## **Corporate presentation**

January 2024



### **Disclaimer**

This presentation has been prepared by Mereo BioPharma Group plc (the "Company") solely for your information and for the purpose of providing background information on the Company, its business and the industry in which it operates or any particular aspect thereof. For the purposes of this notice, "presentation" means this document, any oral presentation, any question and answer session and any written or oral material discussed or distributed during any related presentation meeting.

This presentation has not been independently verified and no representation or warranty, express or implied, is made or given by or on behalf of the Company or any of its subsidiaries, or any of any such person's directors, officers, employees, agents, affiliates or advisers, as to, and no reliance should be placed on, the accuracy, completeness or fairness of the information or opinions contained in this presentation and no responsibility or liability is assumed by any such persons for any such information or opinions or for any errors or omissions. All information presented or contained in this presentation is subject to verification, correction, completion and change without notice. In giving this presentation, none of the Company or any of its subsidiaries, or any of any such person's directors, officers, employees, agents, affiliates or advisers, undertakes any obligation to amend, correct or update this presentation or to provide the recipient with access to any additional information that may arise in connection with it. To the extent available, the data contained in this presentation has come from official or third-party sources. Third party industry publications, studies and surveys generally state that the data contained therein have been obtained from sources believed to be reliable, but that there is no guarantee of the accuracy or completeness of such data. While the Company believes that each of these publications, studies and surveys has been prepared by a reputable source, the Company has not independently verified the data contained therein. In addition, certain of the data contained in this presentation come from the Company's own internal research and estimates based on the knowledge and experience of the Company's management in the market in which the Company periates contracted by the Company believes that such internal research and estimates and such other data are reasonable and reliable, they, and, where applicable, their underlying methodology and assumptions, have not been verified by

#### **Forward-Looking Statements**

This presentation contains "forward-looking" statements that involve substantial risks and uncertainties. All statements other than statements of historical fact contained in this presentation are forward-looking statements within the meaning of Section 27A of the United States Securities Act of 1933, as amended, and Section 21E of the United States Securities Exchange Act of 1934, as amended. Forward-looking statements relate to future events, including, but not limited to, statements regarding future clinical development, efficacy, safety and therapeutic potential of clinical product candidates, including expectations as to reporting of data, conduct and timing and potential future clinical activity and milestones and expectations regarding the initiation, design and reporting of data from clinical trials. Forward-looking statements are often identified by the words "believe," "expect," "anticipate," "plan," "intend," "foresee," "should," "would," "could," "may," "estimate," "outlook" and similar expressions, including the negative thereof. The absence of these words, however, does not mean that the statements are not forward-looking. These forwardlooking statements are based on the Company's current expectations, beliefs and assumptions concerning future developments and involve risks and uncertainties that could cause actual results, performance, or events to differ materially from those expressed or implied in such statements. Such risks and uncertainties include, among others, the uncertainties inherent in the clinical development process; the Company's reliance on third parties to conduct its clinical trials and provide funding for its clinical trials; the Company's dependence on enrollment of patients in its clinical trials; and the Company's dependence on its key executives. You should carefully consider the foregoing factors and the other risks and uncertainties that affect the Company's business, including those described in the "Risk Factors" section of its latest Annual Report on Form 20-F, reports on Form 6-K and other documents furnished or filed from time to time by the Company with the Securities and Exchange Commission. You should not place undue reliance on any forward-looking statements, which speak only as of the date hereof. The Company undertakes no obligation to publicly update or revise any forward-looking statements after the date they are made, whether as a result of new information, future events or otherwise, except to the extent required by law. This presentation also contains estimates, projections and other information concerning the Company's business and the markets for the Company's product candidates, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research, or similar methodologies is inherently subject to uncertainties and actual events, or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, the Company obtained this industry, business, market and other data from reports, research surveys, clinical trials studies and similar data prepared by market research firms and other third parties, from industry, medical and general publications, and from government data and similar sources.



# Unlocking the potential of novel targets for rare diseases

Our mission is to improve the lives of people living with rare diseases





### 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 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





## A mid-late-stage company with validating partnerships

### **Achievements and fundamentals**

### Two rare disease programs in-licensed and ready for pivotal studies within five years

- **Setrusumab** for Osteogenesis Imperfecta (OI) in Phase 3 under a partnership with rare disease leader Ultragenyx
- Alvelestat for Alpha-1 Antitrypsin Deficiency-associated Lung Disease (AATD-LD) successfully completed Phase 2, with Phase 3 endpoints agreed in principle with FDA and EMA

### Financial discipline delivers cash runway into 2026

- Cash runway into 2026: \$62.4 million as of September 30, 2023
- Active cost management runway through key inflection points
- Leverage investigator-led studies to expand data sets



## A mid-late-stage company with validating partnerships

### **Corporate development**

### Management team with a proven track record in rare diseases and corporate development

- Setrusumab acquired from Novartis and alvelestat in-licensed from AstraZeneca
- Setrusumab partnered with Ultragenyx whilst retaining European rights
- Navicixizumab global rights licensed to OncXerna and leflutrozole licensed to ReproNovo

Upside potential from etigilimab (an anti-TIGIT antibody) and acumapimod (p38 MAP kinase inhibitor)



