Corporate presentation

November 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 which have already received significant investment and retain global or regional rights where possible (initially in Europe)
- Partner our programs where it makes strategic sense and target monetization of royalty streams for non-core programs

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A late-stage rare disease company with a capital efficient model

Achievements and fundamentals

Two rare disease programs in-licensed and progressed to pivotal stage:

- **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

- $80.5 million of cash and cash equivalents as of September 30, 2024
- Active cost management – runway through key inflection points
- Leverage investigator-led studies to expand data sets

A late-stage company with validating partnerships

Corporate development
Management team with a proven track record in corporate development • Setrusumab acquired from Novartis • 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)

ultragenyx pharmaceutical

AstraZeneca

NOVARTIS

Late-stage clinical pipeline with core rare disease programs

Product candidate	Phase 1	Phase 2	Phase 3	
Setrusumab Osteogenesis Imperfecta			Orbit (5 -25 yrs old) Cosmic (2 - <7 yrs old) ultragenyx pharmaceutical	Orphan drug designation in US and EU, PRIME (EU),BTD (US) Pediatric disease Priority Review Voucher designation
Alvelestat* AATD-Lung Disease Bronchiolitis Obliterans Syndrome**			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) for ATTD

*Also completed Phase 2 studies in bronchiectasis, COPD (including bronchitic COPD), cystic fibrosis and COVID
**Investigator-Sponsored Study performed under non-Mereo IND

“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

- 80-90% linked to a mutation in Type I collagen[1,2] (Type I, III and IV)
- 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
- Early diagnosis in utero or shortly after birth with symptoms often already present

Market Opportunity

- 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 source of support and valued resource
- OI is a progressive condition, without clear care pathways, especially for adult patients
- Potential market opportunity of >$1Bn[4]

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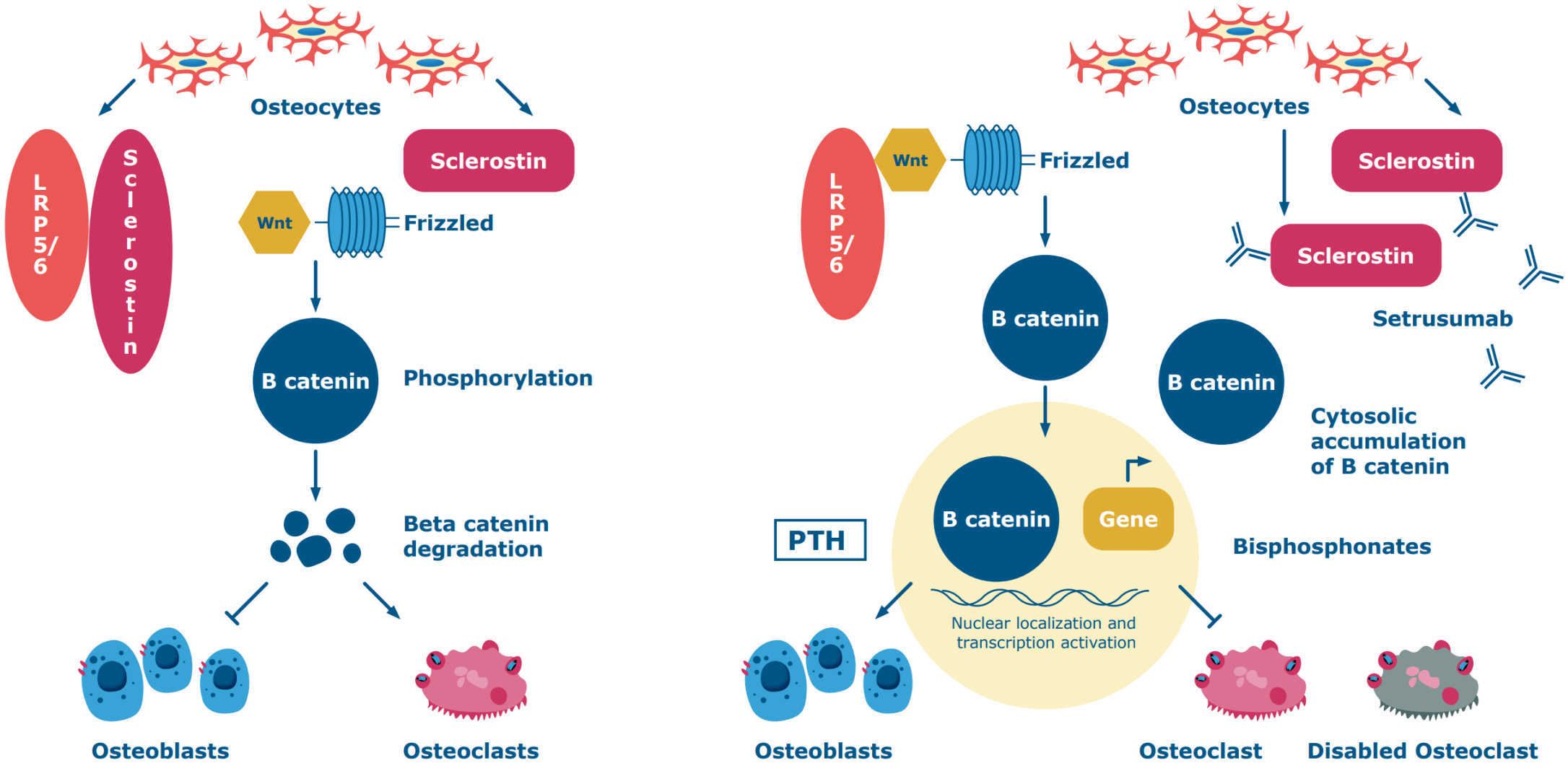
1. Based on Osteogenesis Imperfecta Foundation estimates; 2. Based on Orphanet estimates; 3. Internal BD forecast; 4. Based on Cantor Fitzgerald estimates of Net Peak Sales in the US and EU5
*OIFE: Osteogenesis Imperfecta Federation Europe; OIF: Osteogenesis Imperfecta Foundation

Setrusumab – Mechanism of Action



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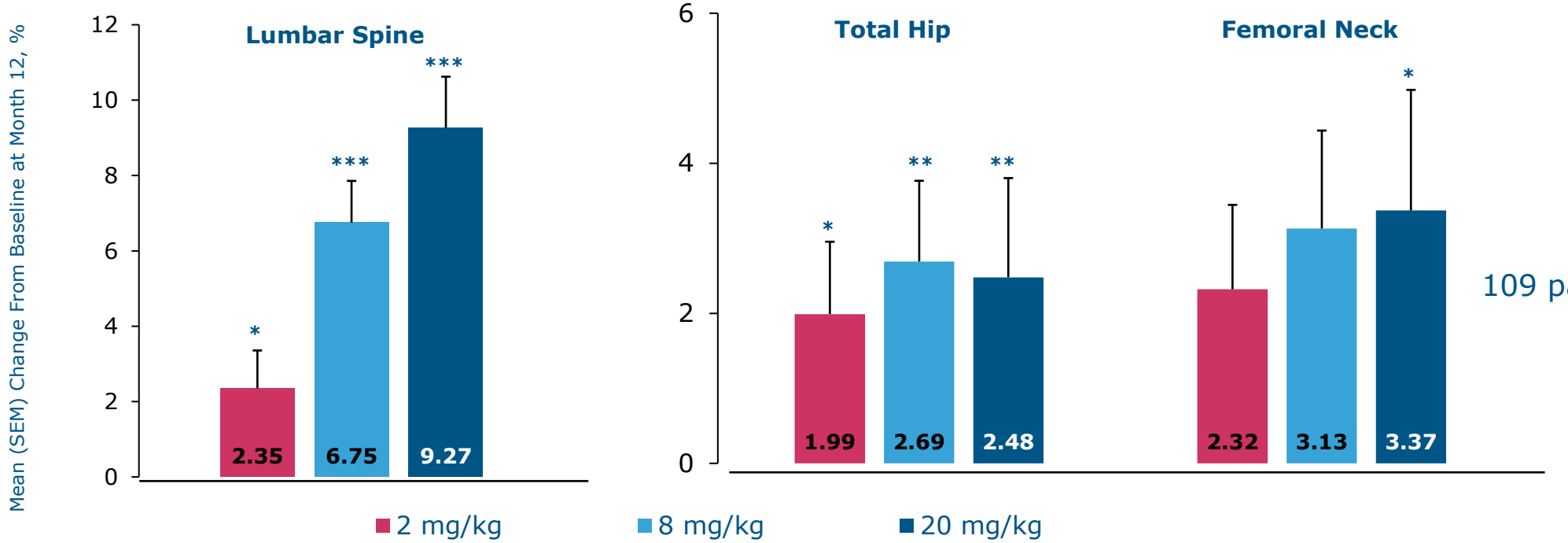
Increased BMD and bone strength, decreased fracture rate

