Corporate presentation

June 2024

Mereo BioPharma

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Unlocking the potential of novel targets for rare diseases

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

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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

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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 2027

- Cash runway into 2027:
  - $48.7 million as of March 31, 2024; and
  - $50 million gross proceeds from financing in June 2024[1]
- Active cost management – runway through key inflection points
- Leverage investigator-led studies to expand data sets

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1. Excluding underwriting discounts and commissions and estimated offering expenses payable by us.

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 Feng Biosciences 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

Product candidate	Phase 1	Phase 2	Phase 3	
Setrusumab OI	Orbit (5 -25 yrs old) Cosmic (2 - <7 yrs old)		ultragenyx pharmaceutical	Orphan drug designation in US and EU, PRIME (EU), Pediatric disease Priority Review Voucher designation
Alvelestat AATD-LD BOS			THE UNIVERSITY OF ALABAMA AT BIRMINGHAM NIH National Center for Advancing Translational Sciences NIH NATIONAL CANCER INSTITUTE	Orphan drug designation (US), Fast track designation (US)
Etigilimab Rare & Gyn-Onc Tumors OCCC**	ACTIVATE EON		FOCUS FUND	

**Ovarian Clear Cell Carcinoma

"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.

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Setrusumab (UGX143)

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

OIFE Topical Meeting
June 2023

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[1,2]
- Affects approximately 60,000 individuals[3] (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[4]

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, on-label therapy
- Symptoms often present from birth, leading to an early diagnosis
- OI is a progressive condition, without clear care pathways, especially for adult patients

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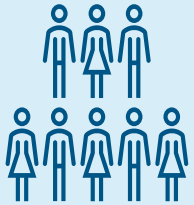
1. Based on Osteogenesis Imperfecta Foundation estimates; 2. Based on Orphanet estimates; 3. Internal BD forecast; 4. Based on Cantor Fitzgerald estimates of Net Peak Sales in the US and EU5
*OIFE: Osteogenesis Imperfecta Federation Europe; OIF: Osteogenesis Imperfecta Foundation

Mutations that effect collagen or collagen synthesis = 80-90% of OI

OI Population	Gene	Impact

 **80-90%[1,2]**	**COL1A1, COL1A2[2]**	• Encodes Type I collagen[2]
		• Different mutations lead to different phenotypes
		• Mutations leading to:
		  • Reduced synthesis of normal collagen in Type 1 (30-50%)[6]
		  • Abnormal collagen in Type I (50-70%), III & IV[3,4]
		• Results in under-modelled and malformed bones[4] and an increased rate of bone turnover[5]

10%[2]	**SERPINF1, CRTAP, LEPRE1, PPIB, SERPINH1, SERPINF1, FKBP10[1,2,3]**	• Encodes proteins involved in collagen biosynthesis, or transcription factors and signalling molecules related to bone cell differentiation and mineralisation[2] • OI Types VI-XI typically caused by these mutations[2]

OI, Osteogenesis Imperfecta

References: 1. Rossi V et al. Curr Opin Pediatr. 2019; 31(6):708-715. 2. Lim J et al. Bone. 2017; 102:40-49. 3. Palomo T et al. Curr Opin Endocrinol Diabetes Obes. 2017; 24(6):381-388. 4. Etich J et al. Mol Cell Pediatr. 2020; 7,9.. 5. Marini JC et al. Osteogenesis Imperfecta. 2020; Endotext. South Dartmouth (MA): MDText.com, Inc.; July 26, 2020 6. Lindahl et al. Eur J Hum Genet 23, 1042–1050 (2015).

Phenotypes are not a scale of severity

Type I

- Bones fracture easily
- Normal or near-normal stature
- Loose joints and muscle weakness
- Hearing loss possible, often beginning in early 20s or 30s
- Blue sclera (whites of the eyes)
- Tendency toward spinal curvature
- Brittle teeth possible

Type II

- Initial classification as lethal at or shortly after birth, often due to respiratory problems
- Some (historical) Type IIs now survive due to medical advances
- Numerous fractures and severe bone deformity
- Small stature with underdeveloped lungs
- Tinted sclera

Type III

- Bones fracture easily with fractures often at birth
- Short stature
- Sclera have a blue, purple, or grey tint
- Barrel-shaped rib cage and spinal curvature
- Respiratory problems possible
- Bone deformity, often severe
- Brittle teeth possible and hearing loss possible

Type IV

- Bones fracture easily
- Shorter than average stature
- Sclera are white or near-white (i.e. normal in color)
- Mild to moderate bone deformity, spinal curvature
- Barrel-shaped rib cage
- Brittle teeth and hearing loss possible

Type I: 50-70%[1,2]
Type III: 10-15%[1,2]
Type IV: 10-25%[1,2]

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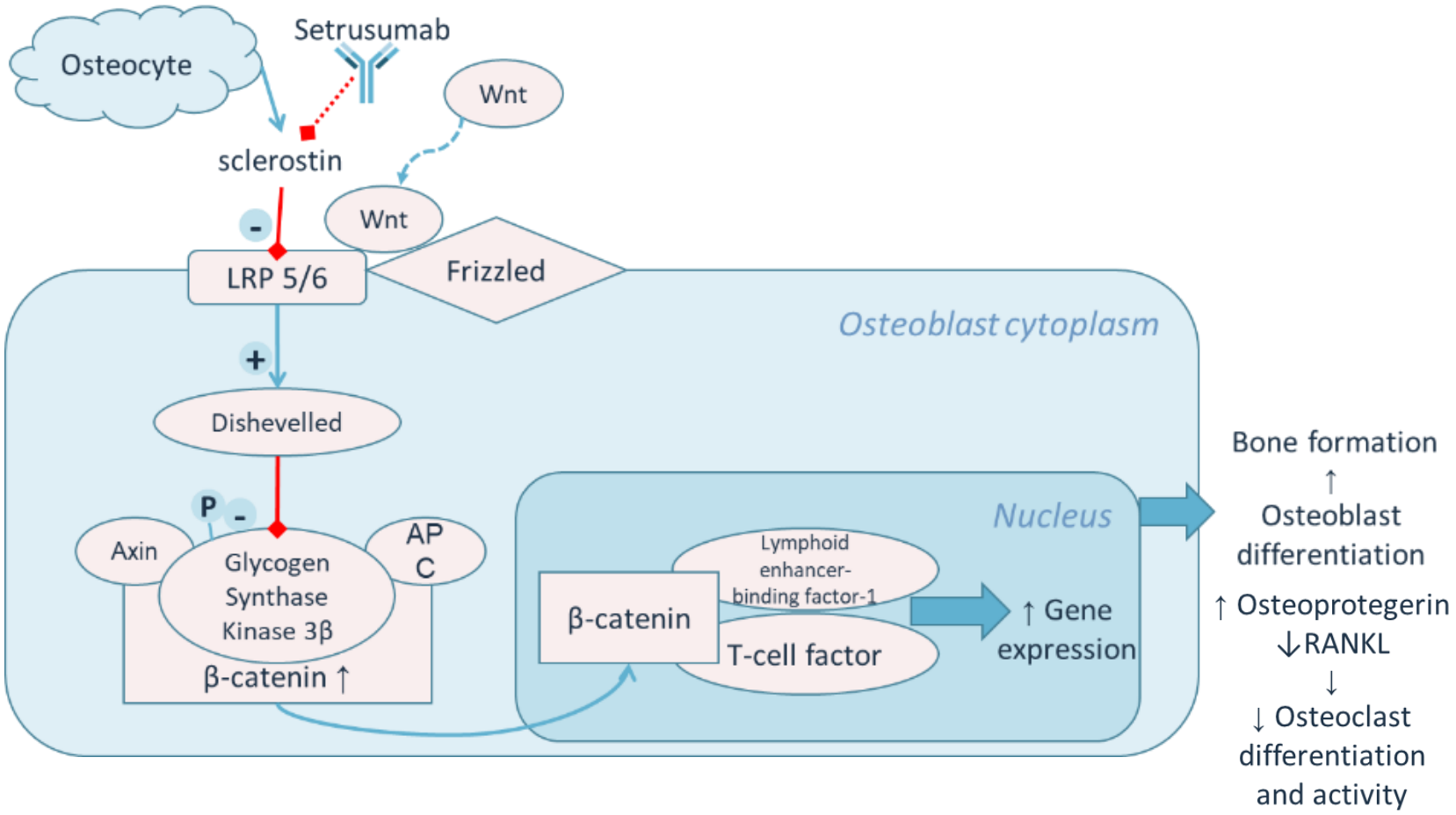
Based on information from the Osteogenesis Imperfecta Foundation website. For a full list of Types visit Living with OI: (oif.org).