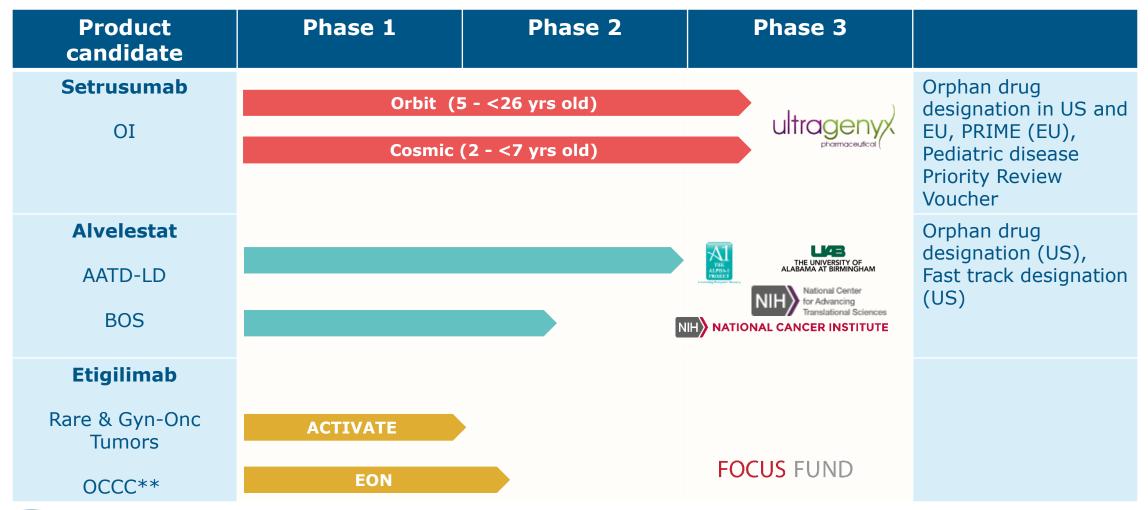








## Late-stage clinical pipeline with core rare disease programs







"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



## A rare genetic bone condition with a high unmet need

### **Osteogenesis Imperfecta**

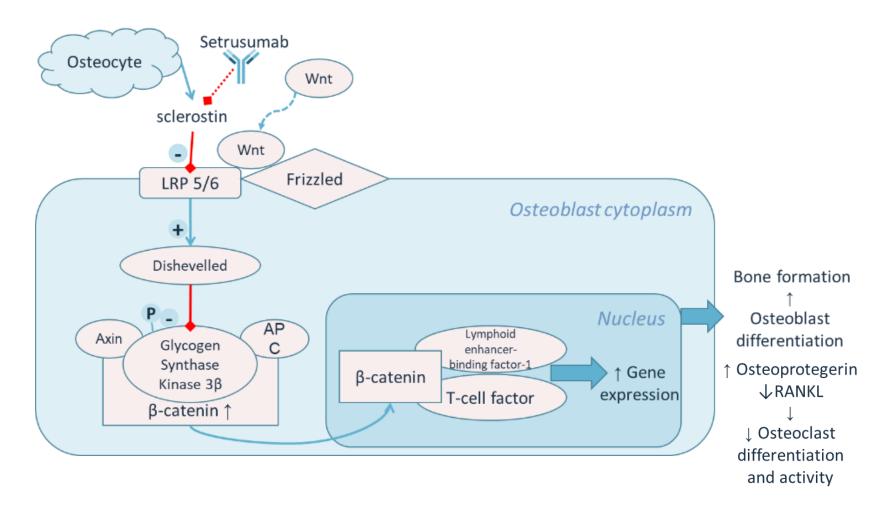
- A rare genetic bone disease, mostly linked to a mutation in Type I collagen<sup>1,2</sup>
- Affects approximately 60,000 individuals<sup>3</sup> (pediatrics and adults) in the US and Europe
- Well-established Community groups (OIFE + national members and OIF)\* are a key support and valued resource
- Potential market opportunity of >\$1Bn<sup>4</sup>

### **Osteogenesis Imperfecta**

- Frequent bone fractures, skeletal deformities, pain, respiratory and gastric problems
- No FDA / EMA approved therapy. Current standard of care, (bisphosphonates) has not been shown to reduce fractures – strong physician appetite for a proven, onlabel therapy
- Symptoms often present from birth, leading to an early diagnosis
- OI is a progressive condition, without clear care pathways, especially for adult patients



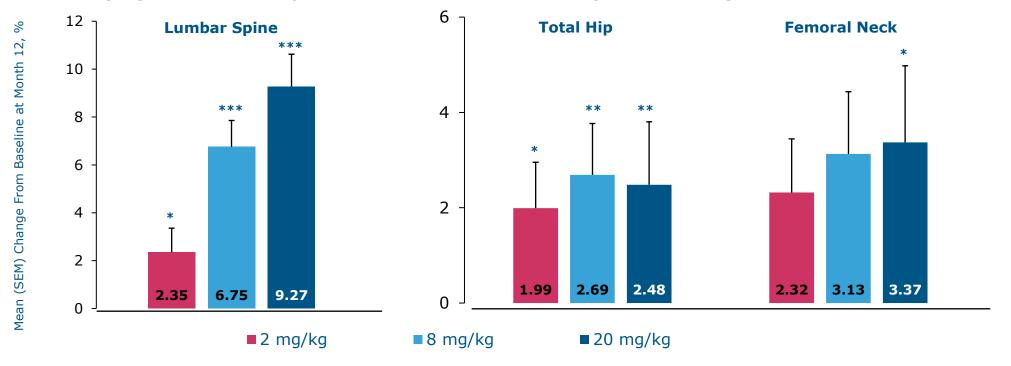
# **Setrusumab mechanism of action particularly well-suited** for **OI**





## Phase 2b ASTEROID study 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. 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).



## Orbit Phase 2 study and Open Label Extension study design

## Phase 2 designed to determine setrusumab dosing strategy based on PK/PD, safety, and available BMD data in subjects with OI

#### **Patients Enrolled**

24 patients ages 5 yrs to <26 yrs with OI Types I, III, or IV and a confirmed *COL1A1* or *COL1A2* mutation. Intended to enroll 12 subjects of <30kg

#### **Dose Cohorts**

Subjects randomized 1:1 to receive 20 or 40 mg/kg of setrusumab administered by monthly infusion.

Open label extension study – subjects remain on allocated dose for 6 months then all switch to 20 mg/kg

#### **Stratification**

Patients with at least 2 fractures over prior 24 months will be enrolled and randomization stratified by number of fractures in the prior 2 years ( $\leq$  3 vs >3) and by age group

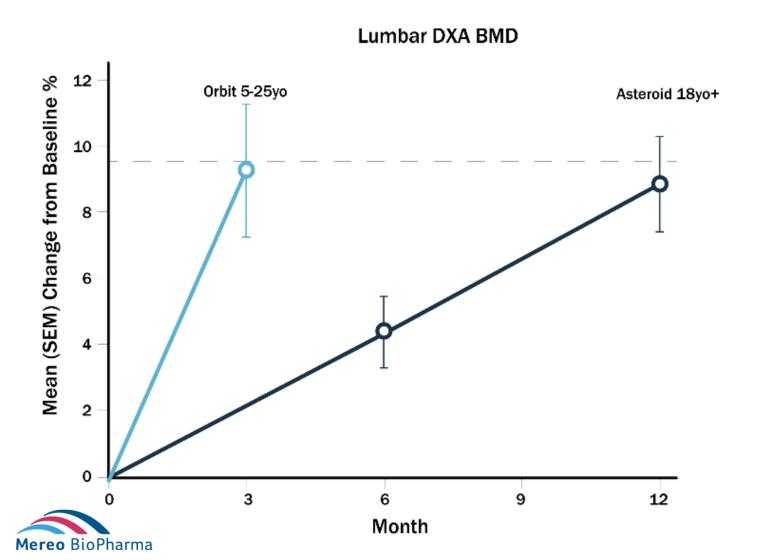
### **Endpoints and data output**

Evaluation of P1NP (propeptide cleavage product of procollagen for bone production), bone mineral density (by DEXA scan), PK parameters and safety.