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



109 patients enrolled

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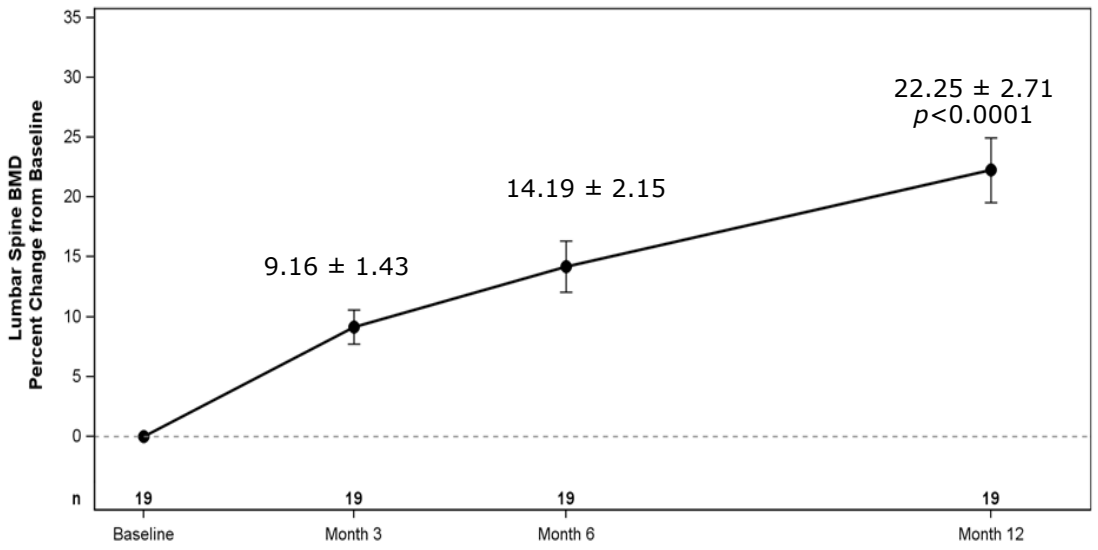
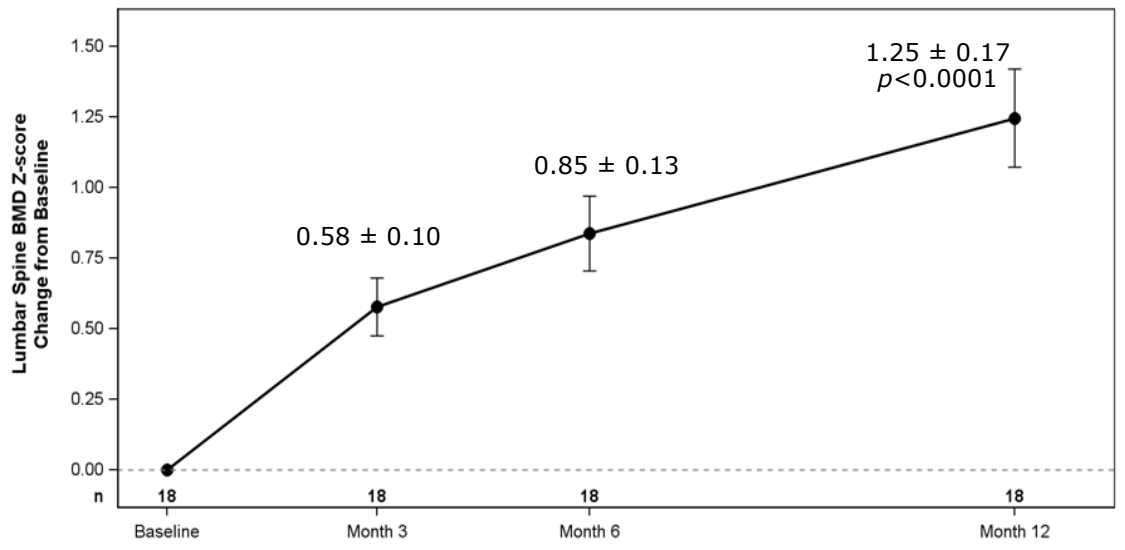
Glorieux F, *et al.* "Setrusumab for the treatment of osteogenesis imperfecta (OI): Results from the Phase 2b ASTEROID Study" ASBMR 2021; Abstract 1016.

Orbit Phase 2 – BMD and Z-score mean increase through month 12[1]
Improvements 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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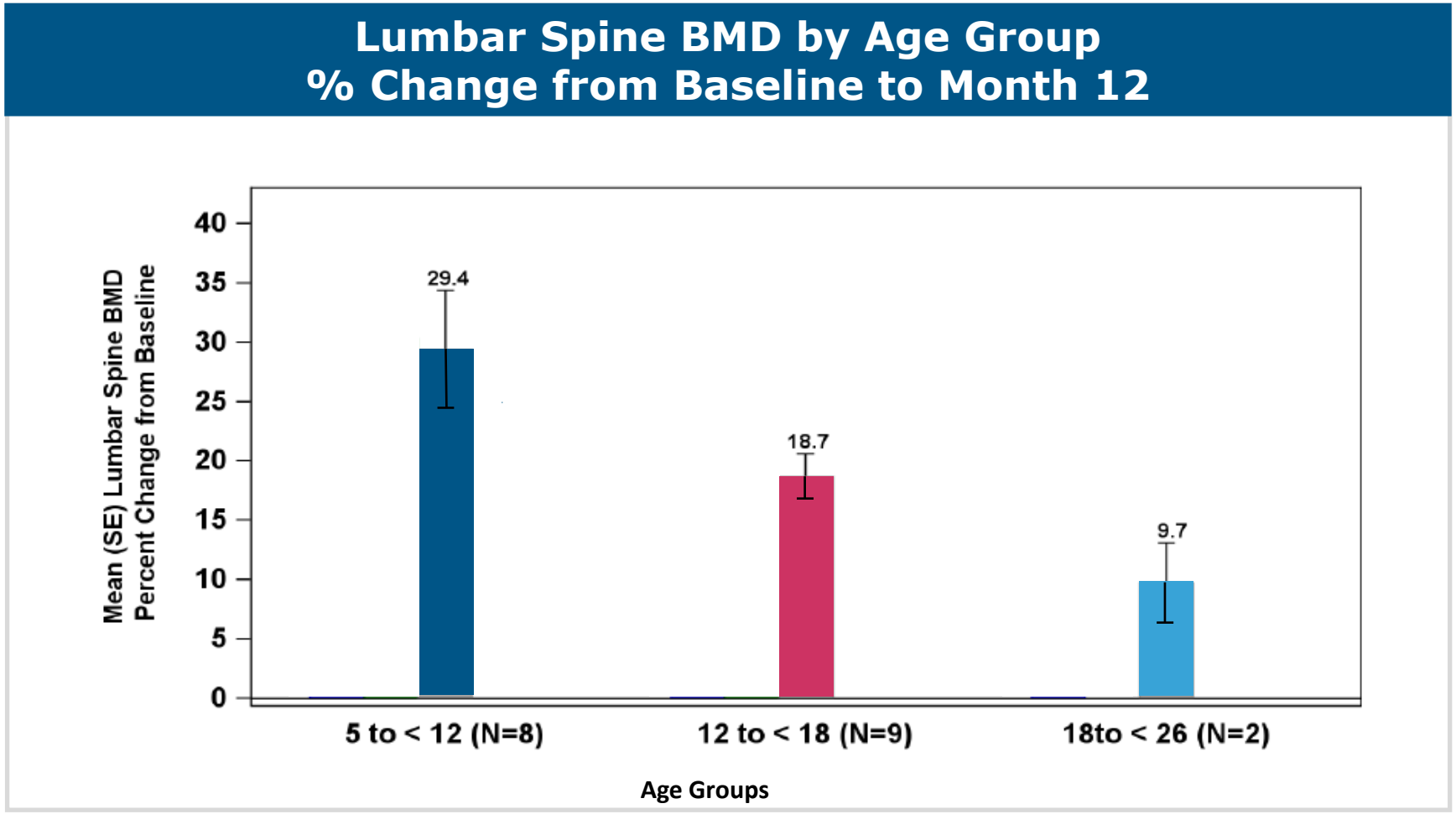
1. Data as of June 2024

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

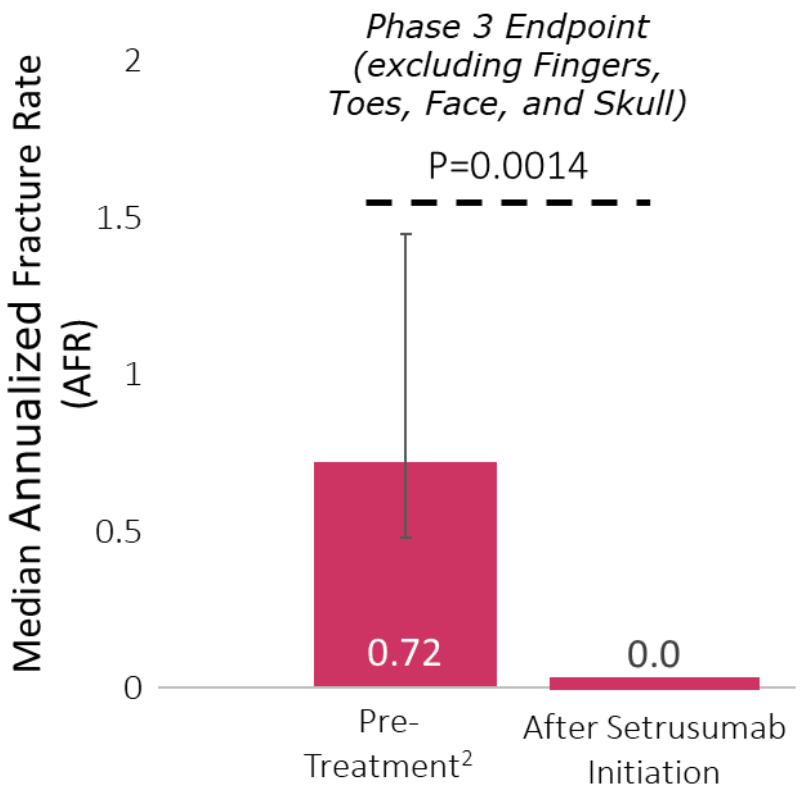


Data consistent with ASTEROID Phase 2 data in adults[2]

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

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

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

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Safety evaluation at 14 months shows setrusumab is well tolerated

No treatment-related SAEs	No unexpected adverse events or safety concerns	No subject discontinued treatment for any adverse event	No drug-related hypersensitivity reactions

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

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

*All related adverse events were mild to moderate in severity

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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* is fully enrolled

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* is fully enrolled

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

Summary of potential timing for Phase 3 readouts

Potential readout	Expected timing	Threshold
Interim Analysis 1 (IA1)*	End of 2024 or early in 2025	p<0.001
Interim Analysis 2 (IA2)*	Mid-2025	p<0.01
Final Analysis	Fourth Quarter 2025	p<0.04

Potential successful readout scenarios driven by baseline fracture variability, accumulated fracture events and p-value stringency

