

# Corporate presentation

October 2024



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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



## 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



# 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

- \$87.5 million of cash and cash equivalents as of June 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 leflutroazole 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	
<b>Setrusumab</b>  Osteogenesis Imperfecta		Orbit (5 -25 yrs old)  Cosmic (2 - <7 yrs old)		Orphan drug designation in US and EU, PRIME (EU), BTD (US) Pediatric disease Priority Review Voucher designation
<b>Alvelestat*</b>  AATD-Lung Disease  Bronchiolitis Obliterans Syndrome**			   	Orphan drug designation (US), Fast track designation (US)



*"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



OIFE Topical  
Meeting  
June 2023

# A rare genetic bone condition with a high unmet need

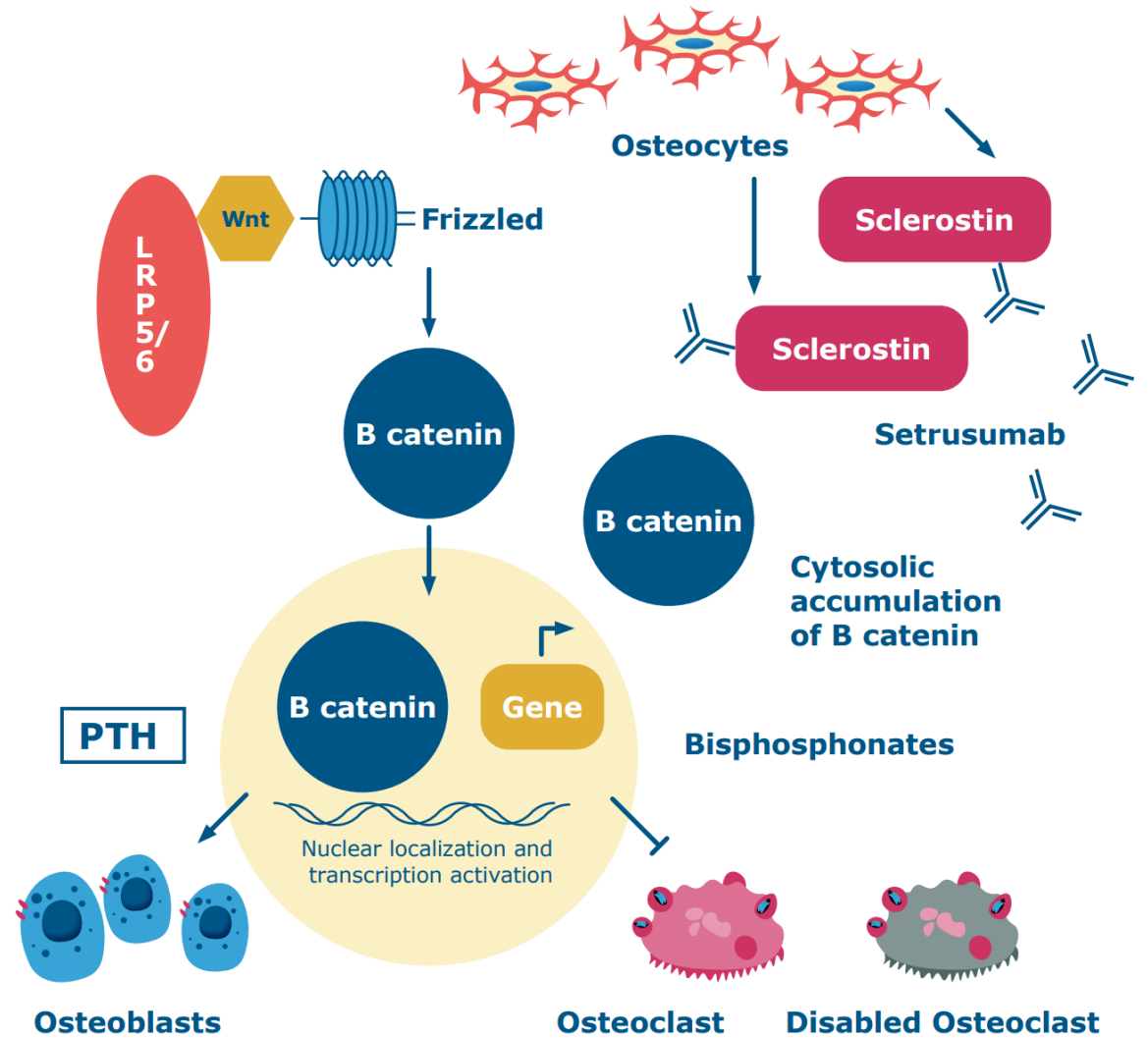
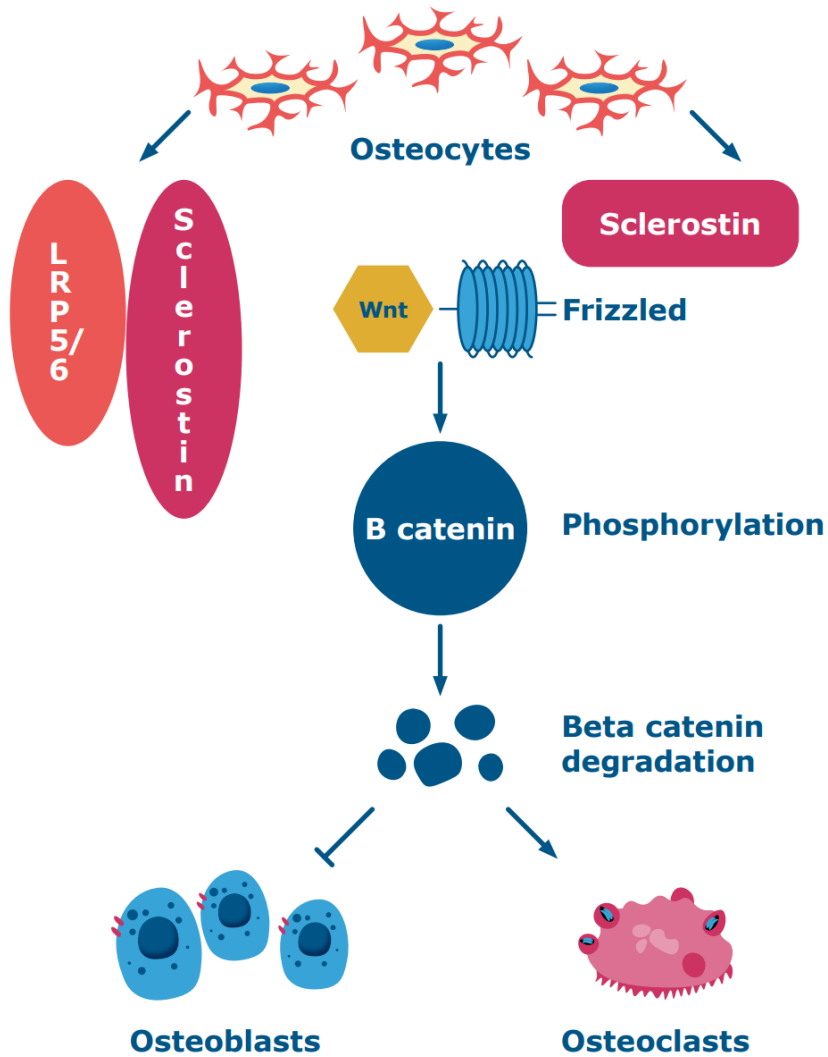
## Osteogenesis Imperfecta