Open label extension study – BMD, Z-score and fracture rate



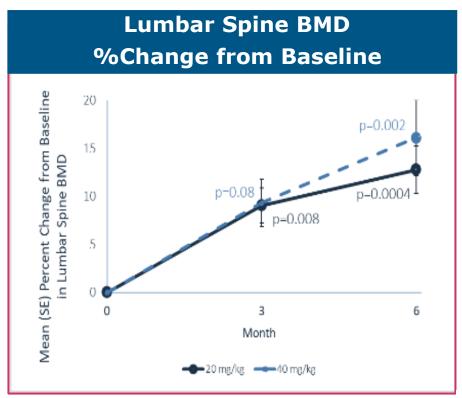
# Younger patients in Orbit achieved increases in Lumbar DXA BMD at 3 months comparable to ASTEROID patients at 12 months





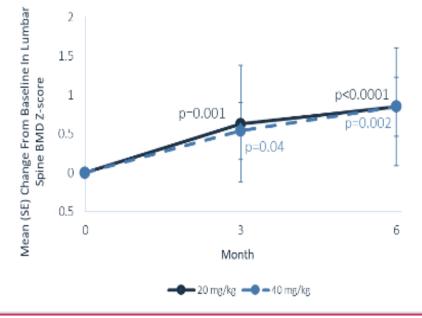
- BMD Z-score change of +0.65 at 3 months for 20 mg/kg
- 1.0 Z-score is equal to 1 standard deviation of the population

## Continuous increase in BMD and Z-score through month 6<sup>1</sup>





# Lumbar Spine BMD Z-Score Change from Baseline

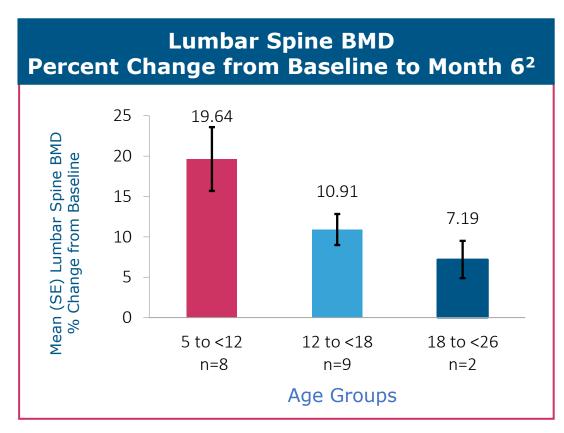


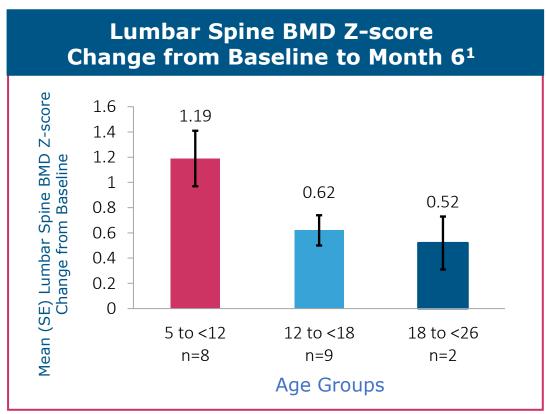
P-values reflect change from baseline

- No significant differences were observed between setrusumab dose groups
- Percentage change in BMD at month 6:
  - 20 mg/kg group=13%
  - 40 mg/kg group=16%
- Change in BMD Z-score at month 6:
  - Both dose groups = 0.85



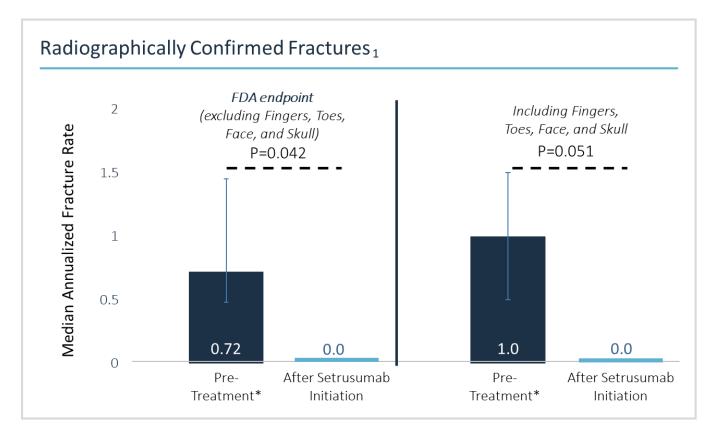
# Increase in BMD observed in all age groups, 1,2 Greatest increase in patients 5-12 years of age



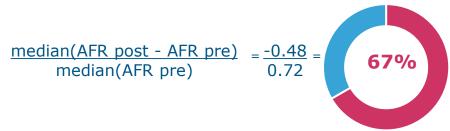




## **Annualized Fracture Rate post-treatment with Setrusumab**<sup>1</sup>



- Median total confirmed Annualized Fracture Rate post-treatment is 0.0
- 67% reduction in annualized fracture rate, excluding fingers, toes, face, and skull
- Mean treatment duration of 9 months (6 – 16 months) in 24 patients



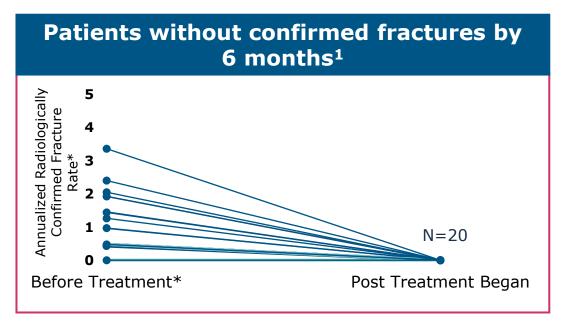
The Phase 2 portion of Orbit was not statistically powered to compare annualized fracture rates between dose groups.

\*Pre-Treatment period includes fractures before screening based on medical record review and patient report, and fractures between screening and first dose



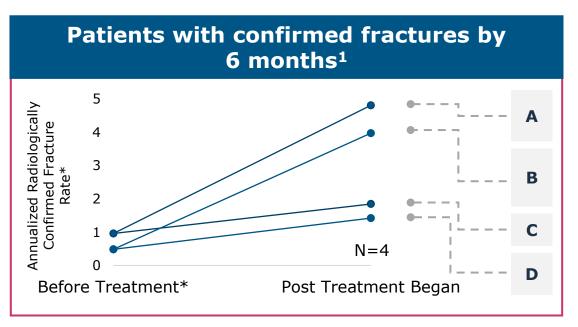
# 20/24 patients did not have radiographically confirmed fractures after 6 months treatment with Setrusumab<sup>1</sup>

### **Radiographically confirmed fractures**



20/24 patients had no radiographically confirmed fractures despite significant historical fracture rates

\*Pre-Treatment period includes fractures before screening based on medical record review and patient report, and fractures between screening and first dose



- A. Slipped on ice (at 1.6 months); stubbed toe (at 6 months)
- B. Fell off tricycle (2 fractures) (at 5.5 months)
- C. Bending over in bed (at 1.1 months)
- D. Tripped and fell on hand (at 7.7 months)



### Safety evaluation 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\*1

Adverse Event	Phase 2 Patients (N=24)
Infusion-related event (not hypersensitivity)	7 (29%)
Headache	3 (13%)
Abdominal discomfort	1 (4%)
Infusion site pain	1 (4%)
Bone pain	1 (4%)
Upper respiratory tract infection	1 (4%)

<sup>\*</sup>All related adverse events were mild to moderate in severity



## Patient with increased mobility after 17 months on study

### Six-year-old male with Type IV OI



## In addition...other high impact events did not result in fracture

### Other high impact events:

- High-impact motor vehicle accident at Month 5.5 of treatment resulted in no fractures
- Patient fell down a flight of stairs with a backpack at Month 4.7 of treatment

**Evaluated: No fractures** 



## **Orbit study - Phase 3\***

## Designed to evaluate the efficacy and safety of setrusumab vs. placebo in children and young adults with OI

Up to 195 subjects ages 5 to < 26 years with OI Types I, III, or IV and a confirmed *COL1A1* or *COL1A2* mutation. Enrolling at 50 sites in 12 countries including USA and Europe.

