Mereo BioPharma

Unlocking The Potential Of Novel Targets For Rare Diseases And Cancer

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Mereo BioPharma Group plc

NASDAQ: MREO

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Mereo BioPharma – A Rare Disease and Oncology Company

Our Mission **To improve the lives of patients with rare diseases and cancer**

Strategic principles guiding us on our journey…

Acquire and develop programs in rare diseases and oncology – partner of choice for in-licensing

Focus on our core competencies and experience in rare diseases including biomarker led approaches

Partner programs where it makes strategic sense and target monetization of royalty streams for non-core programs

Develop pipeline of rare disease programs & retain global or regional rights where possible

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Mereo BioPharma – A Mid-Late-Stage Company with Validating Partnerships

Achievements & Fundamentals

- Pipeline of 3 programs in rare disease/oncology all with advanced clinical data
  - **Setrusumab** for Osteogenesis Imperfecta (OI) under the Ultragenyx partnership, has entered a registrational trial in Q2 2022
  - **Alvelestat** for Alpha-1 Antitrypsin Deficiency-Related Lung Disease (AATD-LD) recently reported positive Phase 2 top-line efficacy and safety data
  - **Etigilimab** an anti-TIGIT antibody, in a Phase 1b/2 solid tumor basket trial; data presented at ASCO 2022
- Management team with a track record of drug development and partnering success
  - Setrusumab and alvelestat acquired/in-licensed from pharma with deal structures dependent on the success of the programs
- Upside potential from successful out-licensing/partnering deals in place, with additional opportunities for partnering

Corporate Partners

ultragenyx pharmaceutical · OncXerna · AstraZeneca · NOVARTIS

Other Partners

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center Making Cancer History® · THE UNIVERSITY OF ALABAMA AT BIRMINGHAM · NIH NATIONAL CANCER INSTITUTE · NIH National Center for Advancing Translational Sciences · ALPHA-1 FOUNDATION

Setrusumab – In Late-Stage Development for the Treatment of OI

Setrusumab is an anti-sclerostin antibody – improves bone mineral density in OI patients

Next milestone:
Phase 2/3 update – late 2022

Setrusumab Overview

- Anti-sclerostin antibody under investigation for the treatment of OI, a rare genetic bone disease with high unmet need and no approved therapies
- **Setrusumab promotes bone formation and inhibits bone resorption**
- Global Partnership with Ultragenyx (NASDAQ: RARE); **Mereo retains European & UK rights**
- Setrusumab has been granted Orphan Drug Designation by both the FDA and EMA, in addition to PRIME status in the EU and eligibility for the FDA's Pediatric Review Voucher (PRV)

Key Clinical Data To-Date

- Reported **positive Phase 2b data showing statistically significant and dose dependent improvements in bone mineral density** in the ASTEROID study
- Setrusumab **was well tolerated, and no safety concerns were observed** (including no cardiac events)

Clinical Development

- Setrusumab **"Orbit" registrational Phase 2/3 study** in 5-25 yr olds initiated in Q2 2022. Phase 3 dose selection expected in late 2022.
- Supportive pediatric study in 2-5 yr olds due to initiate in late 2022
- Mereo providing support in the UK and Europe

OI – A Rare Genetic Bone Condition with No Approved Standard of Care

Osteogenesis Imperfecta

- A rare genetic bone disease, mostly linked to a mutation in Type I collagen[1,2]
- Affects approximately 60,000 individuals[3] (pediatrics and adults) in the US and Europe
- Well established Community groups (OIFE and OIF) are a key support and valued resource

High Unmet Need

- Symptoms include frequent bone fractures, skeletal deformities, pain, respiratory and gastric problems
- **No approved therapy for OI.** Current bisphosphonate standard of care prevents bone resorption but does not reduce fractures
- Symptoms are present from birth leading to an early diagnosis
- OI is a progressive condition, without clear care pathways, especially for adult patients

