levels have been shown to significantly correlate with clinically relevant measures of disease severity in AATD-LD (FEV₁, SGRQ, and CT Density)^{1,2,3}

Disease-modifying

Preliminary data support a protective effect of alvelestat on acute exacerbations in AATD-LD

- Reduction in acute exacerbations observed in Phase 2 program
 - Effect observed across all levels of GOLD severity¹
 - Effect remains consistent when adjusted for exposure
- Augmentation therapy has not shown benefit on exacerbations:
 - Meta analysis of EXACTLE and RAPID trials showed significant 0.29 per year <u>increase</u> in rate compared to placebo, p=0.02²
- Frequent exacerbations are associated with accelerated lung function decline³

% patients with exacerbations by week 16 ATALANTa + ASTRAEUS combined, all doses N=161





Data from two AATD Phase 2 studies, demonstrated good overall safety vs. placebo and builds on extensive safety database

| | Alvelestat 240 mg N=40 (%) | Alvelestat 120 mg N=54 (%) | Placebo N=67 (%) |
|--|-------------------------------|-------------------------------|---------------------|
| SAE | 3 (7.5) | 1 (1.9) | 0 (0) |
| Adverse Events of Special Interest | 11 (27.5) | 10 (18.5) | 18 (26.9) |
| Infections requiring antimicrobial therapy | 10 (25.0) | 10 (18.5) | 18 (26.9) |

Adverse Events of Special Interest

- Across both Phase 2 studies, no discrepancy was observed in number of infections vs placebo
- Single case (240 mg) of prolonged QTc in subject with history of prolonged QTc on concomitant therapy with known QTc effects
- Single case (240 mg) of elevated ALT>5xULN without raised bilirubin; asymptomatic and resolved. No Hy's Law cases.

Adverse events

• Headache was most frequent adverse event, generally mild or moderate and resolving on continued dosing. 3 cases reported as medical important SAEs (240 mg), completely resolved on drug withdrawal.



Including legacy studies, safety database of 1,269 subjects exposed to alvelestat

Well-defined plan for Phase 3 registrational trial in AATD-LD

Earlier stage severe PI*ZZ patients observed to have **greater response** in SGRQ (Total and activity) Clinical (\exists) Data Earlier stage patients (higher FEV₁) may be more likely to show spirometry benefit **Broader** population **Early** → **late stage** – Pi*ZZ genotype maximizes potential Two independent primary endpoints – **SGRQ Total** (FDA) Phase 3 (\Rightarrow) and **lung density by CT** (EMA – p<0.1 may be acceptable) Design for **clinical** and ~220 patients for up to 18 months (240 mg alvelestat) commercial success Opportunity for broad label including earlier stage PI*ZZ patients who may not be eligible for AAT augmentation **Commercial** (\Rightarrow) Payors and HCPs **familiar** with SGRQ Total and CT endpoints **Opportunity Partnering process ongoing** – range of structures





Vantictumab

Osteopetrosis: a rare bone disease with high unmet need



Second rare bone disease opportunity - āshibio partnership autosomal dominant osteopetrosis type 2



- A license agreement with āshibio for vantictumab was announced in August 2025
- āshibio will fund and lead global clinical development for vantictumab in patients with ADO2
- Mereo retains right to commercialise vantictumab in Europe & āshibio has exclusive rights for Ex-Europe
- Deal leverages legacy clinical data on vantictumab in oncology







- āshibio reported promising pre-clinical data at ASBMR 2025 in ADO2 mouse model¹
- Vantictumab significantly decreased areal bone mineral density in the ADO2 mouse model (whole body, femur, and spine)
- Vantictumab also improved measures of bone structure and quality
- Vantictumab rescued the bone phenotype in ADO2 mice supporting clinical development in patients with ADO2

Next Steps: āshibio expect to file an IND in the second half of 2026²



Significant opportunity in underserved rare bone disorder

ADO2 overview¹



ADO2 is an inherited metabolic bone disorder characterized by impaired osteoclast function