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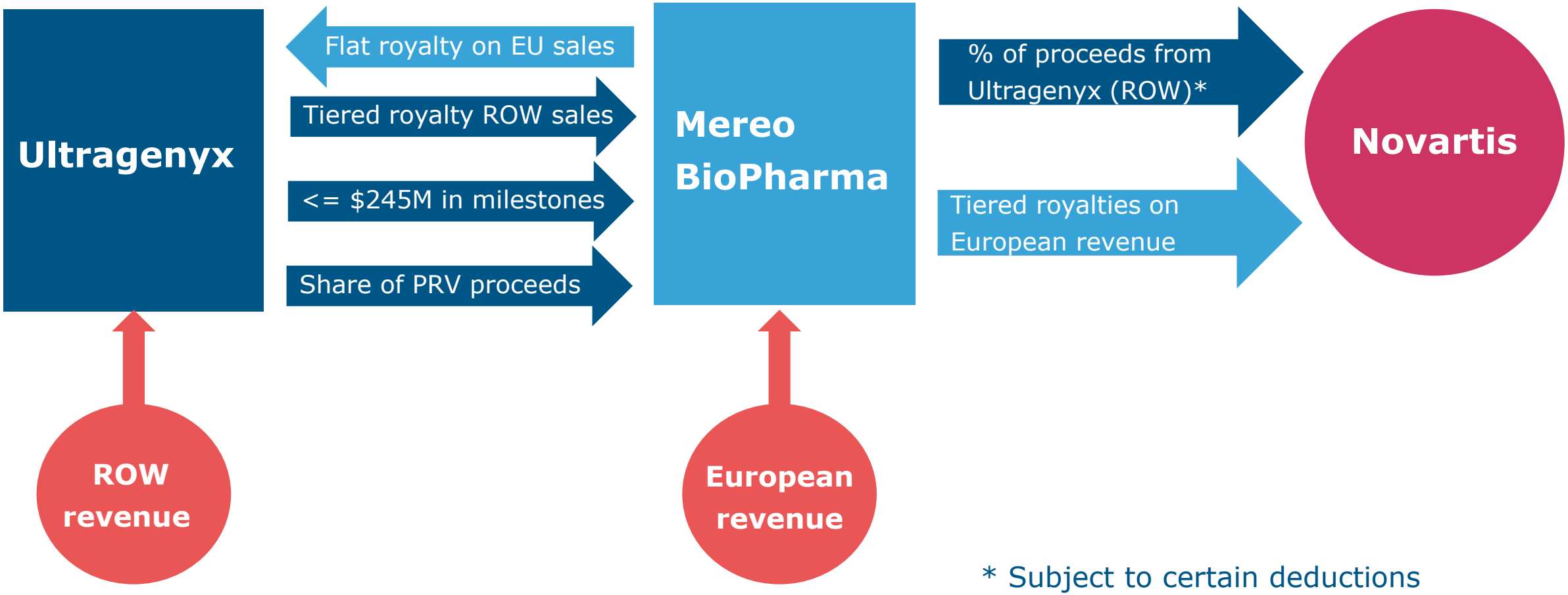
*Only if an interim analysis clears the stringent threshold, would we share that the readout was successful. Topline clinical results would be announced several months later as the study requires patients complete final visits over couple of months and time is required to collect and prepare the data for complete analysis.

The Ultragenyx partnership, a highly effective collaboration

Key terms
• Signed in December 2020 • Ultragenyx leads and funds the global development plan, including CMC • Mereo retains European rights (including UK) and Ultragenyx has 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

Ultragenyx partnership – cash flows



* Subject to certain deductions

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Critical steps toward commercialization
Navigating the EU regulatory and access pathways to unlock value across the region

Sequential process to de-risk the program and build the data sets that HTA committees and payors will require.

Regulatory/ Payor engagement

Engaged early (since 2019) and regularly with stakeholders to understand needs and expectations, including: Prime designation, EUnetHTA and MOCA Mechanism of Coordinated Access to Orphan Medicinal Products. Initial 9 countries represented at EUnetHA.

Real World Evidence

SATURN (Systematic Accumulation of Treatment practices and Utilization, Real world evidence, and Natural history data for OI). Collaborating with existing data sets and OIFE and OIF. Will provide coordinated data set across multiple treatment centers for OI across European countries, to support pricing and reimbursement decisions and scientific publications.

Understanding patients

IMPACT, the largest ever burden of disease survey on the impact of OI on patients, physicians and caregivers, data being published (www.impactsurveyoi.com). 5,000 pediatric and 5,000 adult patients who we believe could be eligible for setrusumab treatment already identified in the key 5 European markets. Scientific publications.

Market opportunity

Intensive engagement with highly networked OI specialized treating physicians indicates high level of interest in safe and effective on-label treatment. Potential relevant rare bone analog X-linked hypophosphatemia (XLH), Crysvita launched 2018/2019 in US and EU, 2023 sales $747M in North America, $256M in EMEA. 1H 2024 sales of $388M in North America and $169M in EMEA (increase of 43% versus 1H 2023).[1]

1. Kyowa Kirin Co., Ltd. Appendix to the Consolidated Financial Summary (IFRS) Fiscal 2023 (January 1, 2023 – December 31, 2023) and Fiscal 2024 Semi Annual (January 1, 2024 – June 30, 2024), respectively.

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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

Disease overview

- 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

Current treatments create high unmet need

- Currently COPD treated and lifestyle changes
- Intravenous plasma-derived augmentation therapy:
  - Clinical efficacy not uniformly recognized
  - IV administration burden
  - Optimal dose uncertain
  - Not uniform access across US and EU and early-stage patients

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 therapy

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 – 16 clinical trials in ~2,000 subjects

- **Phase 1 (6 studies)**
  - Safety, PK and pharmacodynamics support safety and dose-decisions
- **Phase 2 (9 completed, 1 ongoing)**, efficacy from respiratory disorders of Neutrophil Elastase/Anti-Elastase imbalance:
  - **COPD** (2 studies, n~1,500): In one study (n=615) a >100ml increase in FEV_1 observed in bronchitic subset (n~200, p< 0.01)[1]
  - **Bronchiectasis** (n=38): >100ml increase in FEV_1 (p= 0.006); numerical improvement St. George's Respiratory Questionnaire (SGRQ)[2]
  - **Cystic Fibrosis** (n=55): Reduction markers of lung damage (desmosine) p<0.05)[3]
  - **Hospitalized COVID-19** (n=15): Faster 5-day clinical improvement in WHO severity scale[4]
  - **Bronchiolitis Obliterans Syndrome** (ongoing, n=13): Improvement biomarkers of lung damage and fibrosis, with signal of FEV1 stabilization)[5]

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
#MCID of > 4 points reached, but high variability and statistical significance not reached

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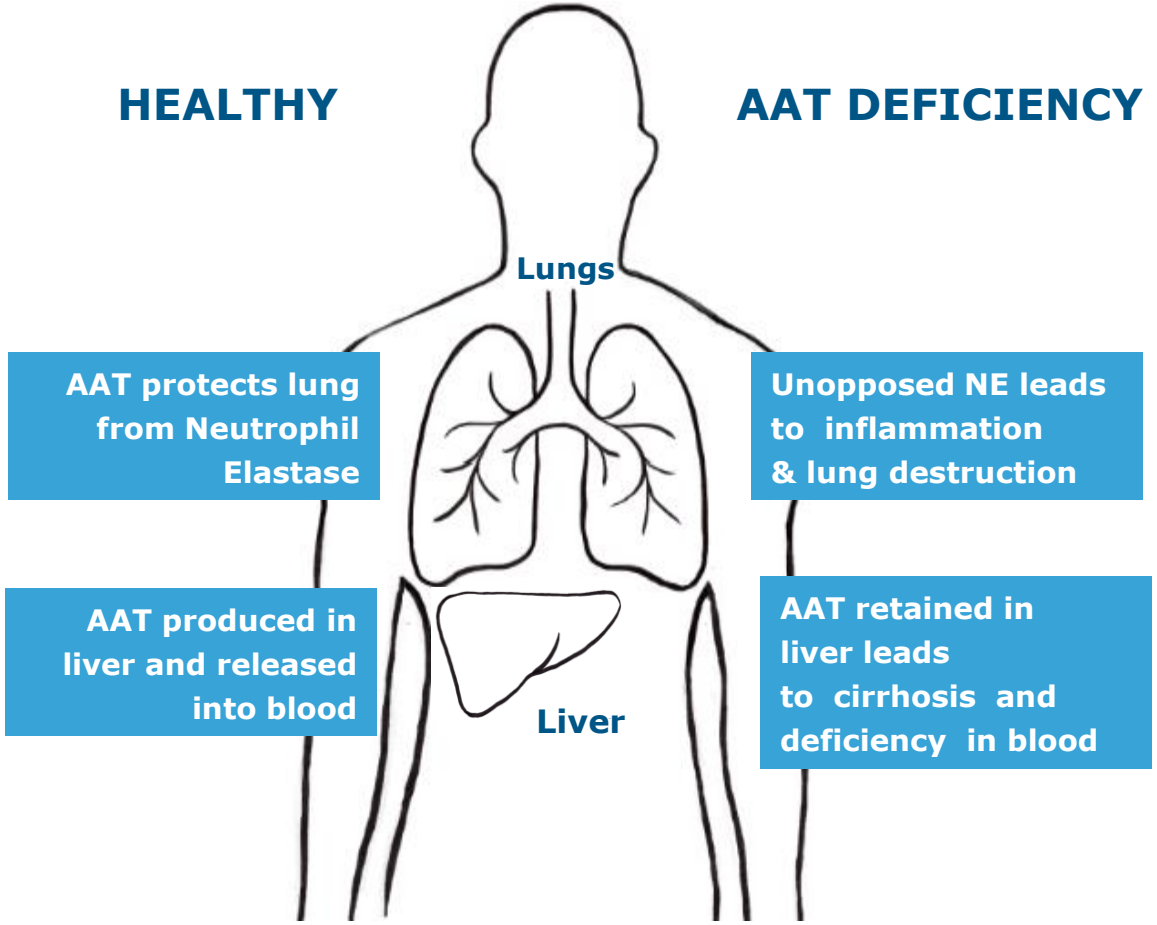
1. Kuna et al Resp. Med 2012; 106:531 supplement; 2. Stockley et al Resp Med 2013;107:524; 3. Elborn et al Eur Resp J 2012; 40:969; 4. Mereo R&D Update March 14 2022; 5. Im et al Blood 2021:138, Supplement 1 1815

AATD – Progressive lung disease driven by Neutrophil Elastase



Alvelestat an Oral Neutrophil Elastase (NE) Inhibitor

- Targets the cause of lung damage
- Potential to treat early stages of lung disease to delay progression

Potential efficacy advantage

- Sustained NE suppression and 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 impairments
- 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