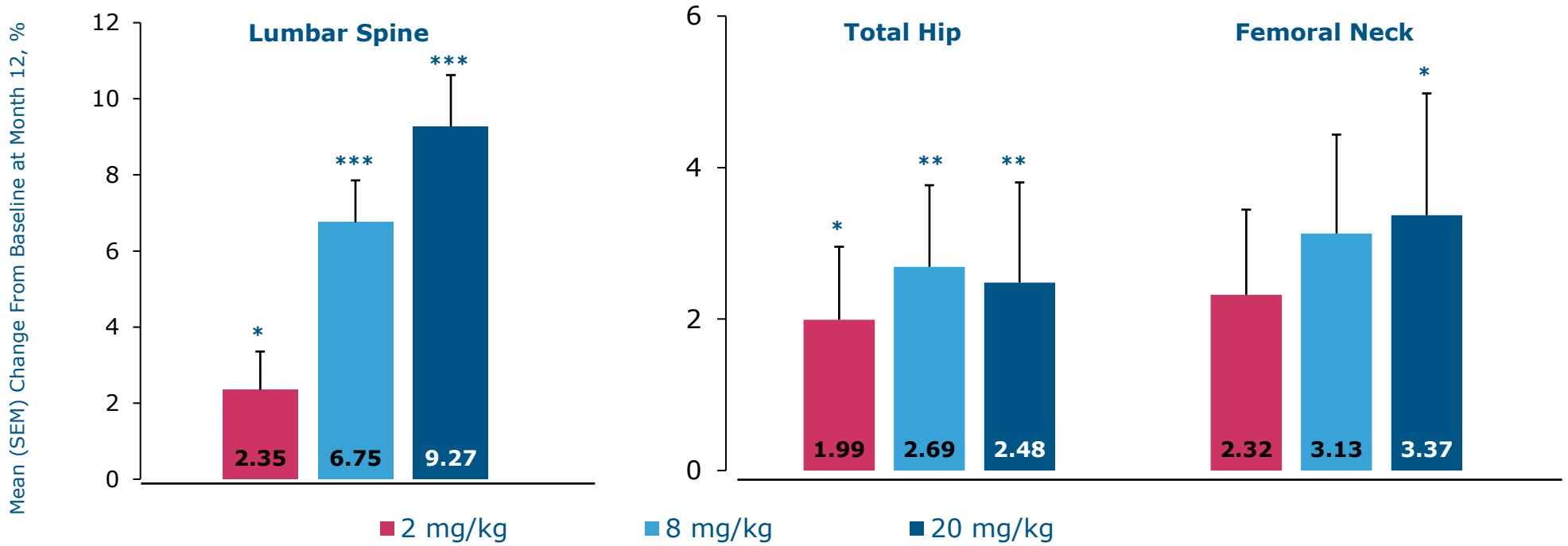
1. Lin X, et al. J Endocrinol Invest. 2024 Jan;47(1):67-77. 2. Lindahl et al. Eur J Hum Genet 23, 1042–1050 (2015).

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).

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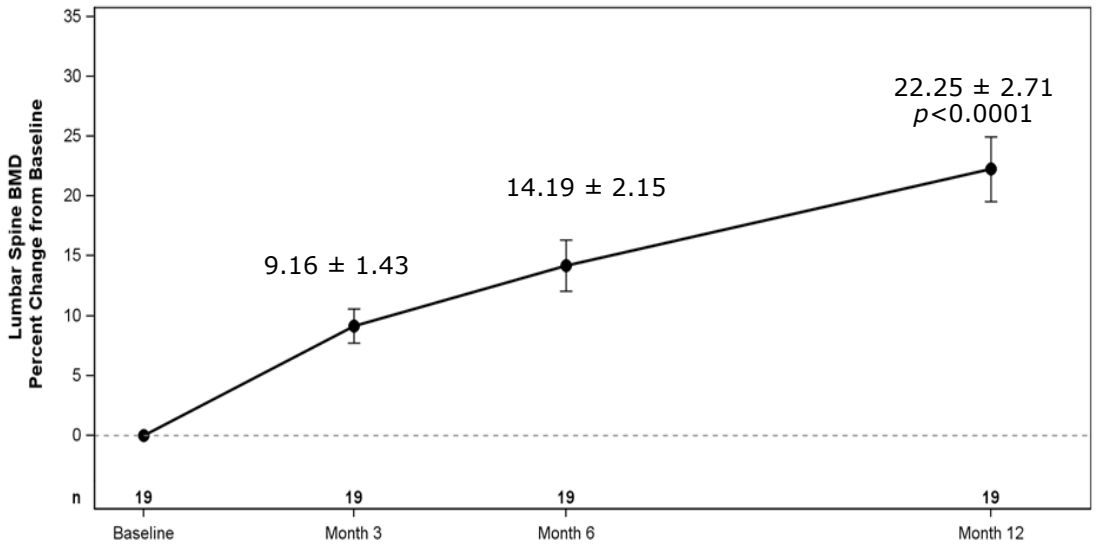
Glorieux F, *et al.* "Setrusumab for the treatment of osteogenesis imperfecta (OI): Results from the Phase 2b ASTEROID Study" ASBMR 2021; Abstract 1016.

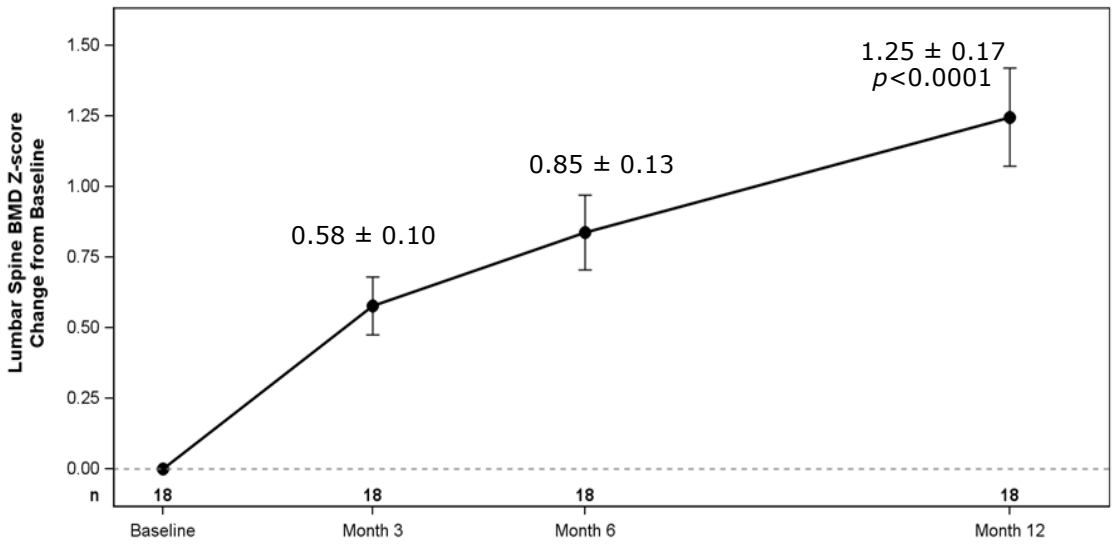
Orbit Phase 2 – BMD and Z-score mean increase through month 12[1]

Improvements in BMD and Z-scores consistent across all OI Types studied

Lumbar Spine BMD[1] % Change from Baseline



Lumbar Spine BMD[1] Z-Score Change from Baseline



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)

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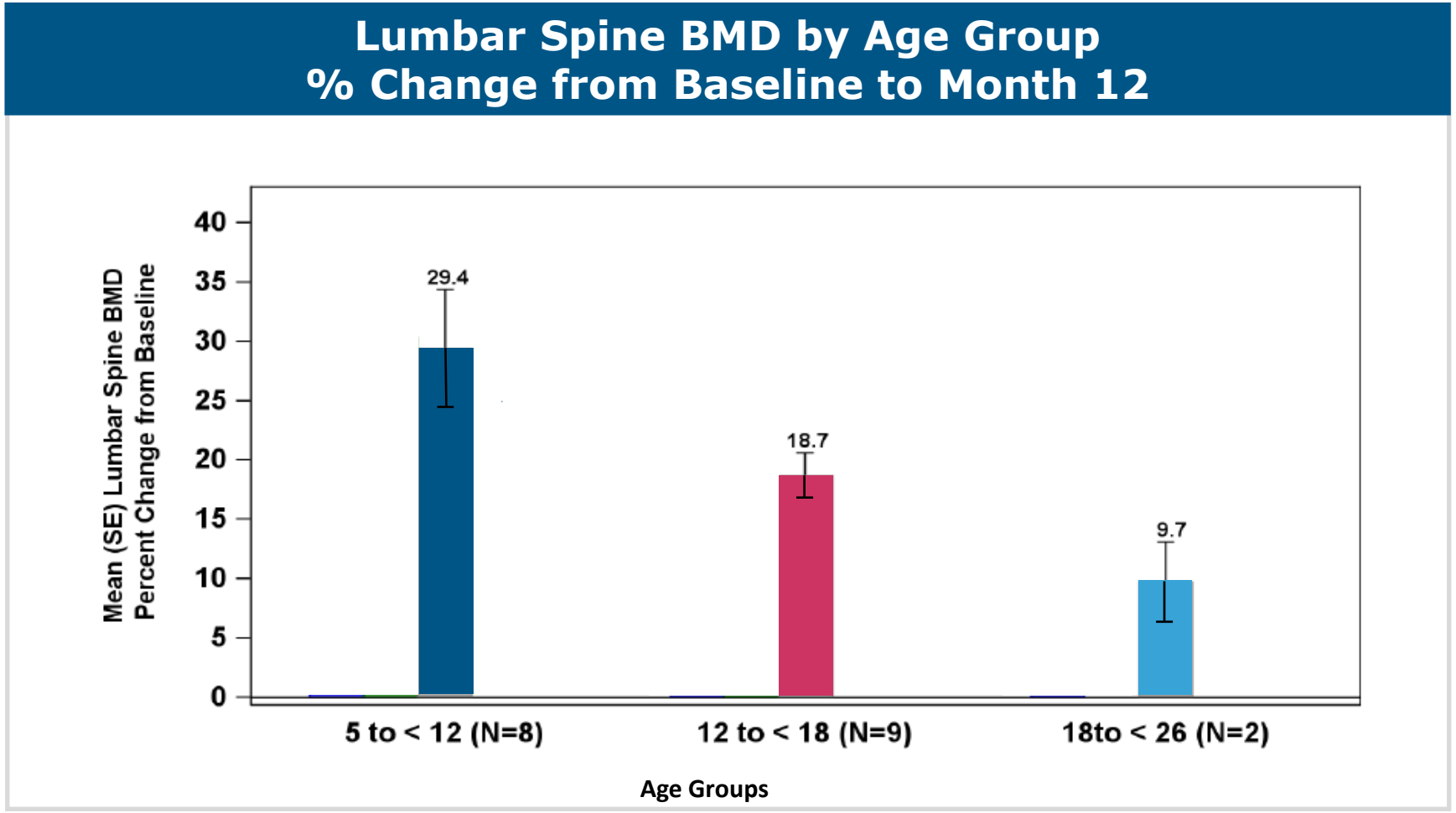
1. Data as of June 2024