Patients with at least 2 fractures over prior 24 months will be enrolled and randomization, stratified by number of fractures in the prior 2 years ( $\leq$  3 vs >3) and age group.

Subjects randomized 2:1 to receive 20 mg/kg of setrusumab administered by monthly infusion or placebo administered IV QM. Study is double blinded.

Primary efficacy endpoint of **annualized clinical fracture rate**. Treatment period of up to two years. Interim analyses being planned to evaluate for overwhelming efficacy and updates in process that may accelerate timeline.



## **Cosmic study - Phase 3\***

## Designed to evaluate the efficacy and safety of setrusumab vs. bisphosphonates in young children with OI

Approximately 65 subjects ages 2 to < 7 years with OI Types I, III, or IV and a confirmed *COL1A1* or *COL1A2* mutation. Enrolling at sites including in the USA and Europe.

Patients with at least 2 fractures over prior 24 months will be enrolled and randomization, stratified by number of fractures in the prior 2 years ( $\leq 3 \text{ vs} > 3$ ) and age group.

Subjects randomized 1:1 to receive 20 mg/kg of setrusumab administered by monthly infusion or existing bisphosphonate by infusion per investigator discretion. Study is open label.

Primary efficacy endpoint of **annualized clinical fracture rate**. Treatment period of up to two years but with open label design.



## **Mereo – Ultragenyx partnership**

### **Key terms**

- Signed in December 2020
- Ultragenyx leads and funds the global development plan, including CMC
- Mereo retains European rights (including UK) and Ultragenyx the USA and Rest of the World rights
- Mereo received \$50M upfront with potential additional \$254M in regulatory and commercial milestones
- Mereo received first milestone payment of \$9M on first patient dosed in Orbit Phase 3 study (July 2023)
- 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



## Mereo - Ultragenyx partnership and long-term plan

### Mereo territories and focus

- Groundwork for reimbursement of setrusumab in Europe and UK
- Intensive engagement with highly networked
   OI specialized treating physicians indicates
   high level of interest in safe & effective on-label treatment
- Collaborating with OIFE and OIF on IMPACT Survey<sup>1</sup>, largest data set on OI; will inform reimbursement
- Project SATURN collaborative European Real World Evidence data collection
- Pilot EUnetHTA process 9 EU countries individual HTA\* bodies in one forum - future evidence requirements; advice from payors through MoCA on a rolling basis

### Significant market opportunity

- OI affects approximately 60,000 pediatrics and adults in the US and Europe
- Relevant rare bone analog X-linked hypophosphatemia (XLH), a rare inherited form of rickets – approximately 48,000 pediatrics and adults – Crysvita launched 2018/2019 in US and EU
- Crysvita sales forecast for 2023 currently \$925M in North America and EMEA with \$230M in revenue in EMEA in 2022\*\*\*
- Initial feedback indicates responsible Crysvitalike pricing potentially acceptable to European healthcare systems



<sup>1.</sup> Rapoport, M., Bober, M.B., Raggio, C. et al. The patient clinical journey and socioeconomic impact of osteogenesis imperfecta: a systematic scoping review. Orphanet J Rare Dis 18, 34 (2023)

\* Health Technology Assessment

<sup>\*\*</sup> Mechanism of Coordinated Access



## **Alvelestat (MPH966)**

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



# **AATD-LD:** a rare progressive lung disease with high unmet need

Lack of AAT results in risk of progressive lung damage and early onset emphysema

### **AATD-LD**

- Presents age 20 to 50, shortness of breath, cough, reduced exercise tolerance
- Severe deficiency patient population estimates:
   ~50,000 in North America and ~60,000 in Europe and the UK, of which 60-80% develop lung disease¹
- Increasing diagnosis rate

### High unmet need

- Currently COPD treated and lifestyle changes
- Specific treatment –
   intravenous plasma-derived
   augmentation therapy:
  - Clinical efficacy not uniformly recognized
  - IV administration burden
  - Optimal dose uncertain
  - Reimbursement access

## Significant market opportunity

- US AAT augmentation revenues reached \$1.2bn in 2021<sup>4</sup>
  - US patients (weekly
     I.V.) \$100-150k/year<sup>5</sup>
  - AATD products forecast to reach \$3.2bn by 2031<sup>4</sup>
- Europe AAT augmentation not widely reimbursed as lack of clinical outcomes data
- Potential first oral treatment



<sup>1.</sup> Blanco I et al. 2017. alpha-1 antitrypsin Pi\*Z gene freguency and Pi\*ZZ genotype numbers worldwide: an update. Int J COPD: 12 561-569

<sup>2.</sup> Evercore estimate

<sup>3.</sup> Based on Cantor Fitzgerald estimates of Net Peak Sales in the US and EU5

<sup>4.</sup> GlobalData estimate

<sup>5.</sup> Evercore estimate

## **Alvelestat – a potent, oral inhibitor of Neutrophil Elastase**

### **Healthy**

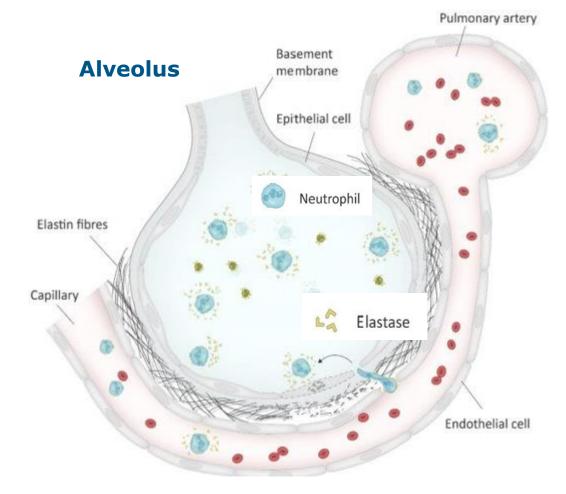
- Alpha-1 antitrypsin (AAT) produced in the liver, released to blood and lungs
- AAT protects from Neutrophil Elastase (NE) a protease that drives tissue destruction in lung

### **AAT Deficiency**

 Lack of AAT – unopposed NE and progressive lung damage initiating in small airways/alveoli

#### **Alvelestat**

- Specific NE inhibitor effective lung penetration
- Twice daily dosing provides sustained >90% inhibition in AATD