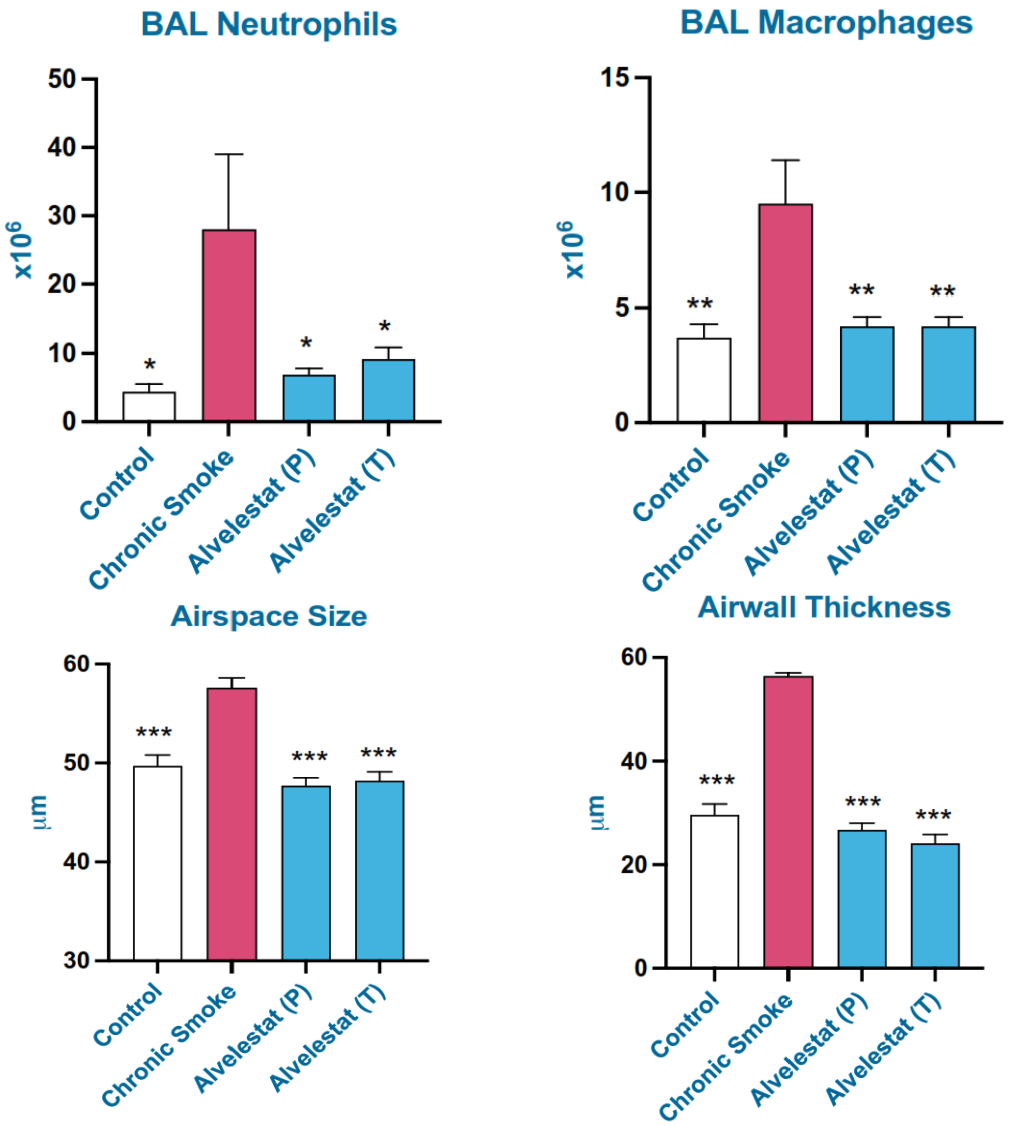
Alvelestat is highly effective in an Animal Model of AATD Lung Disease

Six-month Chronic Smoke (CS)-exposed guinea-pig model of AATD emphysema[1]

- CS inactivates AAT
- Progressive inflammation, airspace enlargement and airway remodeling

At clinically relevant doses, alvelestat, prophylactically (P) and therapeutically (T), completely prevented[2]

- Increases in lavage neutrophils and macrophages
- Airspace enlargement (emphysema) and small airway remodeling



*p<0.03, **p<0.002, ***p<0.001

1.Alam and Mahadeva. Chapter 11. Animal Models of Alpha-1 Antitrypsin Deficiency 2017
2.Stevens et al JPET 339:313–320, 2011

Two Phase 2 studies in AATD-Lung Disease completed across different populations

ASTRAEUS
NCT03636347
12 weeks
N=99

- Placebo bid
- Alvelestat 120 mg bid
- Alvelestat 240 mg bid

Enrolled PI*ZZ patients

No subjects on augmentation
Patients with established disease
Baseline scores (median):
FEV_1 - 59%
*SGRQ total score – 32.2
SGRQ activity – 53.3

Investigator-led study – Mark Dransfield, University of Alabama at Birmingham

ATALANTa
NCT03679598
12 weeks
N=63

- Placebo bid
- Alvelestat 120 mg bid

Enrolled PI*ZZ, PI*SZ and PI*Null patients

~Half of subjects not on augmentation
Patients earlier in their disease process
Baseline scores (median):
FEV_1 – 89%
SGRQ total score – 19.6
SGRQ activity – 25.5

THE UNIVERSITY OF ALABAMA AT BIRMINGHAM
NIH National Center for Advancing Translational Sciences
Funded by NCATS
ALPHA-1 FOUNDATION
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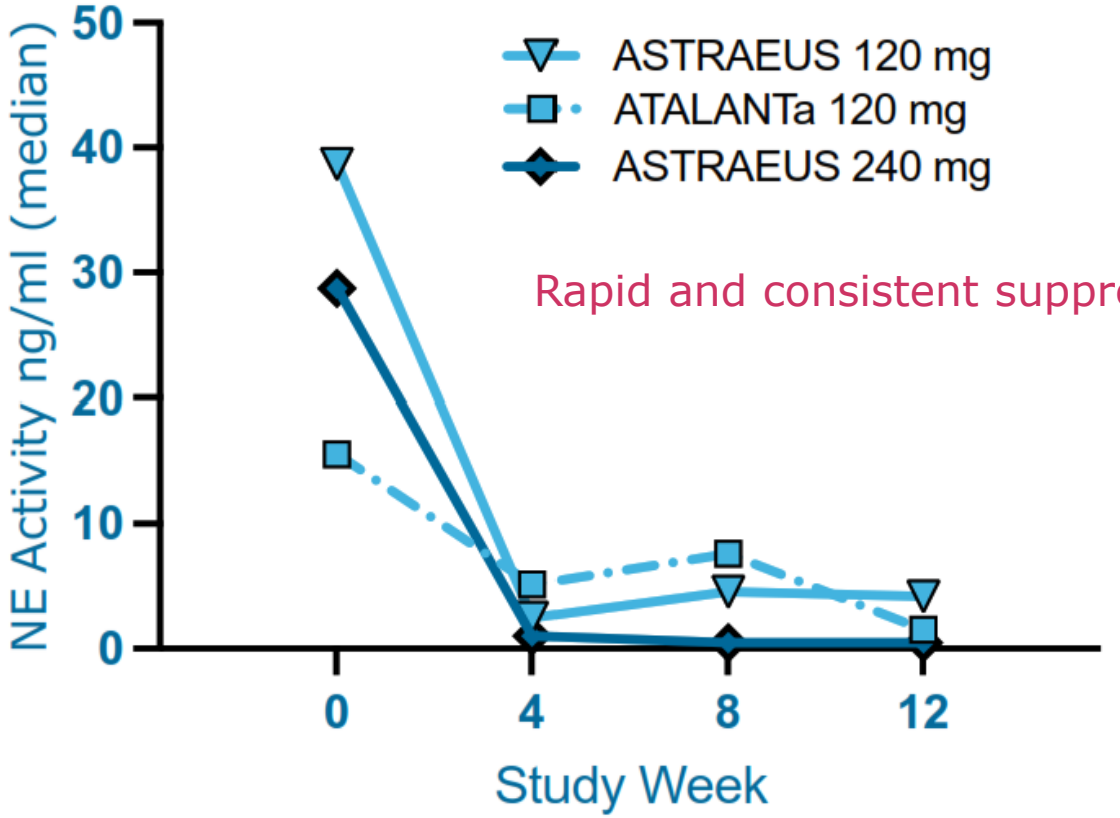
*SGRQ scores out of 100, lower SGRQ scores equate to better status

Alvelestat suppression of Blood Neutrophil Elastase Activity



Rapid and consistent suppression with dose response

- 120 mg reduction at week 12 ASTRAEUS p<0.05 (vs placebo)
- 240 mg reduction at week 12 ASTRAEUS <0.001 (vs placebo)
- 240 mg met target > 90% NE suppression in blood

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Biomarkers and PK modelling confirm 240 mg dose for progression

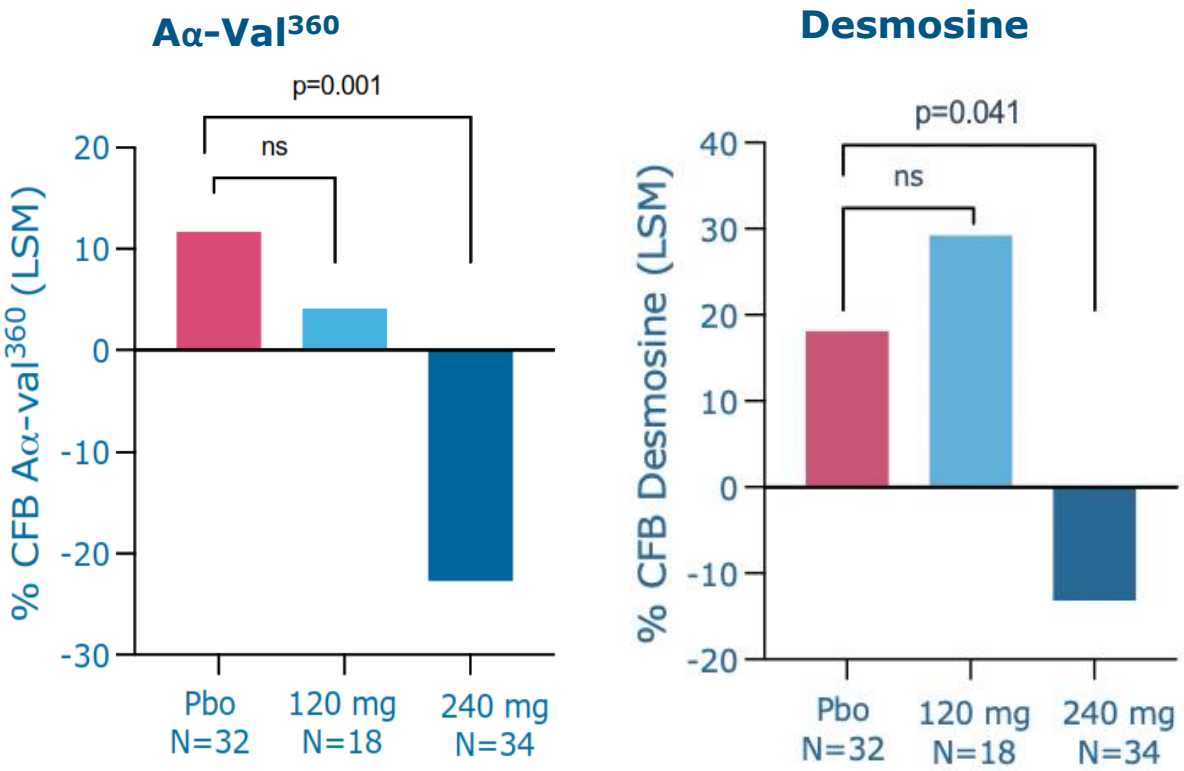
ASTRAEUS

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

ASTRAEUS (Primary Endpoints)