Orbit Phase 2 data – increase in BMD observed in all age groups,[1,2] Greatest increase in patients 5-12 years of age



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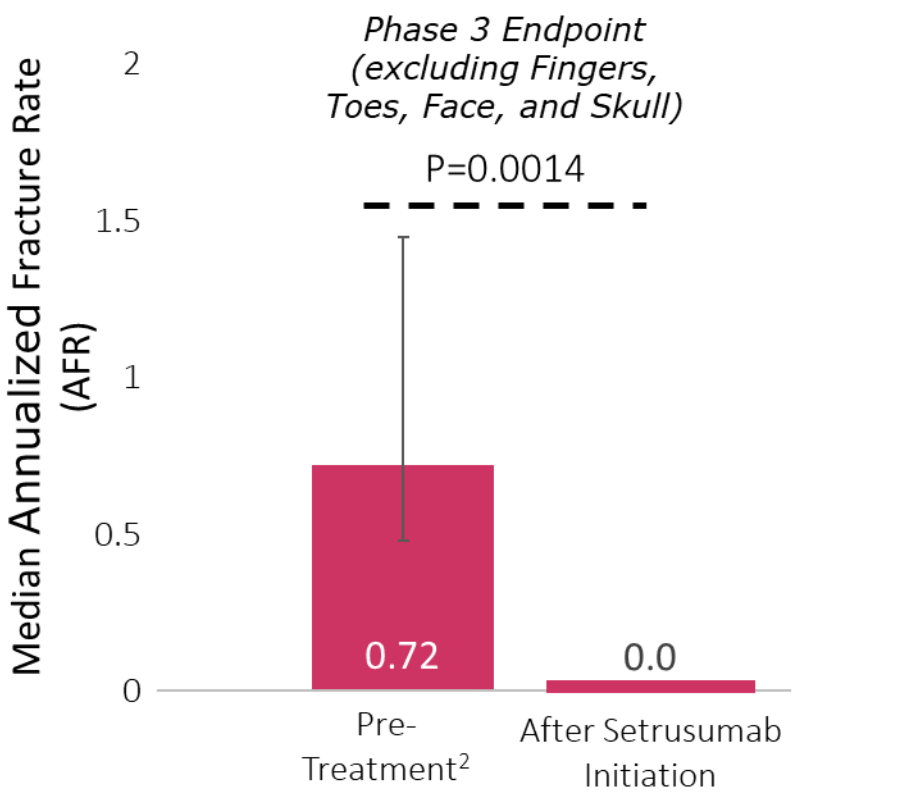
1. Data as of June 2024
2. Lewiecki EM *et al*. Evaluating Setrusumab for the Treatment of Osteogenesis Imperfecta: Phase 2 Data from the Phase 2/3 Orbit Study. Presented at the American Society for Bone and Mineral Research; October 13–16, 2023; Vancouver, BC, Canada. Abstract/Poster LB SAT-650

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

Radiographically Confirmed Fractures[1]



1: Data as of June 2024; updated clinical fractures includes a mean follow-up of 16 months
2: Pre-Treatment period includes fractures in the two years before screening based on medical record review and patient report, and fractures between screening and first dose

6 y/o male patient with Type IV OI, increased mobility after 17 months on study

Safety evaluation at 14 months shows setrusumab is well tolerated

Safety at 14 months

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 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%)

*All related adverse events were mild to moderate in severity

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1. 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

Orbit study – Phase 3*

Designed to evaluate the efficacy and safety of setrusumab vs. placebo in children and young adults with OI	
Enrolled 158 subjects ages 5 to 25 years with OI Types I, III, or IV and a confirmed *COL1A1* or *COL1A2* mutation. Enrolled in 12 countries including USA and Europe (50 sites)	Patients with at least 1 fracture in prior 12 months or 2 fractures in prior 24 months or 1 fracture of tibia, femur or humerus. Stratified by number of fractures in the prior 2 years (≤ 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** (excludes fingers, toes, face and skull)

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*Clinical Trials Identifier: NCT05125809

Cosmic study – Phase 3*

Designed to evaluate the efficacy and safety of setrusumab vs. bisphosphonates in young children with OI	
Enrolled 69 subjects ages 2 to < 7 years with OI Types I, III, or IV and a confirmed *COL1A1* or *COL1A2* mutation. Enrolled at sites including in the USA and Europe.	Patients with at least 1 fracture in prior 12 months or 2 fractures in prior 24 months or 1 fracture of tibia, femur or humerus. Stratified by number of fractures in the prior 2 years (≤ 3 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** (including morphometric fractures)

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*Clinical Trials Identifier : NCT05768854

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 $245M in regulatory and commercial milestones ($9M received 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[1], largest data set on OI; will inform reimbursement
- 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 Crysvita-like pricing potentially acceptable to European healthcare systems

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1. 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
** Mechanism of Coordinated Access
***Kyowa Kirin Co., Ltd. Appendix to the Consolidated Financial Summary (IFRS) Fiscal 2023 Interim (January 1, 2023 - June 30, 2023)

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Alvelestat (MPH966)

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

Alpha 1 Support Group UK Information Day September 2023

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 disease[1]
- 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 $1.4bn in 2022[4]
  - US patients (weekly I.V.) $100-150k/year[4]
  - AATD products forecast to reach $3.2bn by 2031[5]
- Europe AAT augmentation not widely reimbursed as lack of clinical outcomes data
- Potential first oral treatment

1. 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
2. Evercore estimate
3. Based on Cantor Fitzgerald estimates of Net Peak Sales in the US and EU5
4. Cantor Fitzgerald January 2024 Deep Dive: Alpha-1 Antitrypsin Deficiency and Its Destruction of the Lungs and Liver
5. Global data

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Alvelestat – Historical data

- Potent, specific oral Neutrophil Elastase Inhibitor
- Safety profile in >1,000 patients
- Development informed by efficacy signals from trials in disorders of Neutrophil Elastase / Anti-Elastase imbalance:
  - Bronchiectasis, Cystic Fibrosis, Bronchiolitis Obliterans Syndrome, COVID-19

Phase 2 Bronchiectasis (Stockley et al 2013)

- 60 mg alvelestat or placebo BD for 4 weeks
- 38 randomized, 16 alvelestat, 22 placebo