OIFE AGM 2019

** OIFE: Osteogenesis Imperfecta Federation Europe; OIF: Osteogenesis Imperfecta Foundation*

1. Based on Osteogenesis Imperfecta Foundation estimates; 2. Based on Orphanet estimates; 3. Internal BD forecast

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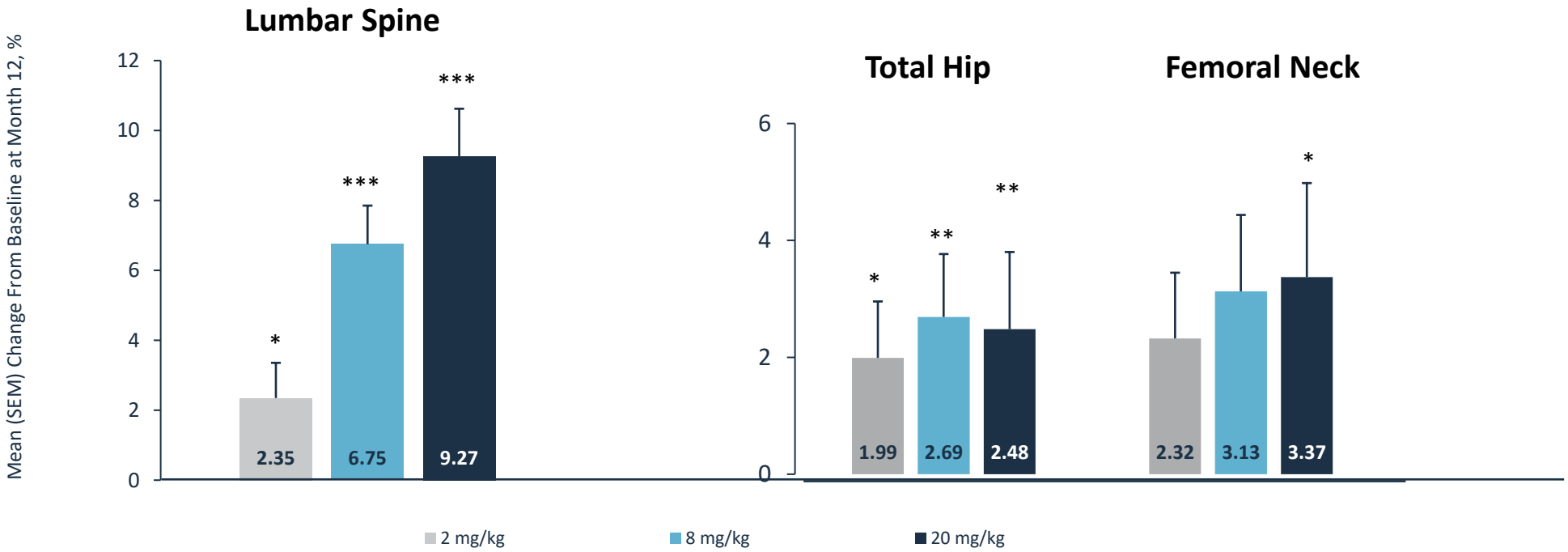
Summary of Phase 2b ASTEROID Results in Adults with OI Types I, III and IV

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.

Primary endpoints: Radial Tb vBMD at 12 months was not significantly changed after setrusumab treatment. However, setrusumab elicited dose-dependent increases in bone strength indices and total vBMD at the radius, with stiffness and cortical vBMD also increased at the tibia (all significant at 20 mg/kg). Significant increases in DXA aBMD were observed at lumbar spine and total hip (all doses), as well as at the femoral neck (20 mg/kg).

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Glorieux F, et al "Setrusumab for the treatment of osteogenesis imperfecta (OI): Results from the Phase 2b ASTEROID Study" ASBMR 2021; Abstract 1016.

Ultragenyx – Mereo Partnership and Long Term Plan

Mereo – Ultragenyx Partnership

- Ultragenyx funding and leading global development plan in pediatrics and adults
- Mereo retains rights to setrusumab in Europe and UK – Ultragenyx US and ROW
- Received $50M upfront with up to $254M for clinical, regulatory and commercial milestones
- Ultragenyx pays Mereo tiered double digit % royalties on net sales
- Mereo pays Ultragenyx fixed double digit % royalty on net sales

Clinical Development Overview

- Phase 2/3 pediatric study in OI initiated in H1 2022 ('ORBIT')*
  - Dose selection based on collagen production (P1NP)
  - Phase 3 – fractures over 15-24 months
- Supportive pediatric study in OI in 2-5 yrs old expected to initiate in **late 2022**
- Registrational pathway for adults with OI under discussion