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

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Safety data from two AATD Phase 2 studies, builds on extensive safety database

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

Adverse Events of Special Interest

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

Adverse events

- Headache was most frequent adverse event, generally mild or moderate and resolving on continued dosing. 3 cases reported as SAEs (240 mg)

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

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Outcome of End-of-Phase 2 and Type C meetings

Phase 3 design

- End-of-Phase 2 meeting with FDA and scientific advice (EMA) to discuss endpoints for Phase 3 registrational trial
  - Subsequent Type C meeting held with the FDA and DCOA*
  - Additional communications following Type C meeting
- SGRQ Total (FDA) and CT-density (EMA) independent primary endpoints
  - For FDA "functional assessment" as key secondary
  - CT – EMA has indicated P<0.1 may be acceptable for approval
- Single study with enrollment of ~220 patients for up to 18 months – PI*ZZ patients with emphysema for full approval
  - Initial qualitative validation study completed to support use of SGRQ in AATD
- Primary endpoints supported by ATALANTa and ASTRAEUS Phase 2 data for SGRQ including biomarker responders and significant correlation of desmosine with CT-density

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*Division of Clinical Outcome Assessment

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 = Activity, Symptoms and Impacts domains
  - Activity domain most impacted in patients with AATD
- Potential tool for "feels and functions" endpoints required by the FDA for registrational trials in AATD
- In AATD studies, **SGRQ Total score** has been shown to deteriorate ~ 1 point per annum[1]
- Phase 2 studies demonstrated a consistent association between the effects of alvelestat (biomarker reductions) and improvement in SGRQ (Total score and Activity Domain)[2,3]
- Effect also observed for the COPD Assessment Test (CAT), another validated patient-reported quality of life tool
- ATALANTa study – greater effect in SGRQ (Total score and Activity domain) 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
3. Fettiplace. Am J Respir Crit Care Med 2024;209:A3298

Earlier stage lung disease patients show greater SGRQ response

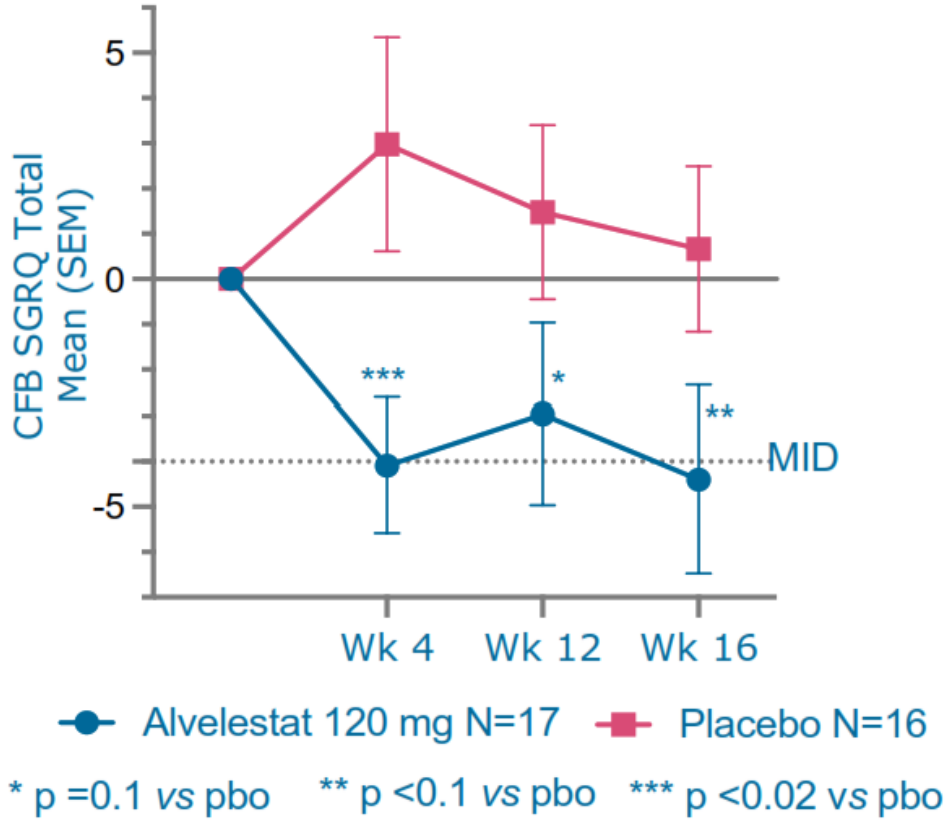
- ATALANTa study – Non-augmentation subgroup (median FEV_1 89.3%). Between group changes at week 12:
  - **SGRQ Total** = 4.7-point improvement (p=0.10)
  - **SGRQ Activity** = 10.0-point improvement (p=0.01)
- Post hoc analysis of ASTRAEUS and **SGRQ Total** change shows earlier stage patients also had the greatest improvement

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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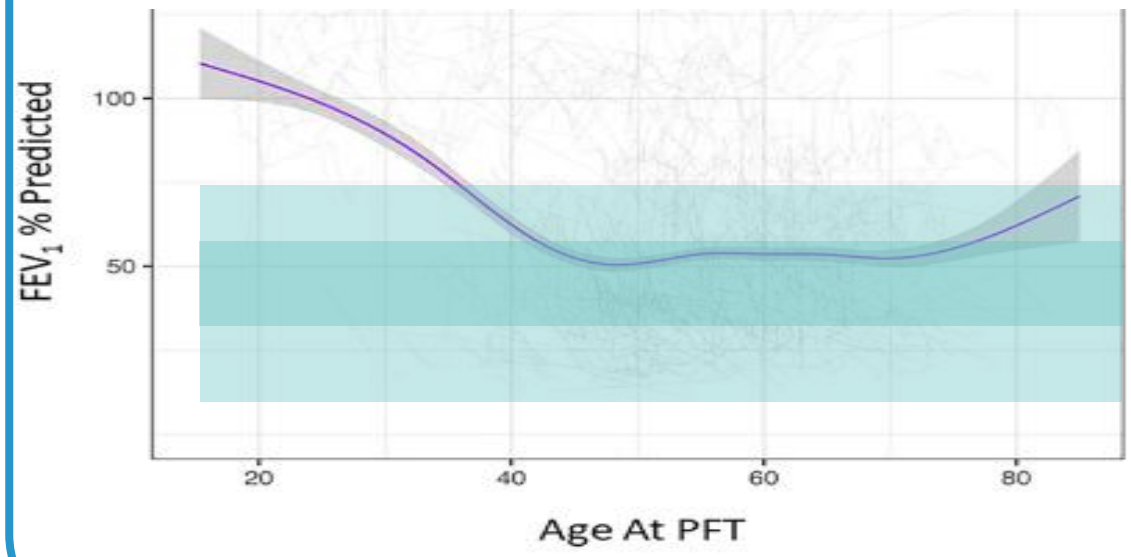
Historical augmentation studies

Limited to FEV_1 <70% or <80%
(Average FEV_1 in RAPID, EXACTLE ~50%)

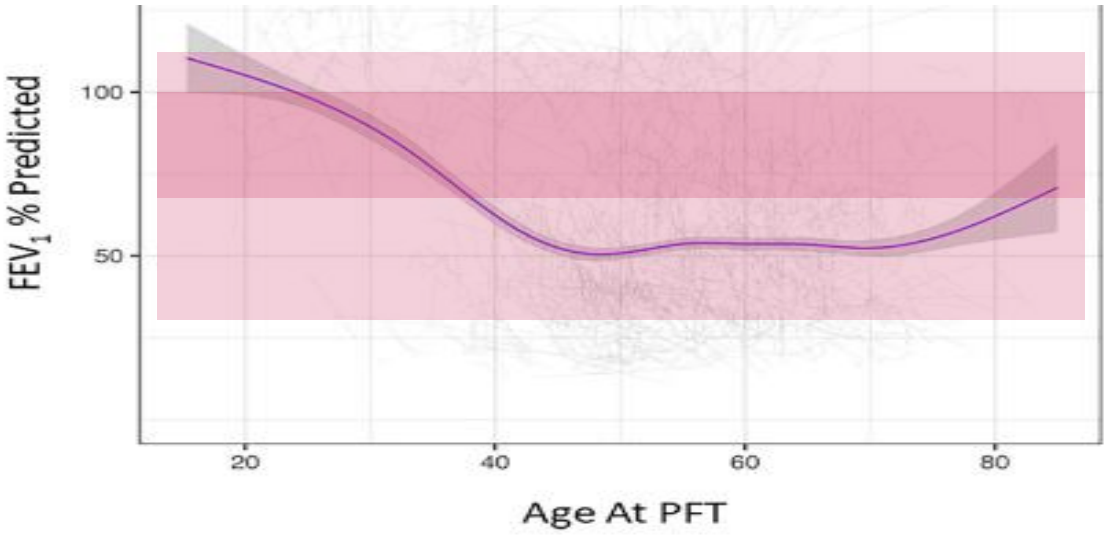
- Patients earlier in their disease not eligible
- Intervening later may limit impact



Mereo's approach to Phase 3

No upper FEV_1 limit

- FEV_1 – weighting towards patients >75%
- More patients eligible, including those not eligible for augmentation therapy
- Intervening earlier may have greater impact



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PFT = Pulmonary function testing

Graphs adapted from Fraughen et al, Am J Resp Crit Care Med 2023 Nov 1;208(9):964-974. Reprinted with permission of the American Thoracic Society.