Spirometry at week 4

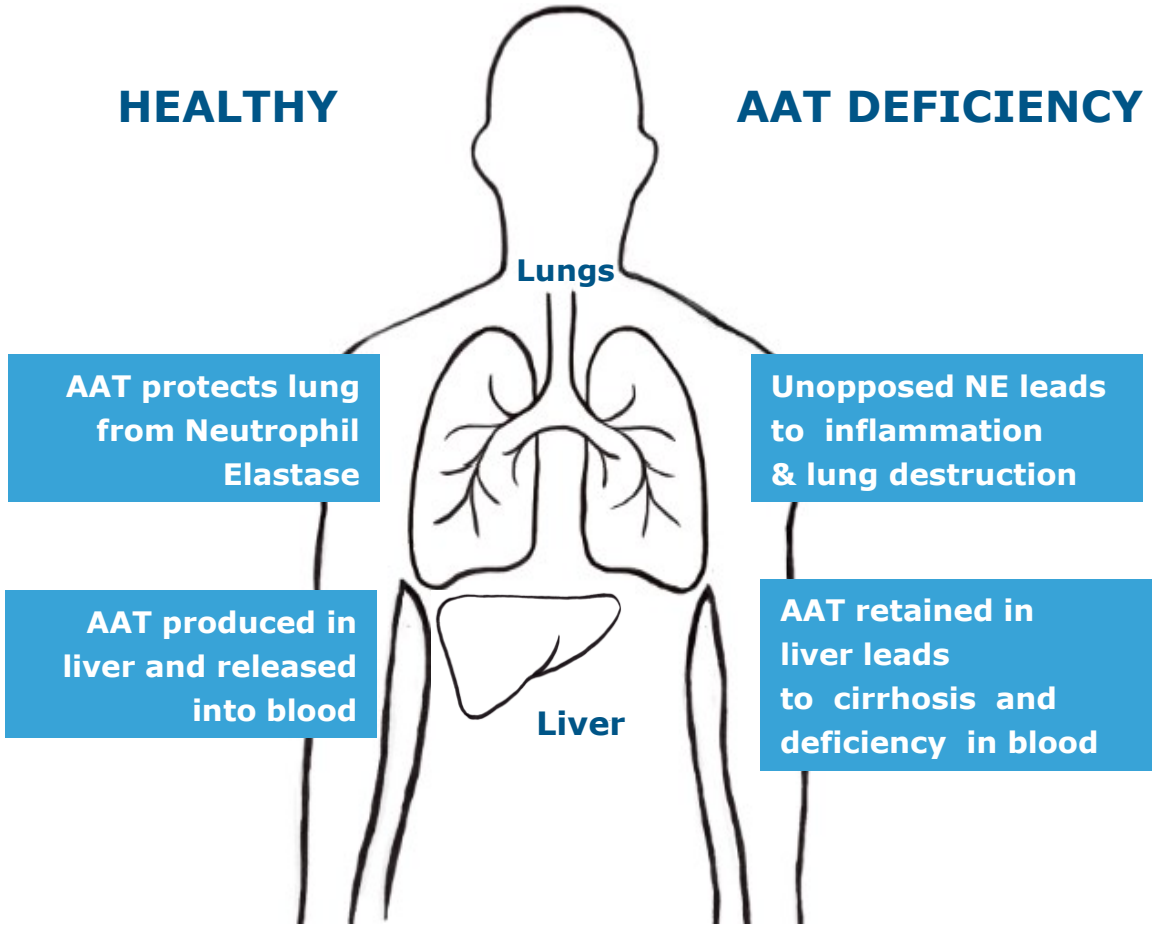
Lung Function	Improvement over placebo LSM(SEM)	P Value
FEV_1	100 mls (34.0)	0.006
SVC	130 mls (74.0	0.079

SGRQ at week 4

	Improvement over placebo LSM(SEM)*	P Value
Total SGRQ	-5.64 (4.65)#	0.236

*Negative value is improvement for SGRQ
#CIM of > 4 points reached, but high variability and statistical significance not reached

AATD – A progressive, lung disease driven by Neutrophil Elastase



Alvelestat Neutrophil Elastase Inhibitor

- Targets the cause of lung damage
- Convenience of oral therapy
- Potential use in early stages of lung disease to delay progression

Potential for efficacy advantage

- Daily dosing for sustained NE suppression
- Effective lung penetration[1]
- Inhibits NE on cell sites inaccessible to AAT[2]

Two complementary Phase 2 trials completed

- 162 patients with AATD-LD, 98 on alvelestat
- 12-week safety and efficacy investigated across range of respiratory impairment
- Data in augmentation naïve and on augmentation
- Phase 3 dose identified

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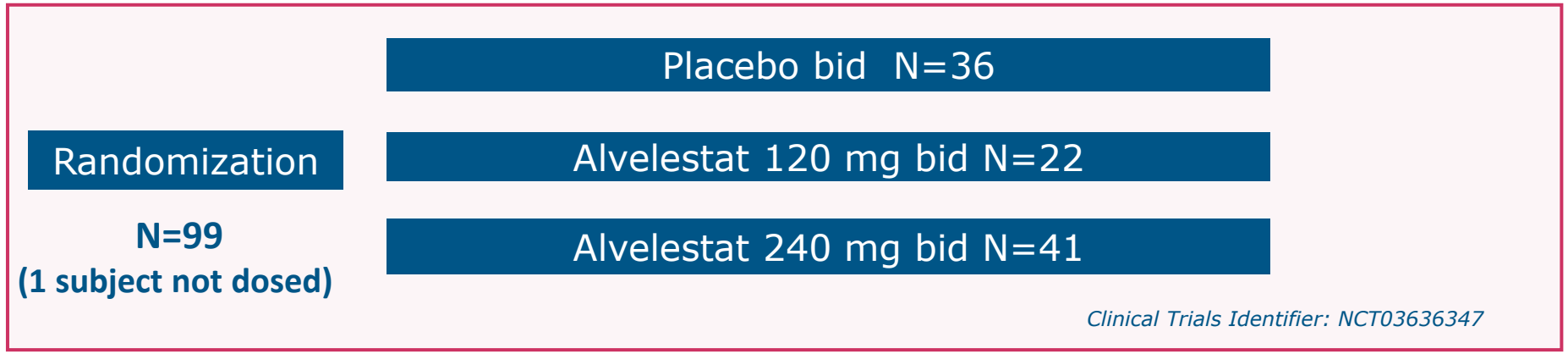
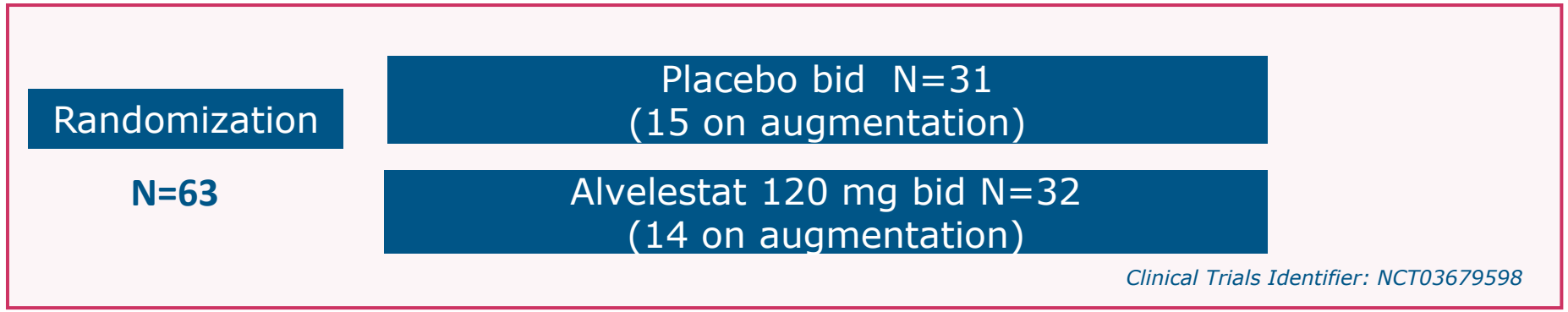
1. Gunawardena et al 2013;
2. Stevens et al 2011

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



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THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

NIH National Center for Advancing Translational Sciences

Funded by NCATS

ALPHA-1 FOUNDATION

ATALANTa and ASTRAEUS deliver safety and efficacy data across early and later stage Lung Disease

ATALANTa was a US study, ASTRAEUS enrolled predominantly in EU

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

- ASTRAEUS studied 120 mg and 240 mg, ATALANTA 120 mg only

Parameter at Baseline (median)	ATALANTa*		ASTRAEUS*
	Augmentation (N=29)	Non-Augmentation (N=34)	Non-Augmentation
FEV_1 (% predicted)	69.8	89.3	59.0
SGRQ Total**	33.7	19.6	32.2
SGRQ Activity	45.4	25.5	53.3

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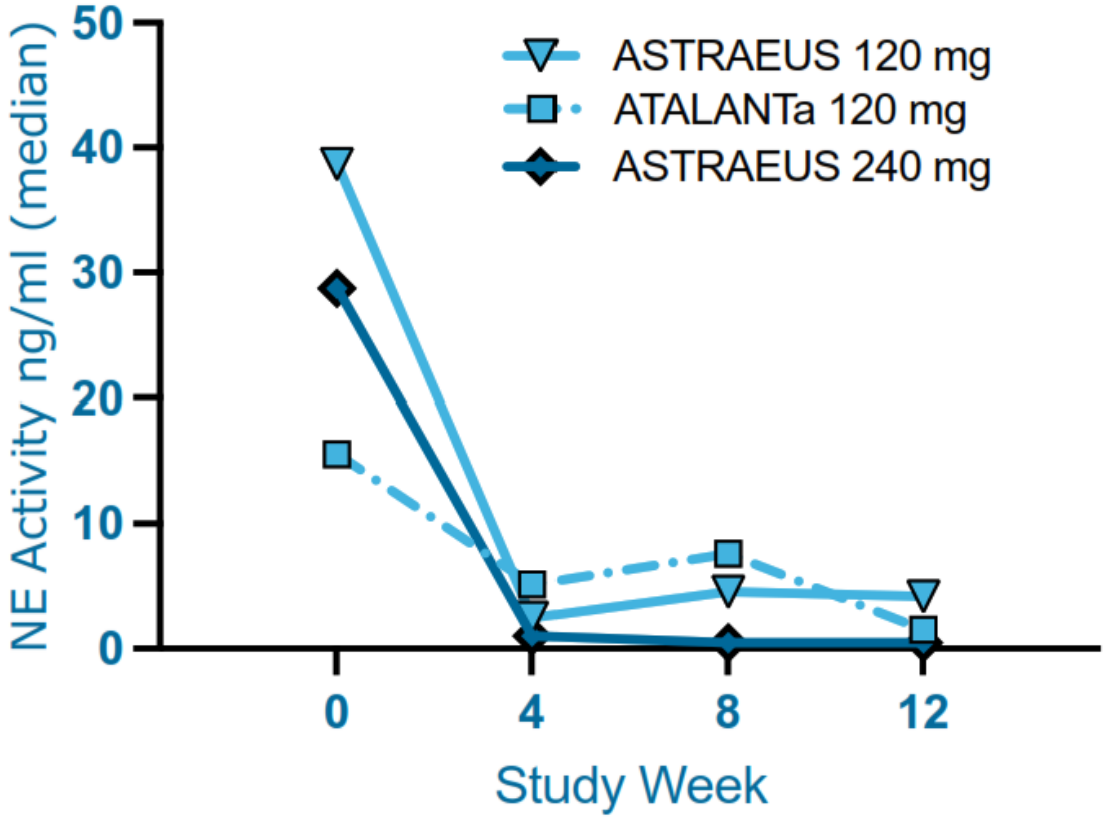
*In ATALANTa 76% of total enrolled were Pi*ZZ, others PiSZ and PiNN. In ASTREAUS 100% PiZZ
**SGRQ scores out of 100; lower SGRQ scores equates to better health status