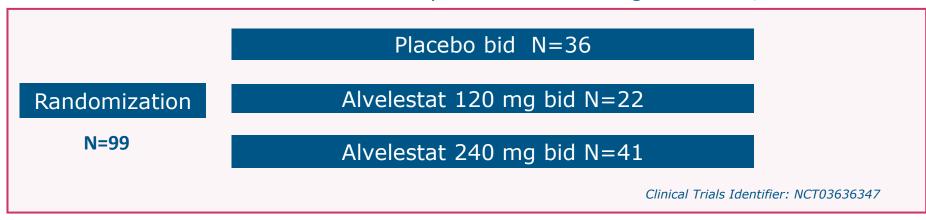
NE breakdown of protein releases **Aa-val**<sup>360</sup>

Breakdown of elastin releases **desmosine** 

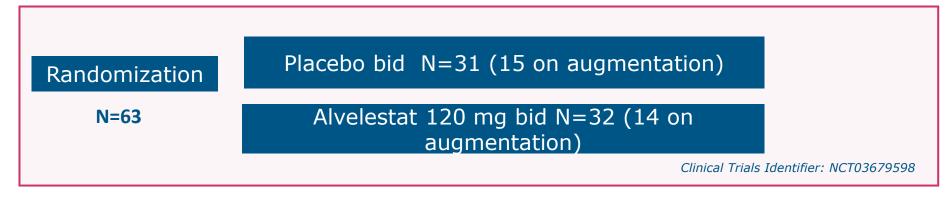


## Two Phase 2 studies of alvelestat in AATD-Lung Disease completed

**ASTRAEUS** – Enrolled PI\*ZZ patients **not** on augmentation, 12 weeks



**ATALANTa** Investigator-led study – Mark Dransfield, University of Alabama at Birmingham Enrolled PI\*ZZ, PI\*SZ and PI\*Null patients including those on augmentation, 12 weeks













## Comparison of ATALANTa and ASTRAEUS patient populations

ATALANTa was a US study, ASTRAEUS enrolled predominantly in EU

- Augmentation available in the US unlike in many EU countries and the UK
- Augmentation population in ATALANTa is similar to the population enrolled in ASTRAEUS
- Non-Augmentation population in ATALANTa has earlier-stage lung disease than in ASTRAEUS

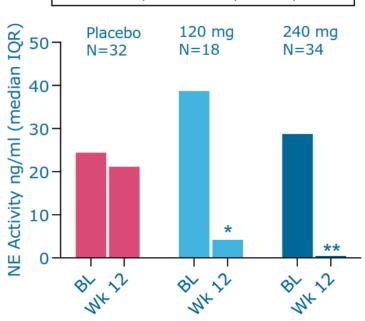
Parameter At Baseline	ATALANTa*		ASTRAEUS	
(median)	Augmentation	Non-Augmentation	Non-Augmentation	
FEV1 (% predicted)	69.76	89.28	59.04	
SGRQ Total**	33.69	19.62	32.24	
SGRQ Activity	45.38	25.49	53.26	

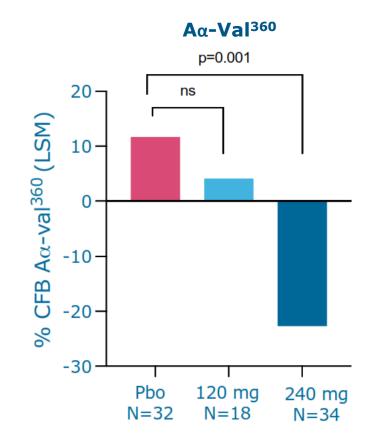


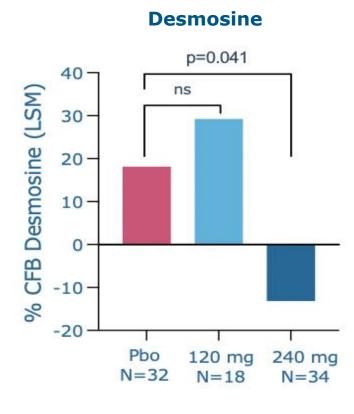
# **ASTRAEUS** Phase 2 study – Dose-related effects on Neutrophil Elastase activity and Disease Activity Biomarkers by 12 weeks

### **Neutrophil Elastase**

\* reduction p <0.05 compared to placebo \*\* reduction p <0.001 compared to placebo







0.5 ng/ml reflects lower limit of detection of assay

- Significant suppression of NE at both doses
- > Sustained 90% suppression of blood NE activity at 240 mg dose
- Only the 240 mg dose significantly reduced other biomarkers

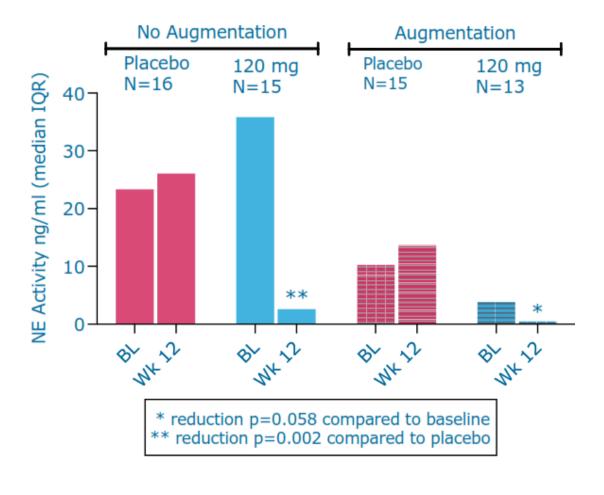
Per protocol analysis



### Biomarker data from ATALANTa confirm dose selection for Phase 3

### **ATALANTa Phase 2 Study**

- Addition inhibition of NE activity observed in patients on augmentation therapy
- With 120 mg dose a significant change (reduction) from baseline in  $A\alpha$ -Val<sup>360</sup> (p=0.03) observed
  - Improved compared to ASTRAEUS data, potentially reflecting earlier stage population
- Consistent with ASTRAEUS data at 120 mg dose – no significant change in desmosine
- Data confirm 240 mg dose twice daily for the pivotal Phase 3 study



0.5 ng/ml reflects lower limit of detection of assay

Full Analysis Set



## **Phase 3 endpoints**

Agency	Phase 3 endpoints	Phase 2 data to support Phase 3 plan
European Medicines Agency (EMA)	Change in CT density P<0.1 could be acceptable	<ul> <li>Change in desmosine observed at 240 mg dose in ASTRAEUS study</li> <li>Significant correlation of desmosine change to CT density change</li> </ul>
U.S. Food and Drug Administration (FDA)	Change in SGRQ Total Score as primary endpoint 'Functional assessment' as key secondary endpoint  Initial SGRQ validation plan agreed with FDA (DCOA)	<ul> <li>Change observed in ATALANTa study of patients with earlier stage diagnosis</li> <li>Change observed in patients with a desmosine response across both Phase 2 studies</li> </ul>