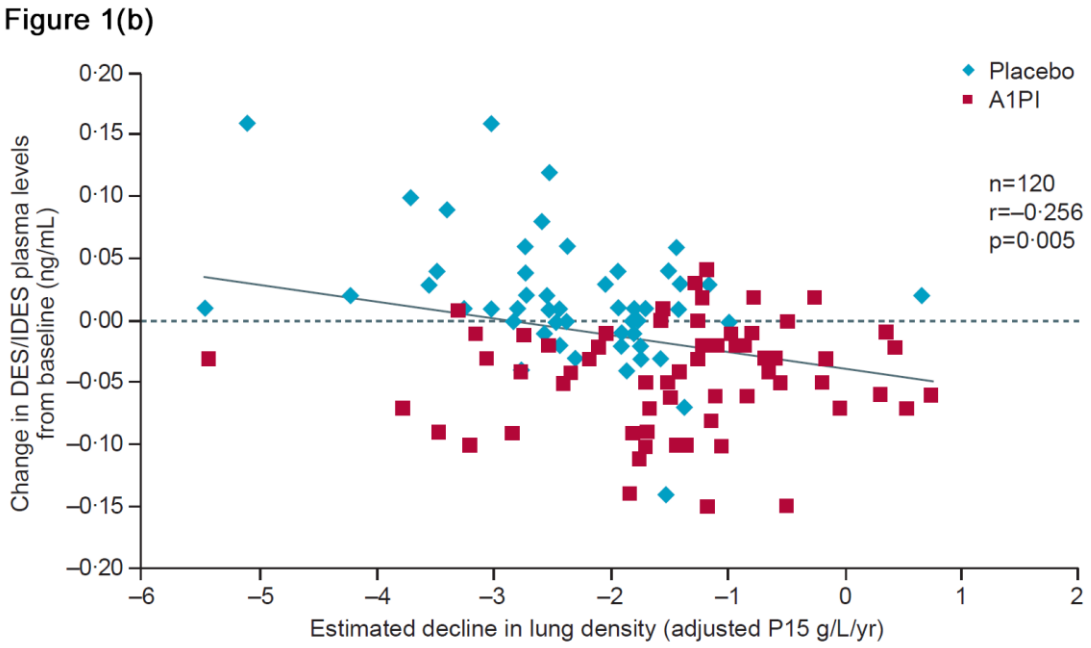
Copyright © 2024 American Thoracic Society. All rights reserved. Showing FEV_1 decline over time in 615 AATD patients

Translating desmosine changes (elastin) to CT efficacy endpoint

		Augmentation therapy[1]	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]

Significant correlation of desmosine reduction 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

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Development strategy for Phase 3 registrational trial

Clinical data	Earlier stage severe PI*ZZ patients observed to have greater response in SGRQ Total and Activity scores Literature indicates 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 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

Broader population maximizes potential for clinical and commercial success

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Other programs, milestones and financials

Key milestones for core programs

Product candidate	2023		2024		2025		Next milestone
	H1	H2	H1	H2	H1	H2	
Setrusumab	Phase 2 Orbit (5 - <26 yrs old) **OLE**						
OI		Phase 3 Orbit (5 - 25 yrs old)					Phase 3 Interim analysis
		Phase 3 Cosmic (2 - <7 yrs old)					Phase 3 Interim analysis
Alvelestat	ASTRAEUS						Potential partnering, Phase 3 initiation
AATD-LD	Phase 2 ATALANTa						Medical conferences
BOS*	Phase 1b		Phase 2				BOS: Phase 2 data

*Bronchiolitis Obliterans Syndrome

Other programs

Other current partnerships

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

- 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

Partnering opportunities

Etigilimab – anti-TIGIT which has completed a Phase 1b basket study in a range of rare tumor types in combination with nivolumab. It is currently in a Phase 1b/2 investigator led study at the MD Anderson in clear cell ovarian cancer in combination with nivolumab, which has been expanded from the initial 10 patients to 20 patients. This study is funded by the Focus Fund.

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

Financial highlights

Cash runway into 2027
$80.5 million as of
September 30, 2024

Cap Table *(September 2024)*	**ADSs** *(in thousands)*
Shareholders > 2% holding	86,026
Shareholders < 2% holding	68,709
Share capital – Issued and outstanding as of September 30, 2024[1]	**154,734**
Potential Future Dilution:	
Warrants[2]	1,401
Convertible loan notes	3,421
Employee share schemes[3]	11,028

1 *ADS equivalents of 773,672,299 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.*

Source: Shareholding based on the 13G & 13F filings (as of June 30, 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.

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APPENDIX

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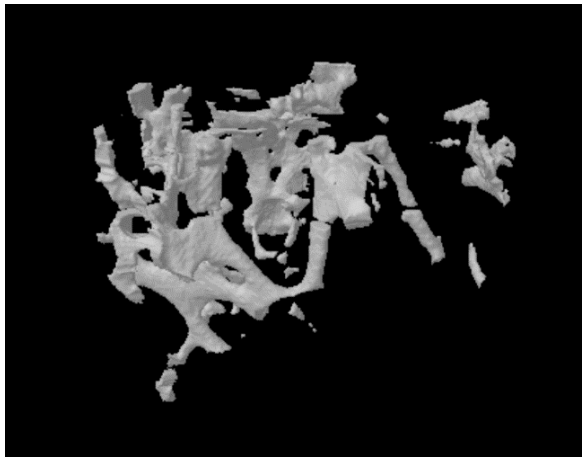
Setrusumab (BPS-804)

Mouse models and HR-pQCT

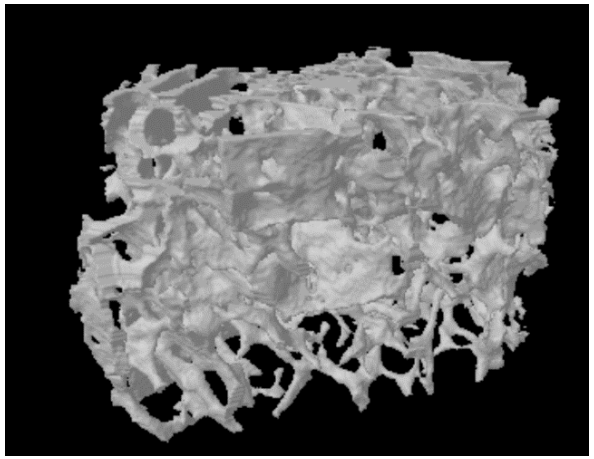
Rare Disease Day
February 2023

Brittle mouse model (Brtl/+)– treatment with BPS-804 (setrusumab)