Alvelestat rapidly and consistently suppresses Blood Neutrophil Elastase Activity, with dose-effect in ASTRAEUS and ATALANTa



- 120 mg reduction at week 12 ASTRAEUS $p<0.05$ compared to placebo
- 240 mg reduction at week 12 ASTRAEUS <0.001 compared to placebo
- 240 mg but not 120 mg dose, met target > 90% NE suppression in blood)

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Biomarkers and PK modelling confirm 240 mg dose for progression

ASTRAEUS

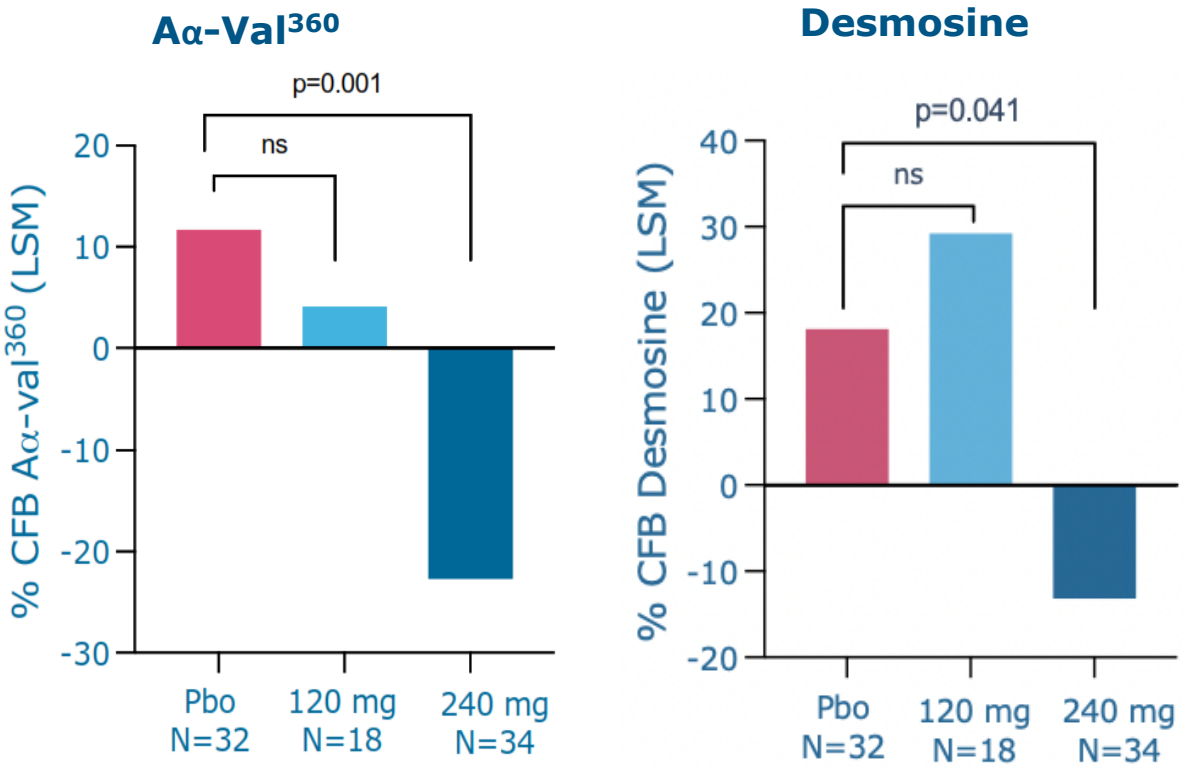
- 240 mg – progressive reduction in biomarkers of NE-driven protein breakdown (Aα-val^{360}) and elastin turnover (desmosine)
- 120 mg – no effect on desmosine

ATALANTa

- Consistent with ASTRAEUS – 120 mg no effect on desmosine
- Significant reduction from baseline in Aα-Val^{360} (p=0.03), but not significant compared to placebo

Population PK modelling predicts 240 mg achieves target drug levels in lung tissue

ASTRAEUS (Primary Endpoint Analysis)



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Association of alvelestat treatment with improvement in Respiratory Health Status (SGRQ)

- St. George's Respiratory Questionnaire – Patient reported outcome in COPD recognized by FDA (Total Score comprising Activity, Symptoms and Impacts domains).
  - Activity Domain most impacted in patients with AATD
- In longitudinal studies in AATD **SGRQ Total score** has been shown to deteriorate ~ 1 point per annum[1]
- In the Phase 2 studies, a consistent association was demonstrated between the effects of alvelestat (disease activity biomarker reduction) and improvement in SGRQ (Total score and Activity Domain)[2]
- This effect was also observed for the COPD Assessment Test (CAT), another validated patient-reported quality of life tool
- ATALANTa study – greater effect in non-augmentation subgroup with earlier stage lung disease (FEV_1)

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1. Chapman et al, Lancet 2015; 386: 360–68
2. Parkin Am J Respir Crit Care Med 2023;207:A2844

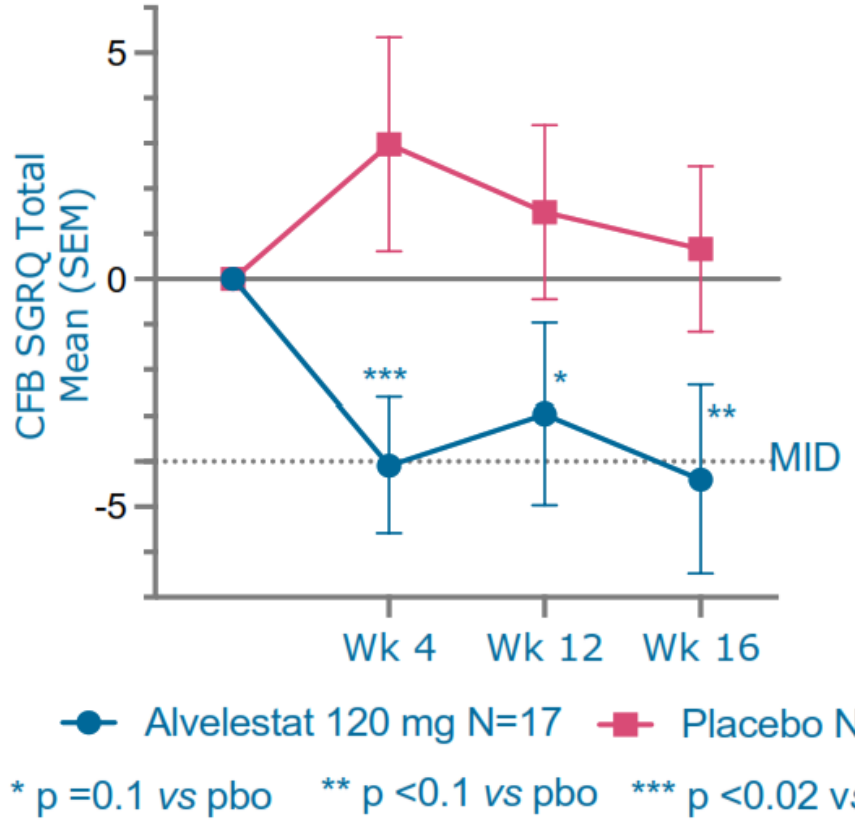
Patients with earlier stage lung disease (FEV_1) show greater SGRQ response - ATALANTa Subgroup Analysis

- ATALANTa study – Non-augmentation subgroup (median FEV_1 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)

Following FDA input, a qualitative validation study has been completed at several US sites to meet the initial requirements for SGRQ as a primary efficacy assessment in Phase 3.
Study concluded:

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

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



MID= Minimal Important Difference for SGRQ Total (COPD)