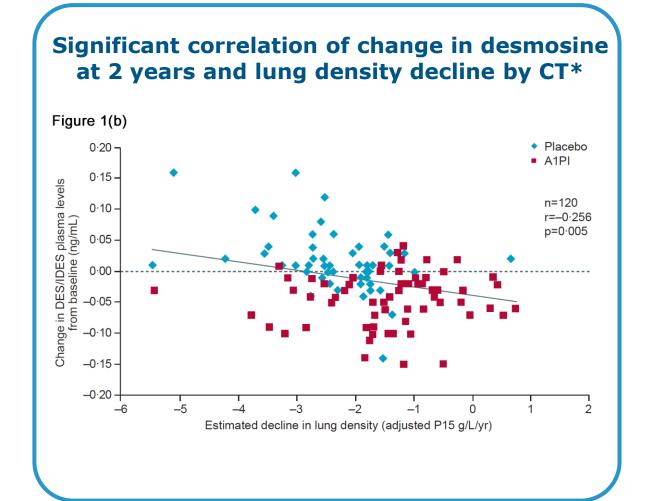


Based on Phase 2 studies to inform the enrolled population, Global Phase 3 study of ~220 participants with 18 months duration

## **CT-density: Linking ASTRAEUS data to the RAPID study**

Reduction in the biomarker desmosine for 240 mg alvelestat at 12 weeks equivalent to Augmentation therapy at 12 months

		Augmentation therapy*	Alvelestat (240mg, ASTRAEUS)
Desmosine (absolute reduction from baseline, mean)	Month 3	-0.013 ng/ml	-0.028 ng/ml <sup>+</sup>
	Month 12	-0.031 ng/ml	Study duration 12 weeks





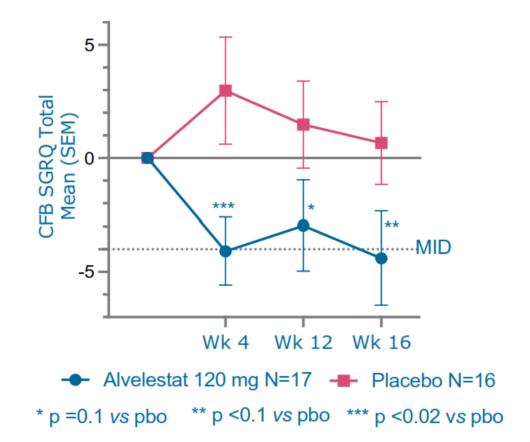
<sup>\*</sup> Ma et al. *Chronic Obstr Pulm Dis.* 2017;4(1):34-44

<sup>†</sup> Per protocol analysis

## St George's Respiratory Questionnaire (SGRQ)

- Validated patient reported outcome recognized by FDA
- Total Score comprises Activity, Symptoms and Impacts;
   Activity key driver of quality-of-life deterioration in AATD
- ATALANTa study greater effect in non-augmentation subgroup with earlier stage lung disease raising potential to use either Total or Activity Domain in Phase 3.
   Between group changes at week 12:
  - **SGRQ Total** = -4.7 (P=0.10 vs placebo)
  - SGRQ Activity = -10.0 (P=0.01 vs placebo)
- Across both Phase 2 studies, patients who had a >5%
  reduction in desmosine saw greatest SGRQ benefit in
  both SGRQ Total Score and the SGRQ Activity Domain
  Score†
  - This effect was also observed for the COPD Assessment Test (CAT), another validated patientreported quality of life tool

## ATALANTa study (non-augmentation subgroup) – Change in SGRQ Total Score

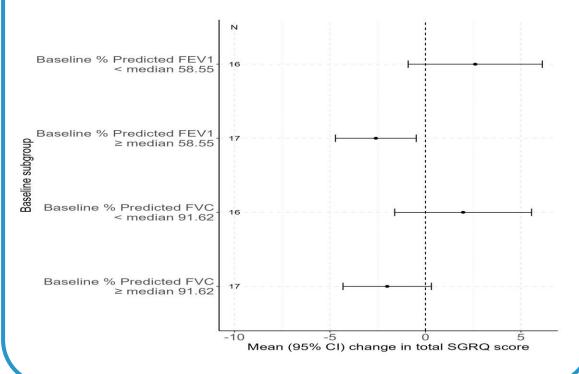




## Earlier stage patients - greater SGRQ change and potentially FEV1

### **ASTRAEUS Study**

In addition to effects observed in earlier stage patients in the ATALANTa study, *post hoc* analysis of baseline characteristics of ASTRAEUS and **SGRQ Total** change shows earlier stage patients also had the greatest change

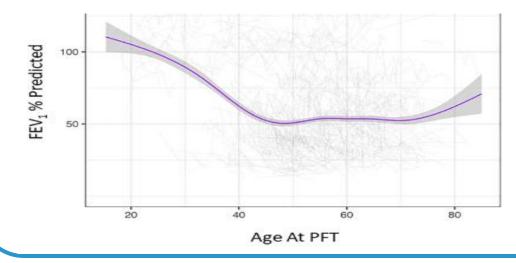


### Fraughen et al, Nov 2023\*

Multinational registry retrospective analysis (N=615, N=365 never received AAT). **FEV1** decline highest 20-50 years old

AAT vs never AAT: significant difference in **FEV1** decline with GOLD stage 2 (50%<FEV1<80%) at time of starting AAT (P=0.007)

"Detecting people with severe AATD as early as possible and initiating therapy before the establishment of COPD should be the goal to improve survival"





# Consistent safety data in AATD-LD in ASTRAEUS and ATALANTa

	ATALANTa		ASTRAEUS		
	Alvelestat 120mg N=32 subjects (%)	Placebo N=31 subjects (%)	Alvelestat 120mg N=22 subjects (%)	Alvelestat 240mg N=40 subjects (%)	Placebo N=36 subjects (%)
SAE	0	0	1 (4.5)	3 (7.5)	0
Adverse Events of Special Interest	5 (15.6)	11 (35.5)	5 (22.7)	11 (27.5)	7 (19.4)
Infections requiring antimicrobial therapy	5 (15.6)	11 (35.5)	5 (22.7)	10 (25.0)	7 (19.4)

#### **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
- Lab monitoring and IDMC review did not identify any safety signals of concern in either study

#### **Adverse events**

• Headache was most frequent adverse event, generally mild or moderate and resolving on continued dosing. 3 cases reported as SAEs (240 mg) but evidence from ISS study using 240 mg shows reduction of headache frequency with a dose-escalation regime



Including legacy studies, safety database of 1,268 patients exposed to alvelestat

#### **Development strategy for Phase 3 pivotal clinical trial**

#### **Clinical data**

Earlier stage severe PI\*ZZ patients appear to have greater reductions in SGRQ Total and Activity

Literature shows that earlier stage patients with higher  $\text{FEV}_1$  may be more likely to show spirometry benefit

### **Execution of** the Phase 3

Study population of AATD patients with a broad range of stage of disease (early → late stage) may accelerate enrollment