Dense, brittle bones lead to multiple fractures, osteomyelitis, bone pain, low blood counts, significant morbidity



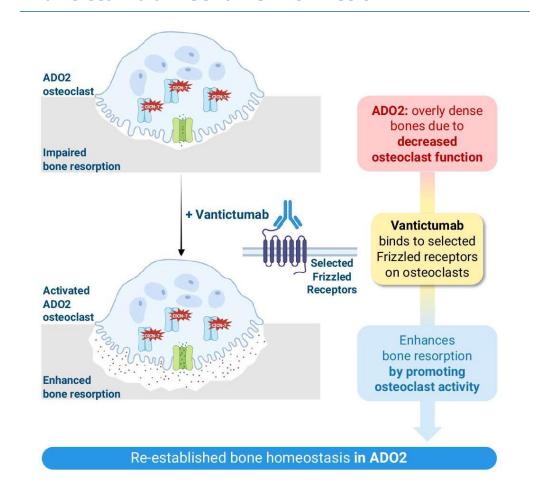
No approved therapy



1 in 20,000 incidence with onset typically in late childhood

Clear unmet need for a therapy that rescues osteoclast function, improves bone structure, and reduces morbidity

Vantictumab Mechanism of Action²







Key milestones, other programs and financials



Mereo is in a strong position to execute into 2027

Financial discipline delivers cash runway into 2027. Mereo is in a strong position to execute through 2025, including critical pre-commercialization activities for setrusumab.

Alvelestat Setrusumab Orbit (p<0.039) and Cosmic (p<0.05) Partnering process progressing final analyses – around the end of 2025 Phase 3 initiation Building health economic value models -Orphan Designation granted January 2025 SATURN and IMPACT Investing in commercial supply Other pre-commercial activities



Other programs could hold future upside

Other current partnerships

Leflutrozole – global rights out-licensed to ReproNovo for further development in infertility in men with low testosterone

Upfront plus up to \$64 million in milestones and royalties

Navicixizumab – global rights out-licensed to Feng Biosciences for further development in ovarian cancer

Payments of up to \$300 million in milestones plus royalties

Partnering opportunities

Etigilimab – anti-TIGIT which has completed a Phase 1b basket study in a range of rare tumor types in combination with nivolumab and a Phase 1b/2 investigator led study at the MD Anderson in clear cell ovarian cancer in combination with nivolumab. This study was funded by the Cancer Focus Fund.

Acumapimod – a P38 MAP kinase inhibitor which has successfully completed a Phase 2 study in Acute Exacerbations of chronic obstructive pulmonary disease (AECOPD) in 282 patients



Financial highlights



| Cap Table (September 2025) | ADSs (in thousands) |
|---|------------------------|
| Shareholders > 2% holding | 95,729 |
| Shareholders < 2% holding | 63,368 |
| Share capital – Issued as of June 30, 2025 ¹ | 159,097 |
| Potential Future Dilution: | |
| Warrants and other equity ² | 2,580 |
| Employee share schemes ³ | 12,638 |

ADS equivalents of 795,484,404 ordinary shares, with one ADS representing five ordinary shares. Assumes a market price of \$4.00 per ADS and cashless exercise. The maximum number of



warrants outstanding is 1.2m.

³ Excludes 0.2m ADSs for employee share awards with an exercise price in excess \$8.00; Most employee share awards have an exercise price between ~\$1.00 - \$6.00.



Appendix



Mereo IP strategy

| Candidate | European IP Strategy |
|---|--|
| Setrusumab Osteogenesis Imperfecta | Setrusumab antibody (2028) Use of setrusumab for treating osteogenesis imperfecta (2037) Possibility of SPC to 2041/2042 Potential additional IP to 2042 |
| Alvelestat AATD-LD | Tosylate salt of alvelestat (2030) Use of alvelestat in patients with AATD who have not responded to AAT treatment (2041 – granted) and broader applications (2041, not yet granted) Possibility of SPC to extend to at least 2045/2046 Potential additional IP to 2044 |



Thank you

With a special thank you to members of our community, who generously agreed to be featured in this presentation.