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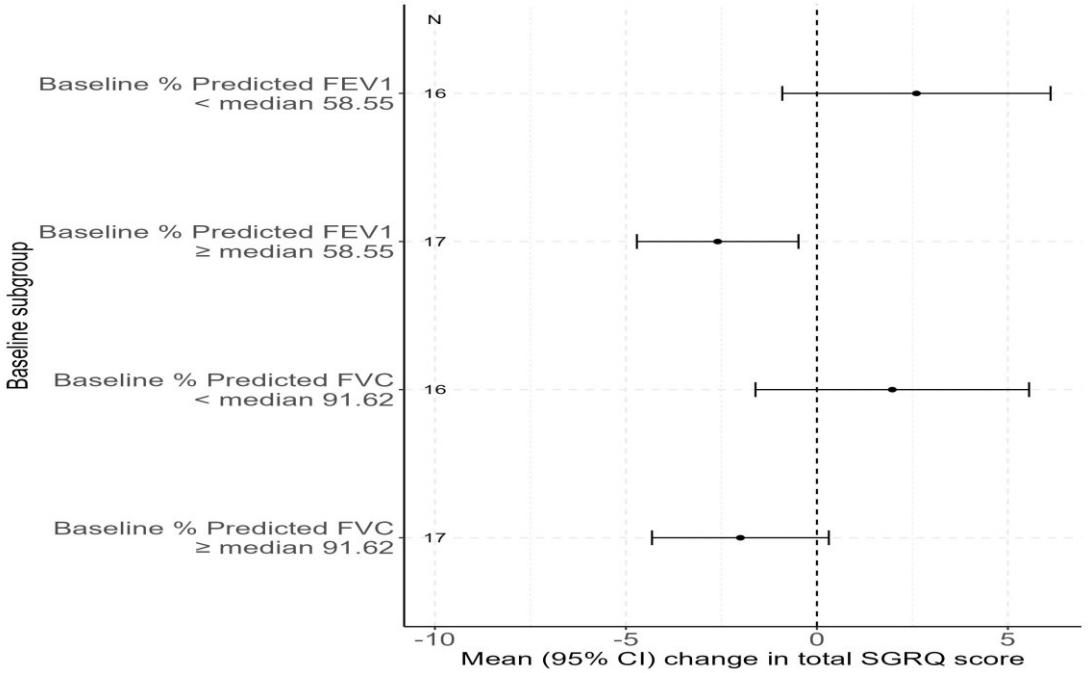
Earlier stage patients – greater SGRQ change and potentially FEV_1 - optimizing the Phase 3 population

ASTRAEUS Study

- Patients with less advanced lung disease may be more able to show improvement than those with extensive damage
- Post hoc analysis of baseline characteristics of ASTRAEUS and **SGRQ Total** change shows earlier stage patients also had the greatest change

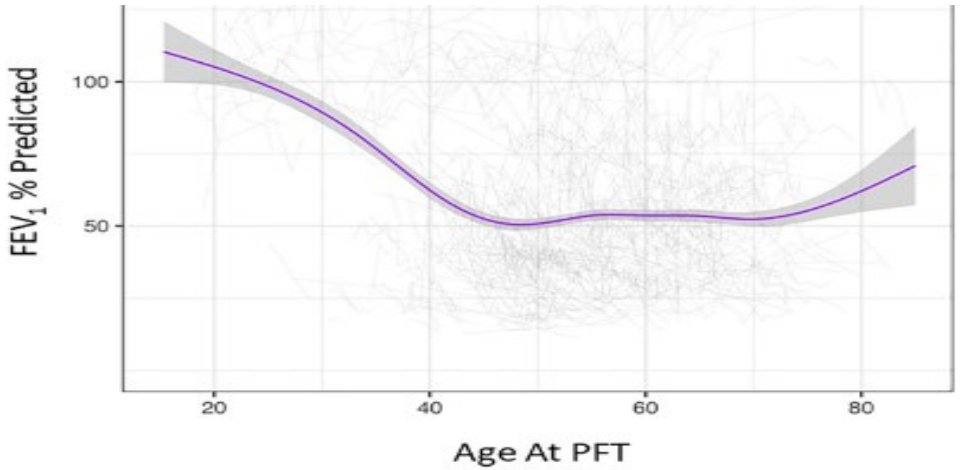


Fraughen et al, Nov 2023[1]

Multinational registry retrospective analysis (N=615, N=365 never received AAT). **FEV_1** decline highest 20-50 years old

AAT vs never AAT: significant difference in **FEV_1** decline with GOLD stage 2 ($50\% < FEV_1 < 80\%$) 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"



1. Fraughen et al, Am J Resp Crit Care Med 2023 Nov 1;208(9):964-974 Reprinted with permission of the American Thoracic Society.
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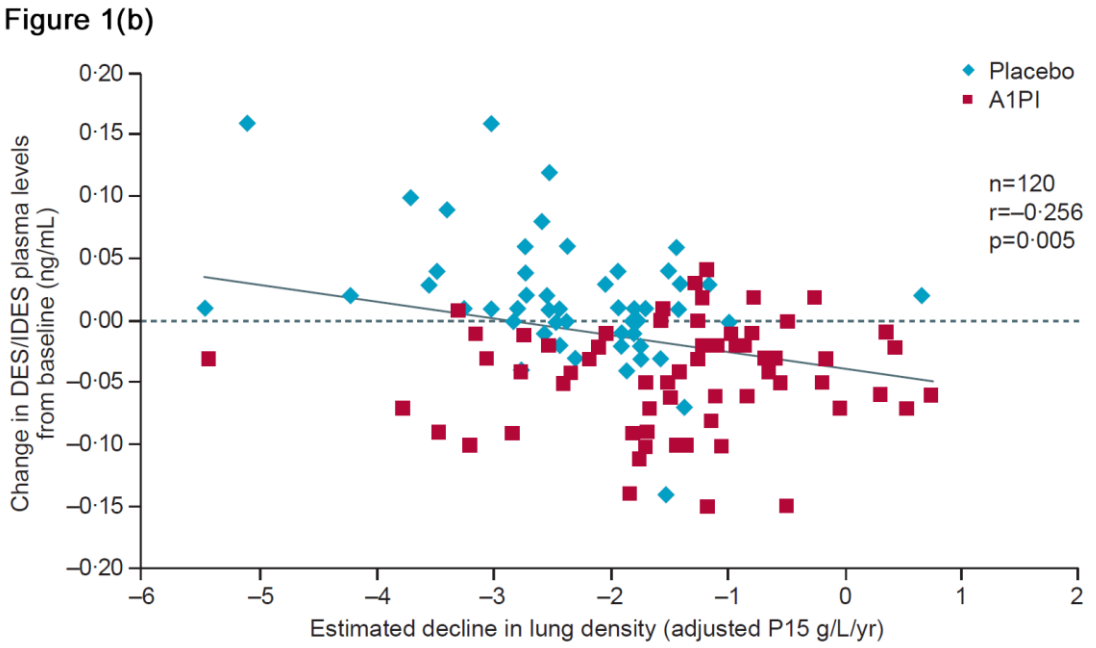
Translating effects on elastin breakdown (desmosine) to CT efficacy endpoint required by European Regulatory Agency

Reduction in desmosine for 240 mg alvelestat at 12 weeks comparable to Augmentation therapy at 12 months

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

Effects progressive over 12 weeks and from augmentation experience expected to continue over the course of 2-4 years[1]

~ 30% lung tissue is elastin and there is a significant correlation of reduction in accelerated elastin turnover (desmosine) and rate of lung tissue loss by CT density in AATD[1]



† Per protocol analysis

1. Ma et al. *Chronic Obstr Pulm Dis*. 2017;4(1):34-44

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)

*one case with concurrent AESIs of infection and infection and prolonged QTc

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

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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	• Change in desmosine observed at 240 mg dose in ASTRAEUS study • Significant correlation of desmosine change to CT density change in longtitudinal study (Ma et al)
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)	• Change observed in ATALANTa study of patients with earlier stage disease • Change observed in patients with a desmosine response across both Phase 2 studies • SGRQ Total score has been shown to deteriorate ~ 1 point per annum in the placebo arm in other studies

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

Development strategy for Phase 3 pivotal clinical trial

Clinical data	Earlier stage severe PI*ZZ patients appear to have greater response in SGRQ Total and Activity Literature shows that earlier stage patients with higher 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

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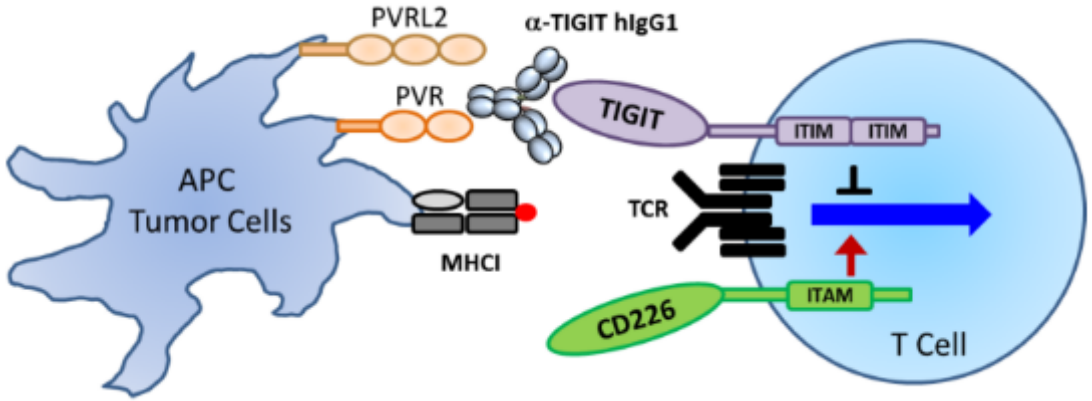
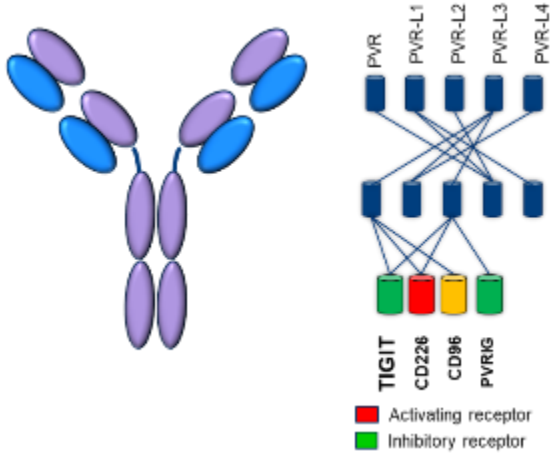
Etigilimab (MPH313)