Mereo Territories & Focus

- Mereo's current focus is laying the groundwork for reimbursement of setrusumab in Europe and UK
- In collaboration with OIFE and OIF Mereo conducted the IMPACT Survey, the largest data set on the impact of OI. Results will support OI advocacy & reimbursement efforts.
- Mereo is participating in the pilot EUnetHTA process – 12 EU countries individual HTA** bodies in one forum for feedback on future evidence requirements; advice from payors through MoCA

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**Clin Trials Identifier: NCT05125809*

***Health Technology Assessment*

Alvelestat – In Development for the Treatment of AATD-LD and BOS*

Alvelestat is a potent, oral inhibitor of Neutrophil Elastase

Next milestone: Expanded Phase 2 ASTRAEUS data & End-of-Phase 2 regulatory discussions – H2 2022

Alvelestat Overview

- Neutrophil elastase (NE) is a protease enzyme that unopposed is believed to drive lung tissue destruction in lead indication, AATD-LD and, also in GVHD BOS
- Alvelestat is a highly specific neutrophil elastase inhibitor that has been shown to inhibit up to 90% of NE at doses in development
- Oral, twice daily dosing with dose regimens for consistent NE inhibition throughout dosing cycle
- Alvelestat has received U.S. Orphan Drug Designation for the treatment of AATD

Key Clinical Data To-Date

- Safe and well tolerated with safety established in >1000 patients
- Recent positive top-line Phase 2 data in AATD–LD, ASTRAEUS[1]
- Biomarker data generated in NE driven diseases (bronchiecstasis, cystic fibrosis, AATD-LD, BOS, COVID)

Two Investigator Initiated Studies

- UAB & the National Cancer Institute, led by Dr. Steve Pavletic. Phase 1b complete, Phase 2 planned to begin in H2 2022
- ATALANTa in AATD-LD, funded by NCATS**, due to read out in H1 2023

*Bronchiolitis Obliterans Sydrome
**NCATS: National Center for Advancing Translational Science

1. Press release: Mereo BioPharma announces Positive Top-Line Efficacy and Safety Data from "ASTRAEUS" Phase 2 Trial of Alvelestat in Alpha-1 Antitrypsin Deficiency- associated Emphysema – 09 May 2022. Further data analysis ongoing.

AATD-LD – A Rare Progressive Lung Disease with High Unmet Need

Alpha-1 antitrypsin (AAT) inhibits the action of neutrophil elastase. Individuals who lack AAT or produce misfolded inactive AAT are at risk from progressive lung damage and early onset emphysema.

AATD-LD

- Presents age 20 to 50, symptoms include, shortness of breath, cough, reduced exercise tolerance
- Target population estimates - 50,000 in North America and 60,000 in Europe and the UK[1,2,3]
- AATD community groups are well established

High Unmet Need

- Treatment options limited to intravenous plasma-derived augmentation therapy
  - Clinical efficacy not uniformly recognized by physicians
  - IV administration burden on patients
  - May require higher doses
  - Inability to titrate dose up for acute lung inflammation

Significant Market Opportunity

US AAT augmentation revenues ~$0.8-1.1bn in 2020 (CAGR 15%; 9.6-25%)[4]

- US patients (weekly I.V.) cost of $110-120k/year
- Market predicted $2.0-$3bn in 2030 driven by increased diagnosis of AATD

Europe AAT augmentation

- Not widely reimbursed
- Opportunity to be first oral treatment of choice including in markets where augmentation is non-reimbursed
- Revenue potential ~30-65% of the US market[5]

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1. Francisco et al (2012) Rare alpha-1-antitrypsin variants: are they really so rare? Therapeutic Advances in Respiratory Disease January 30; 2. Luisetti et al (2004) α1-Antitrypsin deficiency; 3. Epidemiology of α1-antitrypsin deficiency Thorax 59:164-169; 4. US AATD market consensus based on Bernstein, Deutsche Bank, Evercore, LifeSCi Capital, UBS; 5: Internal BD assumption

Linking Biomarkers to Pathological Pathway

AATD-Lung Disease Pathogenic Pathway

Biomarkers of AATD-LD

Blood NE | **Aα-Val^{360}** | **Desmosine** | **CT Density/FEV$_1$**

Elastase Activity → **Unopposed NE** → **Alveolar Elastin Breakdown** → **Lung Tissue Loss/Emphysema**