Both studies confirm 240 mg dose selection

## **Commercial opportunity**

Opportunity for broad label including earlier stage PI\*ZZ patients who may not be eligible for AAT augmentation – payors and HCPs familiar with SGRQ Total and CT endpoints

Partnering process ongoing – range of structures

#### **Phase 3 design**

- SGRQ Total Score and CT-density independent primary endpoints with functional assessment as key secondary
- Enrollment to include earlier stage PI\*ZZ patients
  - All with emphysema
  - Based on defined selection criteria
- ~220 patients for treatment period of 18 months
- For full approval (not conditional)



Broader population with these two independent primary endpoints maximizes potential for clinical and commercial success



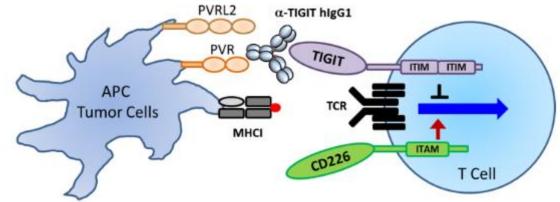
## Etigilimab (MPH313)

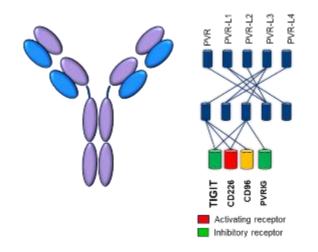
Anti-TIGIT antibody in development in combination with anti-PD1



# Etigilimab: an Anti-TIGIT antibody in development in combination with anti-PD1

- T Cell Immunoreceptor with IG and ITIM domains (TIGIT)
- Anti-TIGIT designed to activate the immune system and enable anti-tumor activity
- Expressed on CD4, CD8 and NK cells and expression is pronounced on regulatory T cells (Tregs)
- TIGIT mediates an inhibitory signal that is thought to prevent T-cells from attacking tumor cells
- Etigilimab is an IgG1 monoclonal antibody designed to balance affinity and ADCC characteristics while limiting side effects
- Completed Phase 1a (etigilimab monotherapy)/1b (combined with nivolumab)
- Phase 1b open label basket study in combination with nivolumab (ACTIVATE) enrollment in selected cohorts; data presented at ASCO 2022 and ESMO 2022 and 2023
- Combination of etigilimab and nivolumab was safe and well tolerated







### **ACTIVATE** efficacy data: select cohorts\*



Objective Responses by RECIST	Cohort					
by necion	Endometrial Cancer (CPI-naïve) (n=10)	Cervical Cancer (n=8)^	Uveal Melanoma (n=8)	De-differentiated Liposarcoma (n=10)	Germ Cell Tumor (n=4)	Total (n=40)
ORR = 10 (25%)						
CR	0	3 <sup>1</sup>	0	0	0	3
PR	3	0	2	1	13	7
SD	3	22	2	4	0	11
PD	4	3	4	5	3	19

Disease Control Rate (CR+PR+SD) = 21 of 40 (52.5%)

All responses confirmed

\*Efficacy analysis set: Best Observed Response (BOR) by investigator-assessed response per RECIST 1.1/clinical progression; data cut-off 3/29/2023. ^ Includes 1 TMB-H cervical pt E025 with CPS >1% by central lab.



<sup>1. 1</sup> CR was on-going and pt withdrew consent; 1 CR off study due to AE; 1 CR on-going at data cut-off

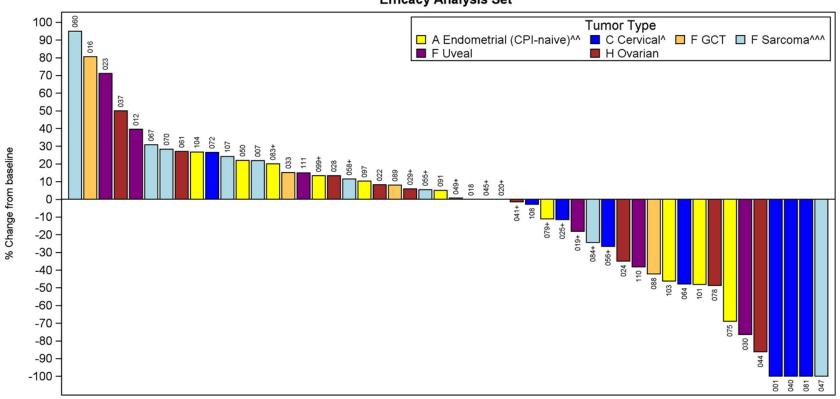
<sup>2. 1</sup> SD on-going at data cut-off, patient died due to unrelated event

<sup>3.</sup> Mixed response, continued treatment, PD-RECIST1.1

# ACTIVATE efficacy data: select cohorts (continued) Live ESVO Congress









<sup>^^</sup> Endometrial cancer - CPI-naïve patient (G101) enrolled in post-CPI cohort

<sup>#</sup>De-differentiated liposarcoma subject F047 is CR for target lesions, but overall PR due to persistent non-target lesion

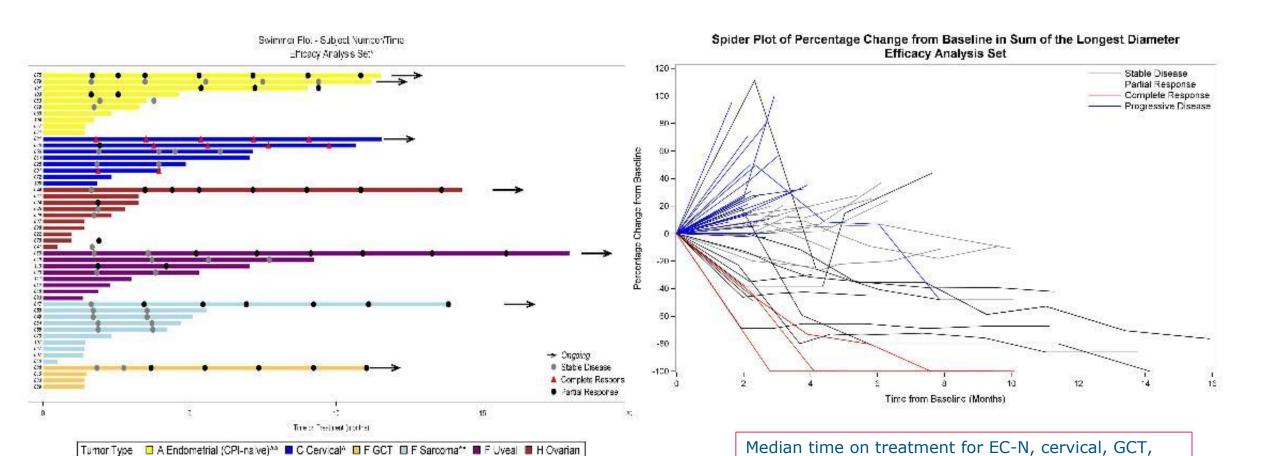


<sup>^^</sup> Sarcoma subjects only include those with de-differentiated liposarcoma