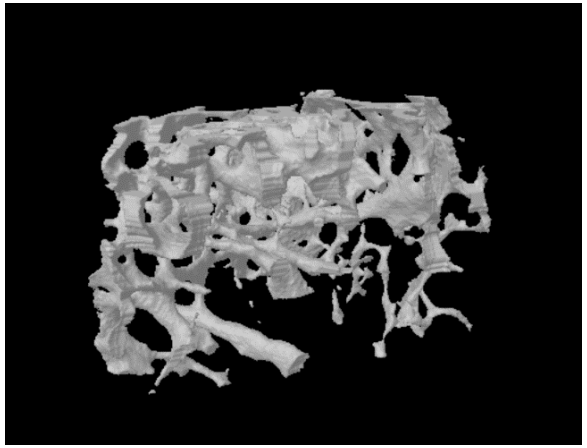
Mature Btrl control



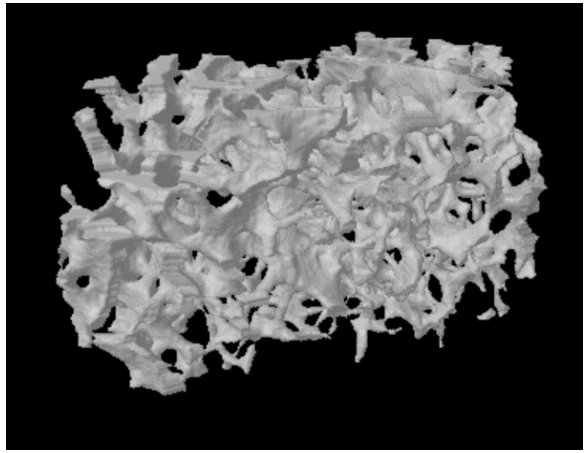
Mature WT Control



Mature Brtl treated



Mature WT Treated



Brtl – brittle mouse model

WT – wild type

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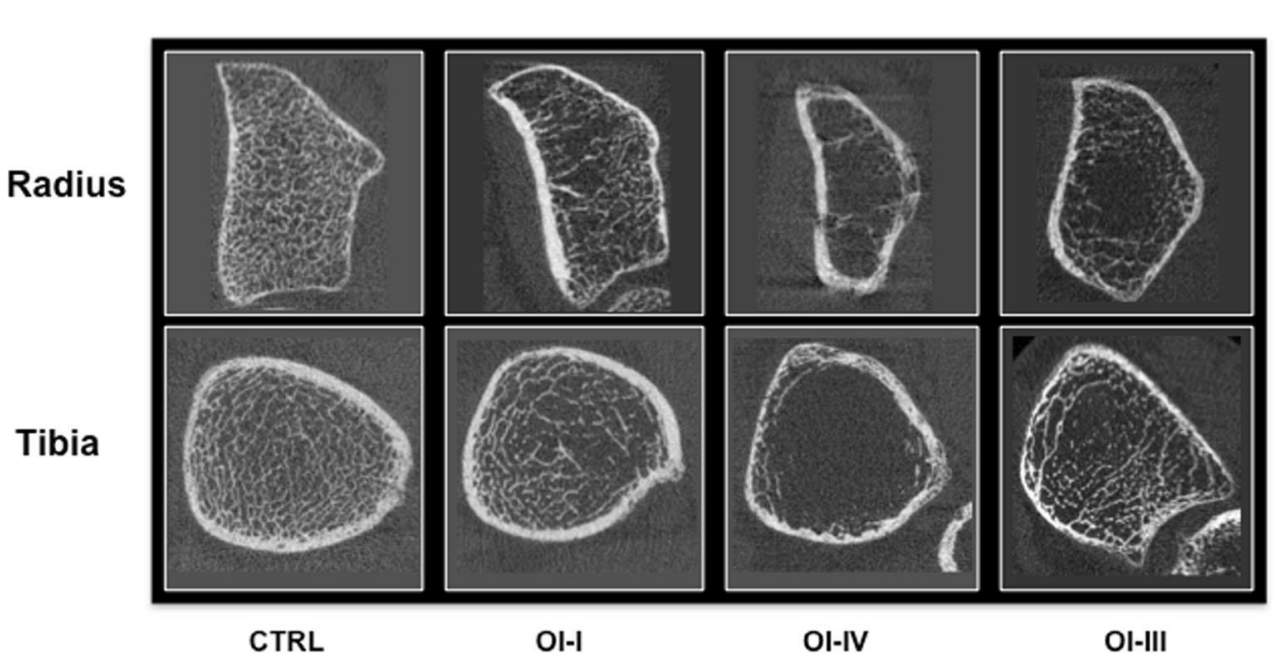
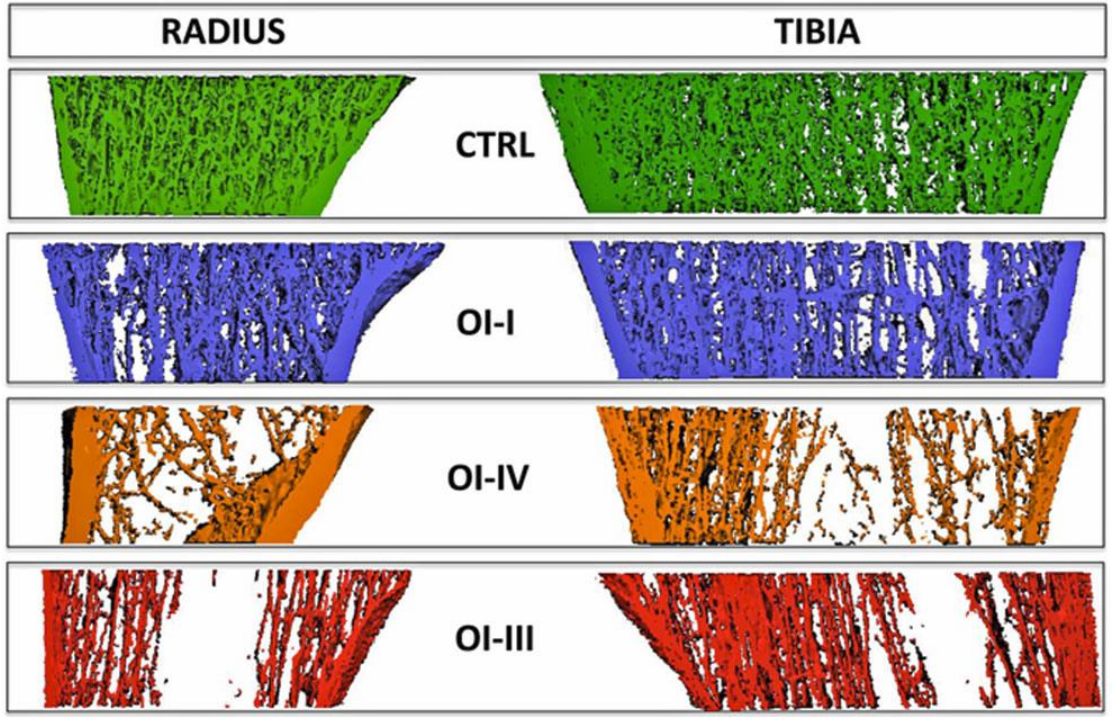
HR-pQCT scans of patients with OI and controls





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The OFLEY STUDY and HR-pQCT

- Prospective study investigating the prediction of fracture (Fx) by bone microarchitecture assessed by HR-pQCT in postmenopausal women
- HR-pQCT used to measure microarchitecture at the distal radius and tibia in 589 women (mean 68 years old)
- During 9 year follow up 135 women sustained a fracture including 81 women with a major osteoporotic fracture
- After adjusting for age, women who had fractures had significantly lower total and trabecular volumetric densities (vBMD) at both sites as determined by HR-pQCT
- OI patients have fewer and thinner trabeculae and increased cortical porosity

Bone Microarchitecture Assessed by HR-pQCT as Predictor of Fracture Risk in Postmenopausal Women Sornay-Rendu et al JBMR March 09 2017

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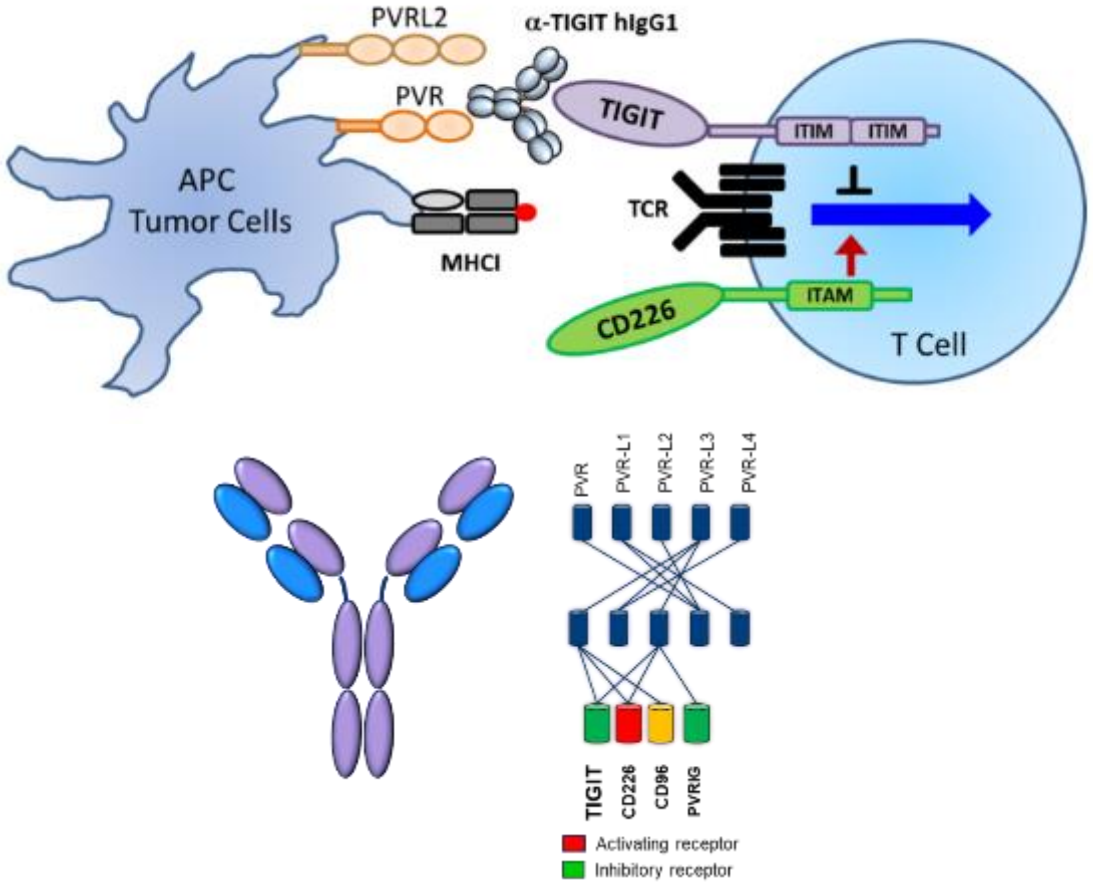
Etigilimab (MPH313)

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



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%)