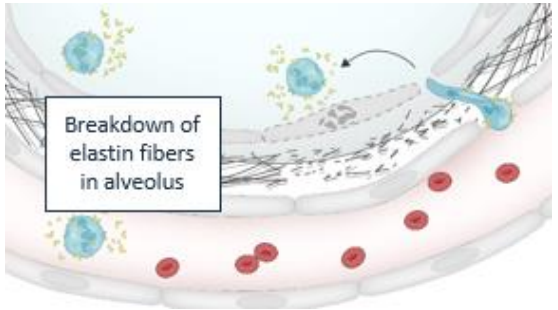
Increased elastase activity

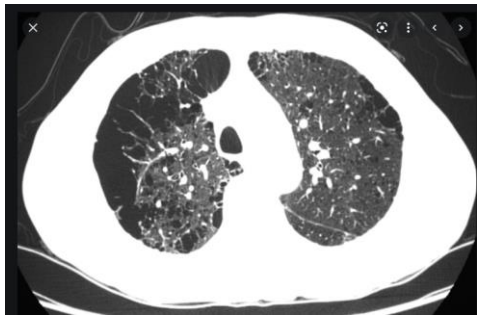
Alvelestat

Increase in elastase-driven target (fibrinogen) breakdown

Correlates with FEV$_1$

Elastin breakdown fragments





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ASTRAEUS – A 12-week Study Treating Participants Who Have alpha-1 antitrypsin-related COPD With Alvelestat (MPH966) or Placebo (NCT03636347)

- A randomized double blind-placebo-controlled study in patients naïve to augmentation or following a 6-month wash-out period. Comparing placebo and two different doses of alvelestat in Pi*ZZ, Pi*Z Null, Pi*Null genotype/phenotype.
- Enrolled 99 patients with 98 dosed (36 placebo, 41 high dose, 22 low dose)

Top-line Data: Expanded analysis expected in H2 2022

- Statistically significant reduction in all three key biomarker primary end-points on the pathogenic pathway of AATD-LD
  - Changes in disease-severity biomarkers (Aα-val360 and desmosine) comparable to those reported with augmentation therapy
- Dose response info will enable selection of a single dose for Phase 3

Safety Summary - No safety concerns identified through lab and adverse event monitoring

Adverse Events of Special Interest:

- One case (high dose) prolonged QTc in subject with history of prolonged QTc, one case (high dose) elevated ALT both resolved
- Known adverse event of headache was more frequent in alvelestat groups, including SAEs. Mitigation planned a through dose-escalation approach.

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Press release: Mereo BioPharma announces Positive Top-Line Efficacy and Safety Data from "ASTRAEUS" Phase 2 Trial of Alvelestat in Alpha-1 Antitrypsin Deficiency- associated Emphysema – 09 May 2022. Further data analysis ongoing.

Etigilimab – An Anti-TIGIT Antibody, in Development in Combination with an Anti-PD-1 Antibody

Etigilimab is an IgG1 anti-TIGIT monoclonal antibody with ADCC characteristics

Next milestone: Additional Phase 1b data – H2 2022

Etigilimab Summary

- An IgG1 monoclonal antibody designed to balance affinity and ADCC characteristics while limiting side effects
- Pharmacodynamic changes consistent with target engagement

Etigilimab Program Clinical Trials

- FIH Phase 1a (etigilimab monotherapy)/1b (combined with nivolumab)- completed[1]
- Phase 1b open label basket study in combination with nivolumab (ACTIVATE) enrolling selected cohorts; data presented at ASCO 2022[2]
- The combination of etigilimab and nivolumab was safe and well tolerated with no new safety signals
- Focus Fund supported Phase 2 MD Anderson study with nivolumab (EON) in clear cell ovarian cancer – initiated and enrolling

Emerging TIGIT Data

- Several pharma/biotech companies are developing inhibitors of TIGIT
- Further Mereo investment pending review of Phase 1b study results and competitive landscape