<sup>+</sup> best overall response of stable diseases. Note 2 subjects with SD had progression (non-target lesion) concurrent with the first scan F049=sarcoma; H045=ovarian; F018 & F020=uveal

## ACTIVATE efficacy data: select cohorts (continued) Live ESVO Congress





<sup>&</sup>quot; Sarcoma subjects only include those with De-differentiated liposarcoma ^Cervical cancer patient (E025) enrolled in TMB-H cohort with PDL-1 CPS>1% ^^Endometrial cancer - CPI naïve patient (G101) enrolled in post-CPI cohort Note E025 death unrelated to study drug or PD. C001 consent withdrew Central lab PD-L1 CPS status pts on study ≥ 335 days:

\* PD-L1 negative; + PD-L1 ≤3; #PD-L1 >3 Data cut-off March 29, 2023; 7 pts on-going (→)



PR (7 pts) = 11 monthsSD (11 pts) = 5.7 months

CR (3 pts) = 11.5 months

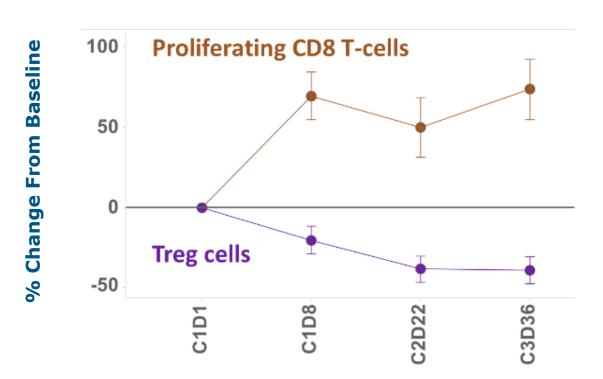
de-differentiated liposarcoma, uveal patients



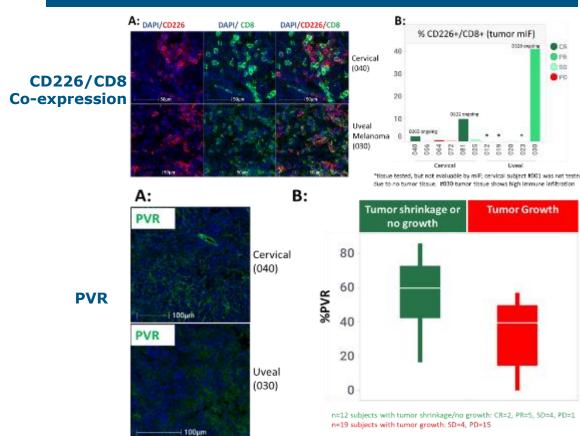


# Etigilimab shows robust target engagement in patients and exploratory biomarker correlation with clinical response

### Etigilimab shows robust target engagement



## Baseline tumor expression: correlation with reductions in target lesions





Sarikonda et al, ESMO, 2022

# **EON\*** investigator-led study at MD Anderson Phase 1b/2 in Clear Cell Ovarian Carcinoma

tumor Pre-treatment tumor expression **FOCUS FUND** Etiqilimab + and immuno-profiling Recurrent platinum resistant clear cell ovarian carcinoma **Nivolumab** On-combinatioion treatment and immuno-profiling Until disease Two-stage design: 1<sup>st</sup> stage: **N=10**, if ≥2 then progression or unacceptable 2<sup>nd</sup> stage for additional toxicity up to 24 N=10months express Total **N=20** evaluable CT CT 8 weeks a8wk

Two Stage Phase 1/2 Design with stopping boundaries for efficacy and toxicity. Based on responses from initial 10 patients, study is being expanded to 20 patients.

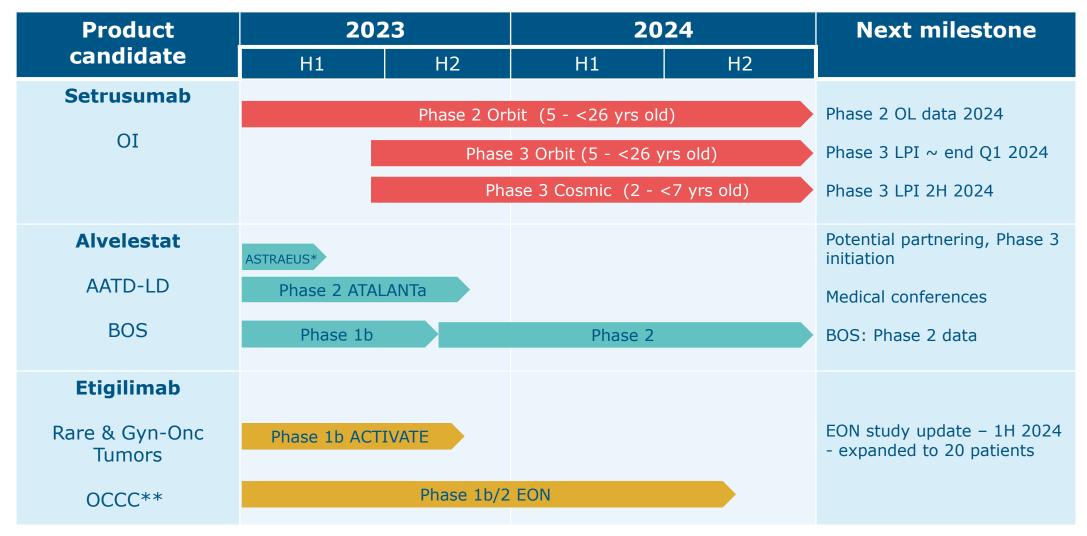




Other programs, milestones and financials



### **Upcoming key milestones for core programs**





#### Other programs: current partnerships

#### Other current partnerships

- Navicixizumab global rights out-licensed to OncXerna for further development
- Payments of up to \$300 million in milestones plus royalties
- OncXerna initiated a Phase 2 basket study in a range of solid tumors in 2H 2022
- **Leflutrozole** global rights out-licensed to ReproNovo for further development
- ReproNovo is a reproductive medicine company
- Upfront plus up to \$64 million in milestones and royalties



### **Financial highlights**



Cap Table (December 2023)	ADSs <sup>1</sup> (in thousands)	
Shareholders > 2% holding	72,563	
Shareholders < 2% holding	67,625	
Share capital - Issued and outstanding	140,188	
Potential Future Dilution:		
Warrants <sup>2</sup>	1,360	
Convertible loan notes	3,421	
Employee share schemes <sup>3</sup>	11,405	



One ADS represents five ordinary shares
Assumes a market price of \$3.00 per ADS and cashless exercise. The maximum number of warrants outstanding is 1.8m.

<sup>3</sup> Excludes 1.4m 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.

### Thank you

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



### Mereo BioPharma Group plc

4<sup>th</sup> Floor, One Cavendish Place London W1G 0QF United Kingdom +44(0)333 023 7300