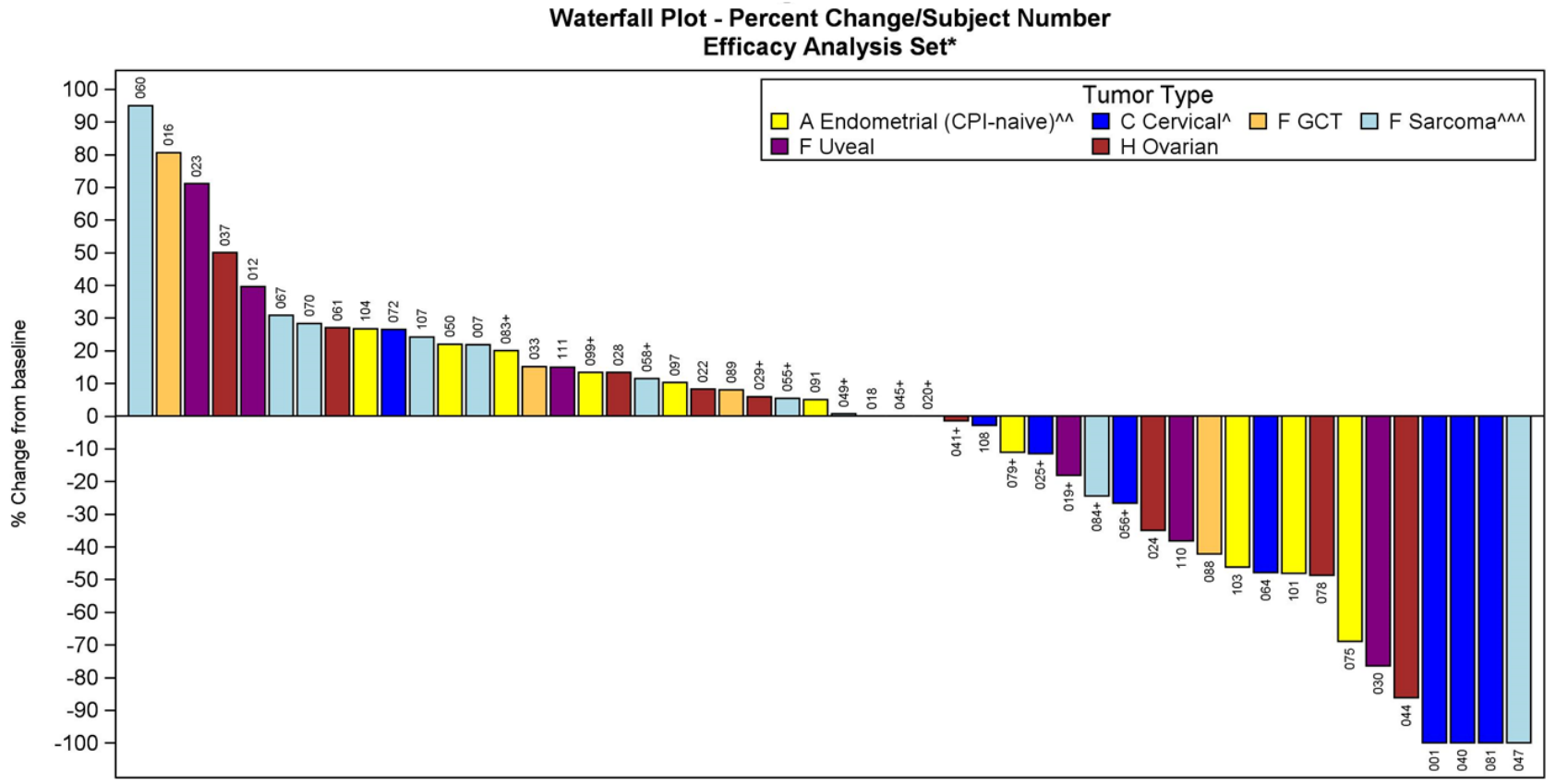
All responses confirmed

*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

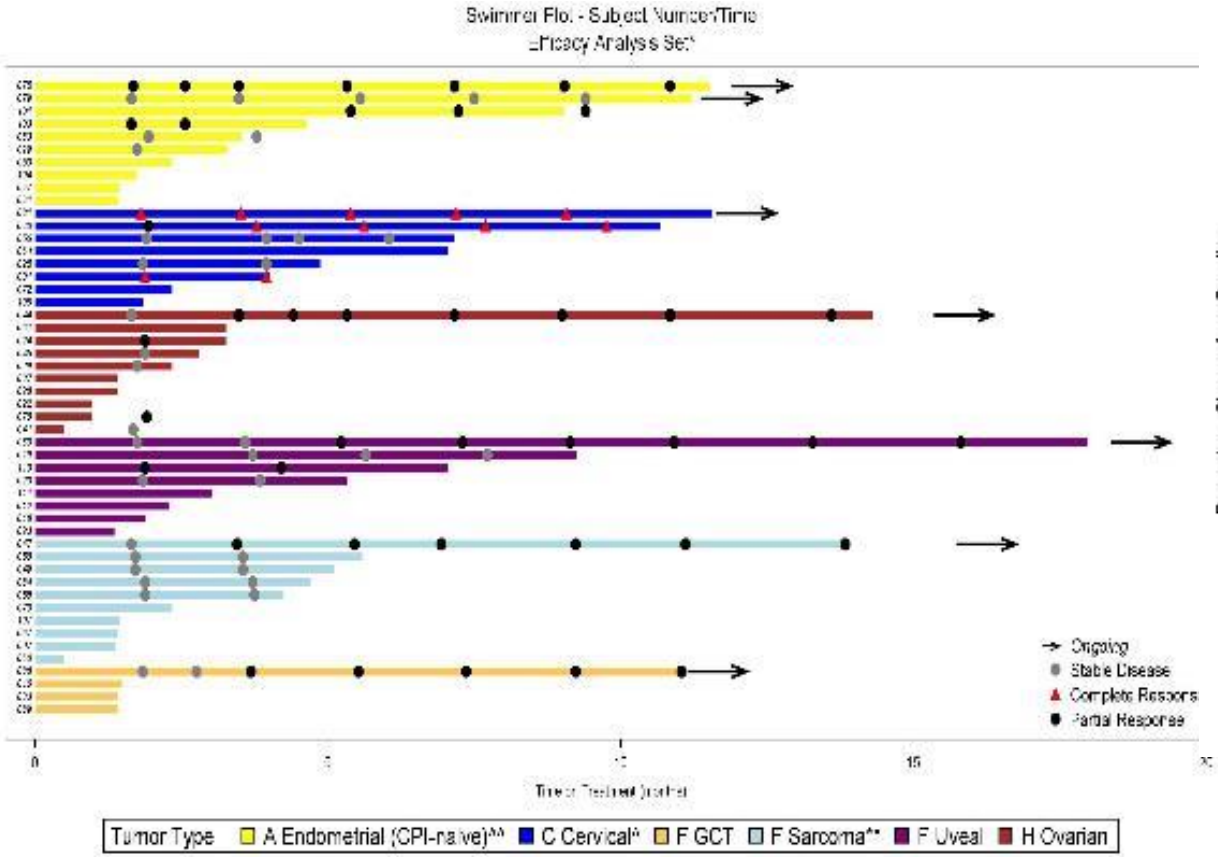
Central lab PD-L1 CPS % for ORR pts: F088 germ cell=0; F047 sarcoma=1; F030 uveal=0; A075 endometrial=3; A103 endometrial=3; G101 endometrial=3; C081 cervical=51; C040=20; C001 cervical and F110 uveal had no tissue for central lab; pathology report for C001 indicated >90%.

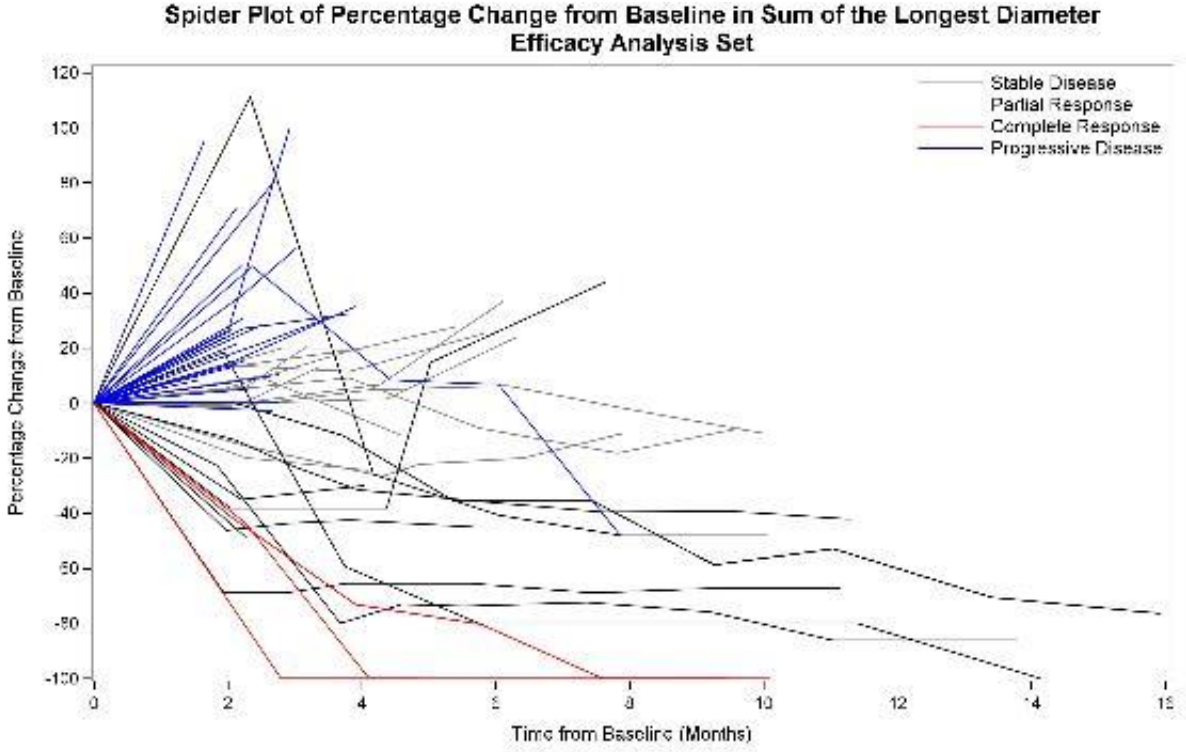
ACTIVATE efficacy data: select cohorts (continued)



^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)



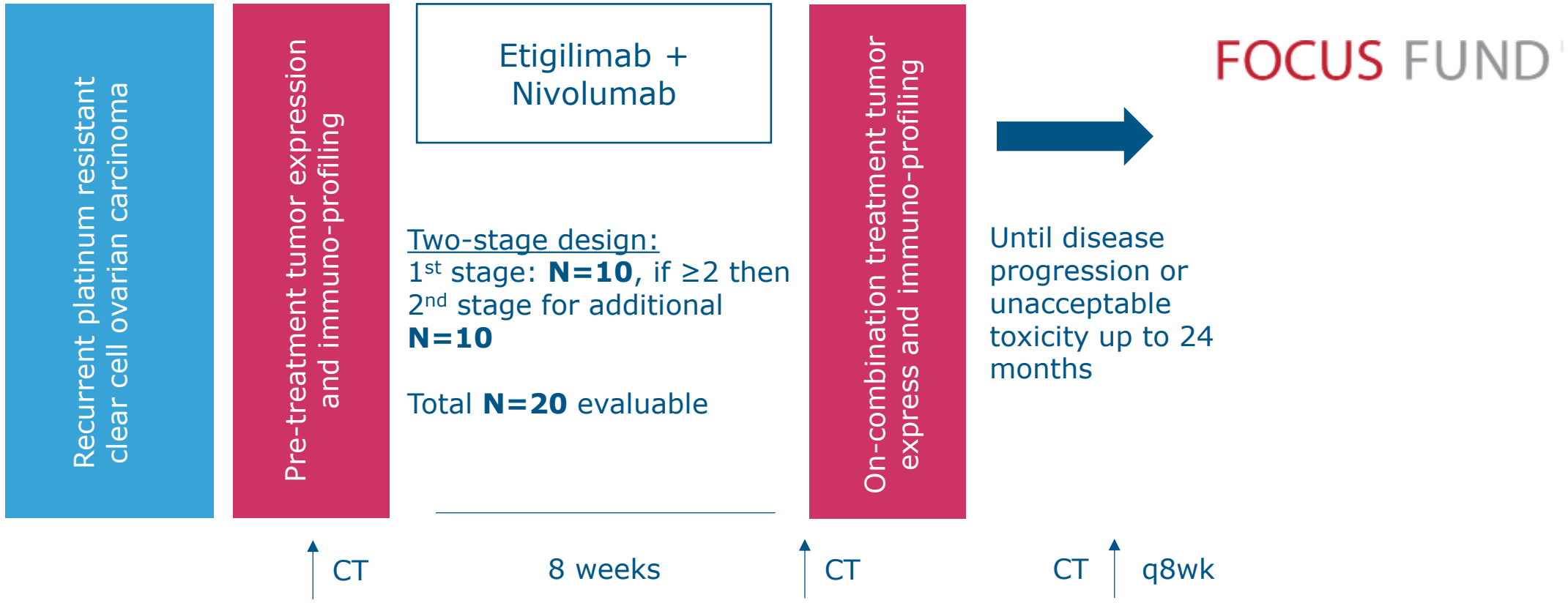


" Sarcoma subjects only include those with De-differentiated liposarcoma
^Cervical cancer patient (E025) enrolled in TMB-H cohort with PDL-1 CPS>1%
^^Endometrial cancer – CPI naïve patient (G101) enrolled in post-CPI cohort
Note E025 death unrelated to study drug or PD. C001 consent withdrew
Central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

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*Clinical Trial Identifier NCT05715216

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