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





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1. Mettu et al., CCR, 2021; 2.McKean et. al., ASCO, 2022; 3. Sarikonda G et al., ESMO, 2022

ACTIVATE efficacy data: select cohorts*

Objective Responses by RECIST	Cohort					
	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[1]**	**0**	**0**	**0**	**3**
PR	**3**	**0**	**2**	**1**	**1[3]**	**7**
SD	**3**	**2[2]**	**2**	**4**	**0**	**11**
PD	**4**	**3**	**4**	**5**	**3**	**19**

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

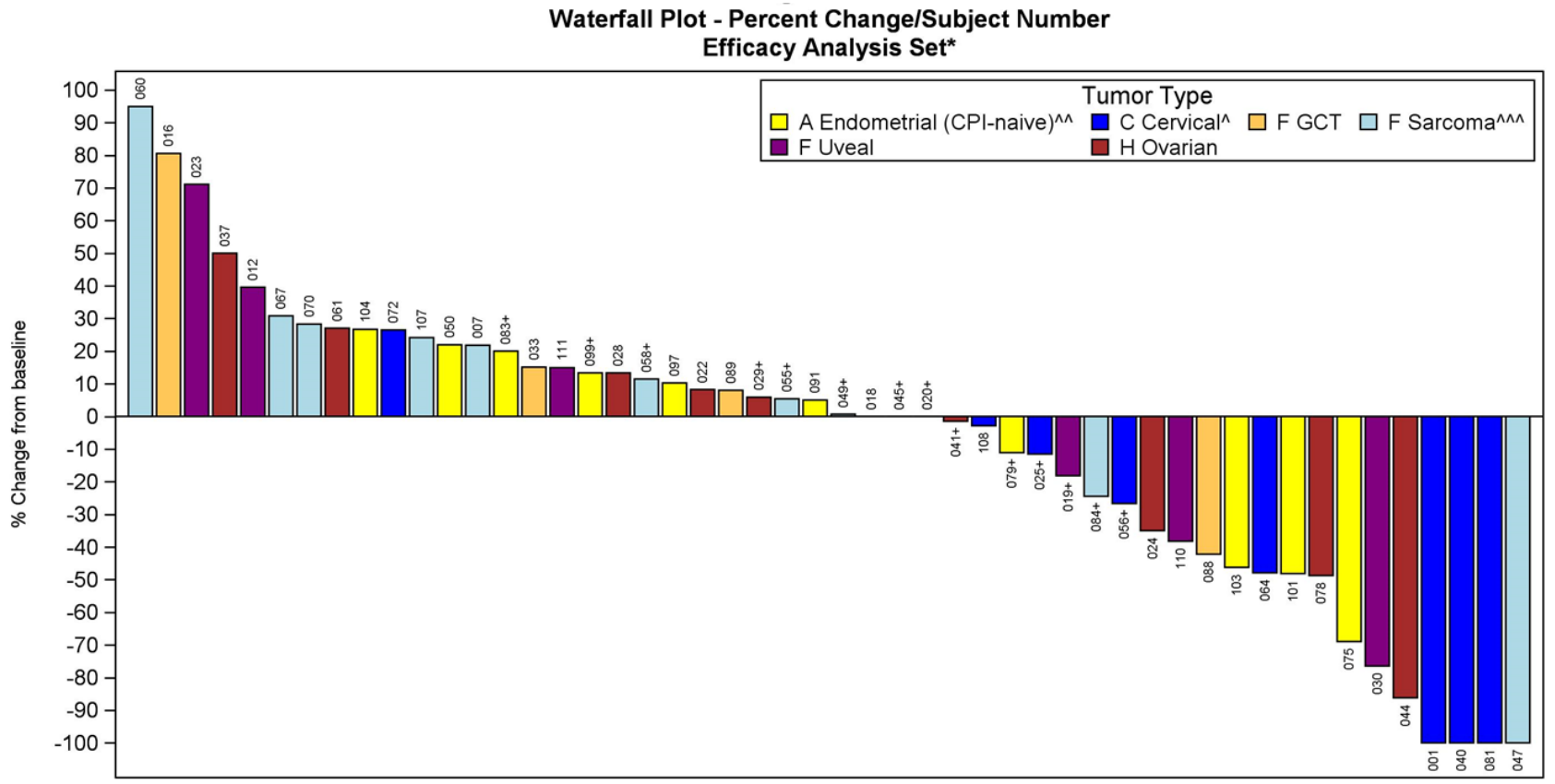
All responses confirmed

*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.

1. 1 CR was on-going and pt withdrew consent; 1 CR off study due to AE; 1 CR on-going at data cut-off
2. 1 SD on-going at data cut-off, patient died due to unrelated event
3. Mixed response, continued treatment, PD-RECIST1.1

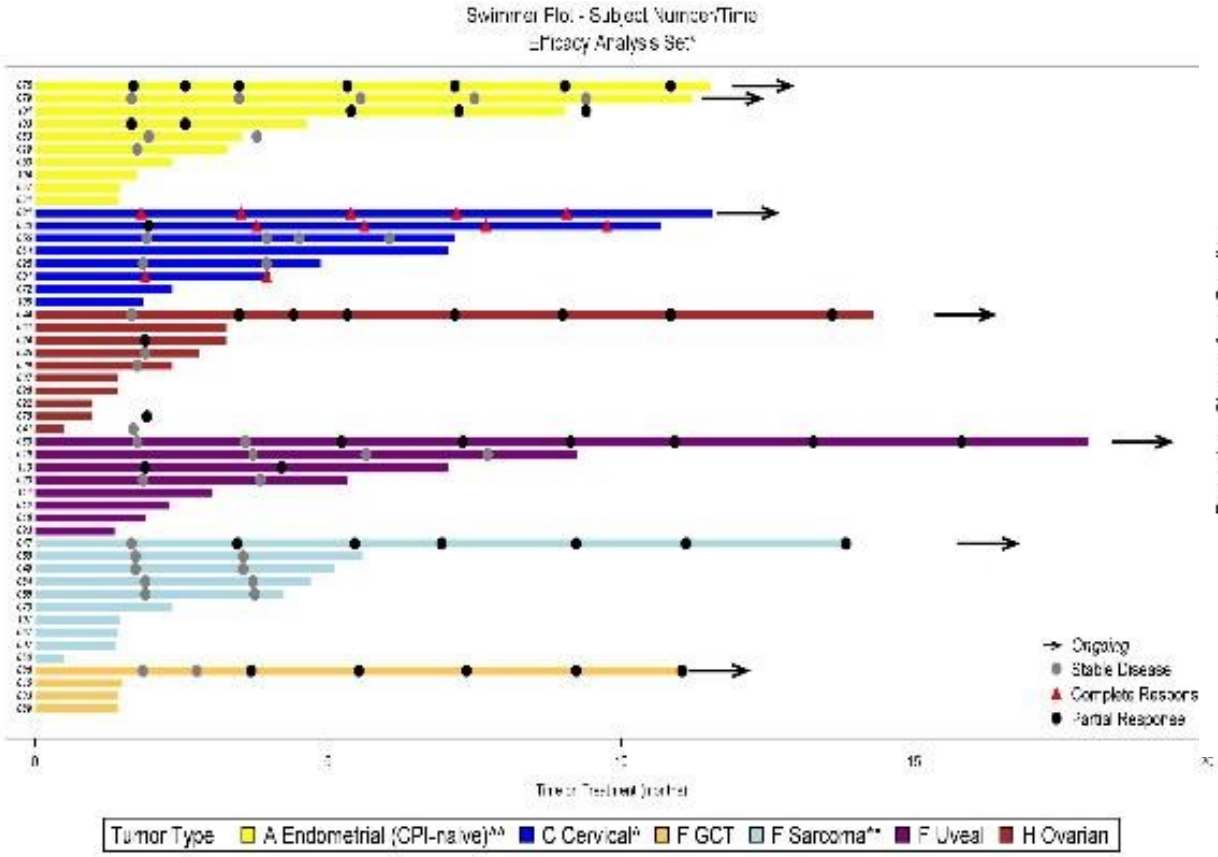
Central lab PD-L1 CPS % for ORR pts: F088 germ cell=0; F047 sarcoma=1; F030 uveal=0; A075 endometrial=3; A103 endometrial=3; G101 endometrial=3; C081 cervical=51; C040=20; C001 cervical and F110 uveal had no tissue for central lab; pathology report for C001 indicated >90%.