1.Mettu et al., CCR, 2021; 2.McKean et. al., ASCO, 2022

ACTIVATE Trial – Preliminary Efficacy Data

Response summary (efficacy analysis set; n=38)*

Objective Responses by RECIST	Cohort							
	A Endometrial Cancer (CPI-naïve) (n=1)	C Cervical Cancer (n=5)^	E TMB-H/MSS (n=6)	F (Rare) Uveal (n=6)	F (Rare) Sarcoma (n=7)	F (Rare) GCT (n=4)	H Ovarian (HGSOC) (n=9)	Total (n=38)
CR	**0**	**2[1]**	**0**	**0**	**0**	**0**	**0**	**2**
PR	**0**	**0**	**0**	**1[2]**	**1[3]**	**0**	**2**	**4**
SD	**0**	**2**	**1[4]**	**2**	**3**	**0**	**2**	**10**
PD	**1**	**1**	**5**	**3**	**3**	**4**	**5**	**22**
Overall Response Rate (%): 15.8								
Disease Control Rate (%): 42.1								

Data cutoff date 4/20/2022.
McKean et. al., ASCO, 2022

*Efficacy analysis set: Response evaluable subjects by investigator-assessed response per RECIST 1.1/clinical progression
Excludes 5 non-prioritized histology subjects enrolled prior to amended, current version of protocol (V3.0).
^ Includes 1 TMB-H cervical subject E025 with CPS >1% by central lab.
[1]1 CR and [2]1 PR confirmed respectively after data cutoff date; [3]Dedifferentiated liposarcoma histology, [4] Post-CPI, NSCLC, CPS<1%

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Partnerships Overview

Current Partnerships	
• Ultragenyx leads global development of setrusumab, Mereo retains rights to Setrusumab in Europe and the UK • Received $50 million upfront, up to $254 million in additional milestones plus royalties • Registrational trial initiated	ultragenyx pharmaceutical
• Navicixizumab out-licensed global rights to OncXerna for further development • Payments of up to $300 million in milestones plus royalties • Recently received $2 million CMC milestone payment • Following regulatory interactions, OncXerna has stated intention to initiate a Phase 3 trial of navicixizumab in late line ovarian cancer	OncXerna THERAPEUTICS™
Partnering Opportunities on Other Programs	
• Leflutrozole – a novel once weekly oral aromatase inhibitor has completed a successful Phase 2b study in obesity-associated male hypogonadotropic hypogonadism (HH)	**Open-to-Partnership**
• Acumapimod – an oral p38 MAP kinase inhibitor has completed a successful Phase 2 study as first-line therapy for severe acute exacerbations of chronic obstructive pulmonary disease (AECOPD)	**Open-to-Partnership**

Upcoming Key Milestones & Opportunities

Upcoming Milestone For Core Programs								
Product Candidate	Indication	2022		2023		2024		Next Milestone
		H1	H2	H1	H2	H1	H2	
Setrusumab	OI	Pediatric Phase 2b/3 ORBIT (5-25 years)						Phase 2/3 dosing update & Phase 3 transition Supportive study initiation (Age 2-5)
			Pediatric study (2-5 years)					
Alvelestat	AATD-LD	ASTRAEUS*						**AATD-LD ASTRAEUS:** Phase 2 additional data
		Phase 2 ATALANTa						
	BOS	Phase 1b	Phase 2					**BOS:** Phase 2 initiation
Etigilimab	Rare & Gyn-Onc Tumors	ACTIVATE Phase 1b						Complete selected Phase 1b cohorts EON: Complete enrollment
	OCCC**	EON Phase 2						

Milestone Achieved *Upcoming Milestone*

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**ASTRAEUS is a proof-of-concept Phase 2 study*
***Ovarian Clear Cell Carcinoma*

Roadmap for Growth

1	**Maintain A Strong Balance Sheet**	• **Cash runway to late 2024** ($111.4 million at March 31, 2022) • Active cost management to maintain cash runway
2	**Invest For Growth**	• Focus on high value rare disease programs. Allocate R&D capital to key value inflection points. • **Alvelestat:** Mereo is evaluating options for next steps. Outcome from FDA End-of-Phase 2 meeting (H2 2022) and EMA Scientific Advice will inform strategy. No additional clinical development expense for this program from current cash resources. • **Etigilimab:** Mereo will complete enrollment in certain cohorts of the Phase 1b ACTIVATE trial (H2 2022). Further investment pending review of Phase 1b results and competitive landscape.
3	**Partnering**	• **Setrusumab:** Highlights track record of partnering /accessing non-dilutive capital, while retaining high value rights to tap long term value • Leveraging investigator-led studies to expand data sets for alvelestat & etigilimab programs (Mereo provides drug supply and expertise)

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