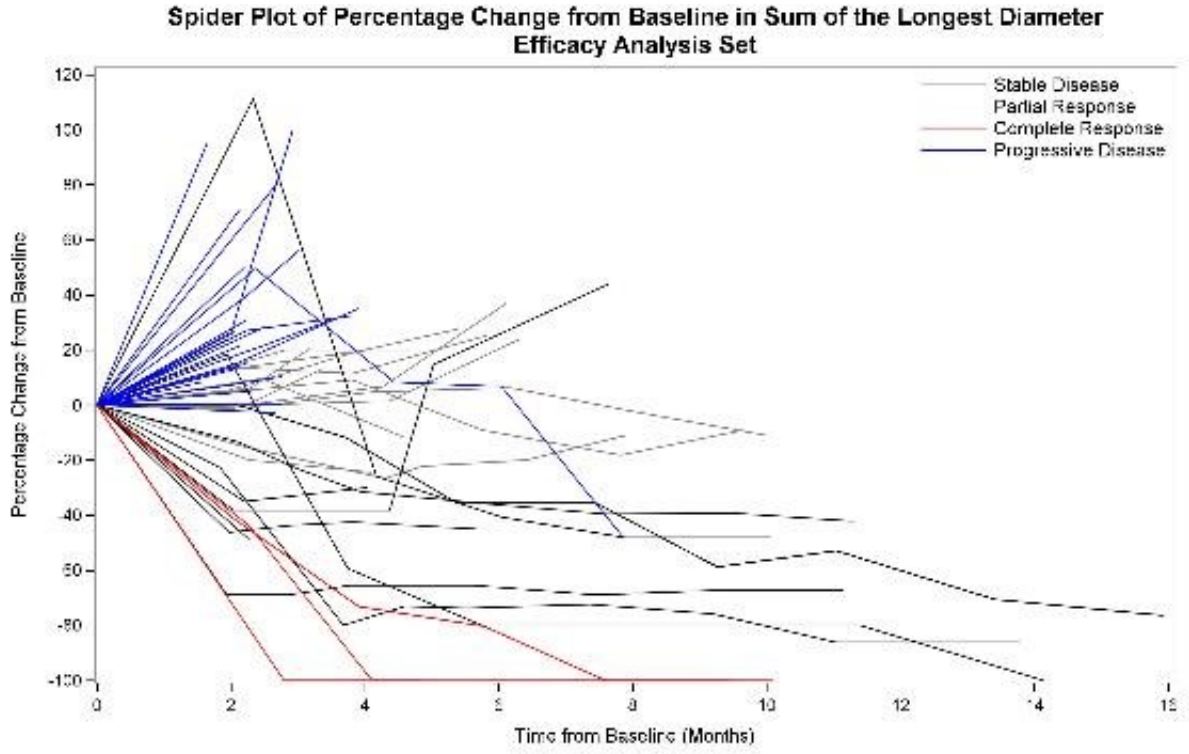
ACTIVATE efficacy data: select cohorts (continued)



^Cervical cancer patient (E025) enrolled in TMB-H cohort with PD-L1 CPS>1%
^^ Endometrial cancer – CPI-naïve patient (G101) enrolled in post-CPI cohort
^^ Sarcoma subjects only include those with de-differentiated liposarcoma
+ 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
#De-differentiated liposarcoma subject F047 is CR for target lesions, but overall PR due to persistent non-target lesion

ACTIVATE efficacy data: select cohorts (continued)



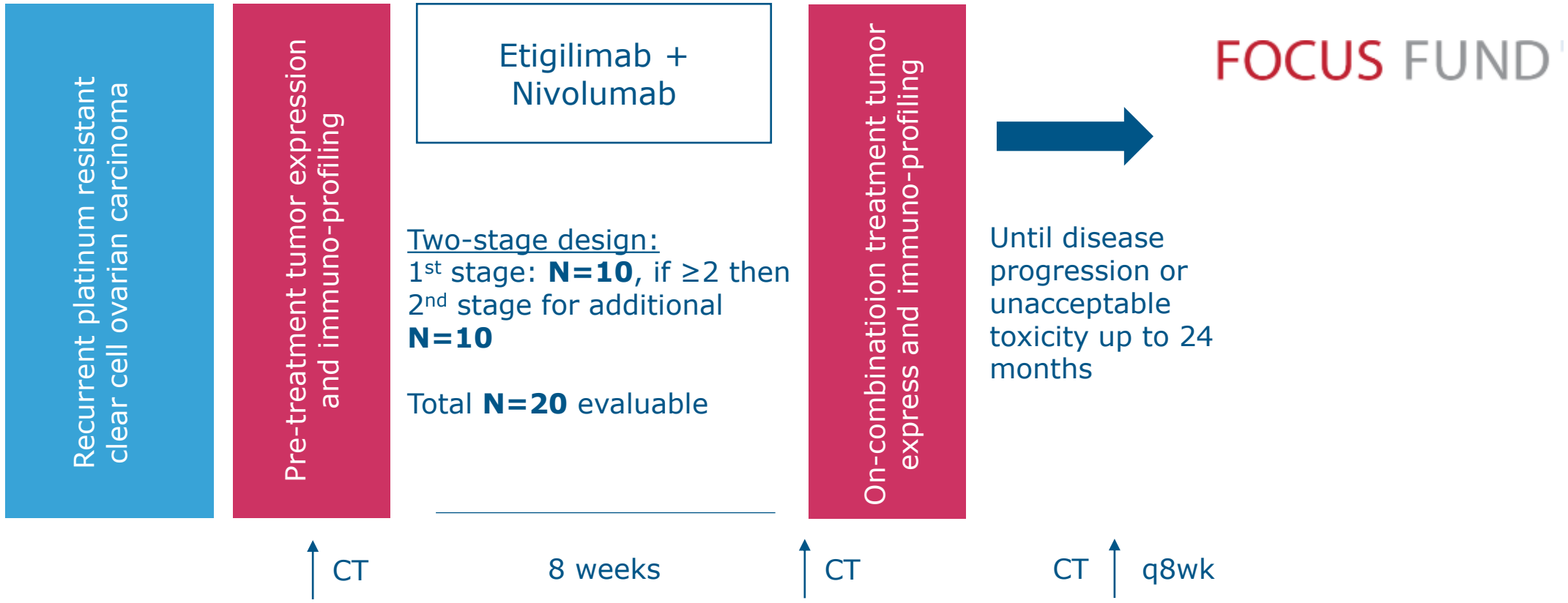


" Sarcoma subjects only include those with De-differentiated liposarcoma
^Cervical cancer patient (E025) enrolled in TMB-H cohort with PDL-1 CPS>1%
^^Endometrial cancer – CPI naïve patient (G101) enrolled in post-CPI cohort
Note E025 death unrelated to study drug or PD. C001 consent withdrew
Central 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 (→)

Median time on treatment for EC-N, cervical, GCT, de-differentiated liposarcoma, uveal patients

- CR (3 pts) = 11.5 months
- PR (7 pts) = 11 months
- SD (11 pts) = 5.7 months

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



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.

*Clinical Trial Identifier NCT05715216

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Other programs, milestones and financials

Upcoming key milestones for core programs

Product candidate	2023		2024		Next milestone
	H1	H2	H1	H2	
Setrusumab OI	Phase 2 Orbit (5 - <26 yrs old)				Phase 2 OL data 2H 2024
	Phase 3 Orbit (5 - 25 yrs old)				Phase 3 Interim analysis
	Phase 3 Cosmic (2 - <7 yrs old)				Phase 3 Interim analysis
Alvelestat AATD-LD BOS*	ASTRAEUS				Potential partnering, Phase 3 initiation Medical conferences
	Phase 2 ATALANTa				
	Phase 1b	Phase 2			BOS: Phase 2 data
Etigilimab Rare & Gyn-Onc Tumors	Phase 1b ACTIVATE				EON study expanded to 20 patients – update 2H 2024/1H 2025
OCCC**	Phase 1b/2 EON				

*Bronchiolitis Obliterans Syndrome
**Ovarian Clear Cell Carcinoma

Other programs: current partnerships

Other current partnerships
Navicixizumab – global rights out-licensed to Feng Biosciences for further development • Payments of up to $300 million in milestones plus royalties **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

Cash runway into 2027

- $48.7 million as of March 31, 2024; and
- $50 million gross proceeds from June 2024 financing[4]

Cap Table *(March 2024)*	**ADSs** *(in thousands)*
Shareholders > 2% holding	74,522
Shareholders < 2% holding	65,748
Share capital – Issued and outstanding as of March 31, 2024[1]	**140,270**
*ADSs issued in June 2024 financing**	*12,531*
Pro-forma share capital – Issued and outstanding following financing	***152,801***
Potential Future Dilution:	
Warrants[2]	1,401
Convertible loan notes	3,421
Employee share schemes[3]	12,940

1 *ADS equivalents of 701,349,434 ordinary shares, with one ADS representing five ordinary shares.*
2 *Assumes a market price of $4.00 per ADS and cashless exercise. The maximum number of warrants outstanding is 1.8m.*
3 *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.*
4 *Excludes underwriting discounts and commissions and estimated offering expenses payable by us.*

Source: Shareholding based on the 13G & 13F filings (as of March 31, 2024), adjusted for subsequent purchases/sales when known.

Thank you

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

Mereo BioPharma

Mereo BioPharma Group plc

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

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