- 80-90% linked to a mutation in Type I collagen<sup>1,2</sup> (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

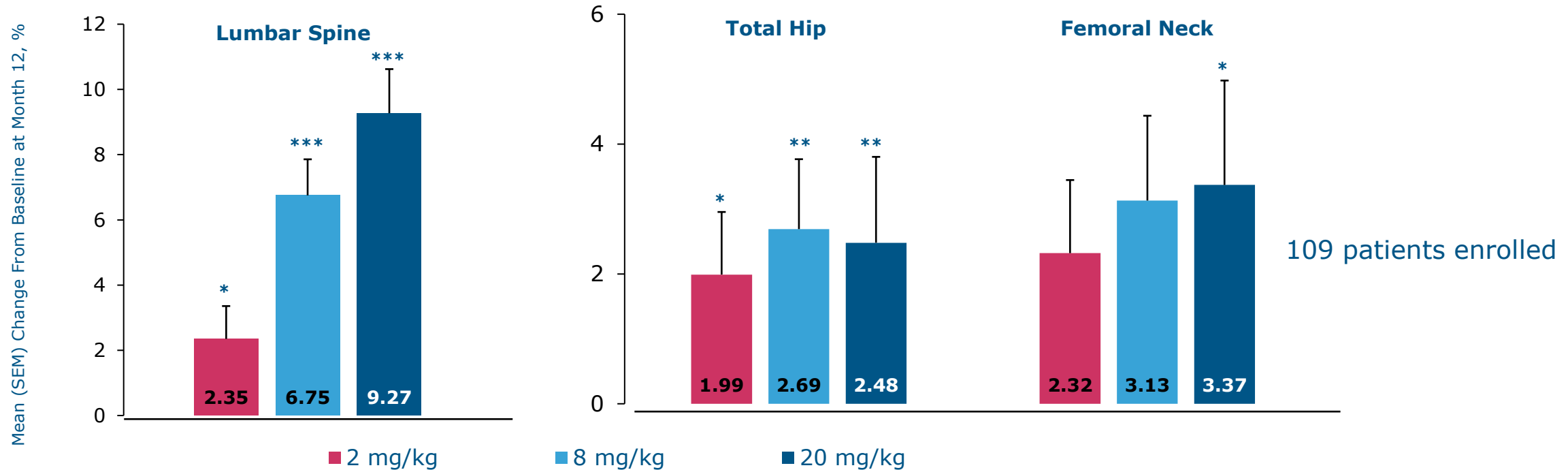
- Affects approximately 60,000 individuals<sup>3</sup> (pediatrics and adults) in the US and Europe
- Well-established Community groups (OIFE + national members and OIF)\* are a key source of support and valued resource
- OI is a progressive condition, without clear care pathways, especially for adult patients
- Potential market opportunity of >\$1Bn<sup>4</sup>

# Setrusumab – Mechanism of Action



# 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

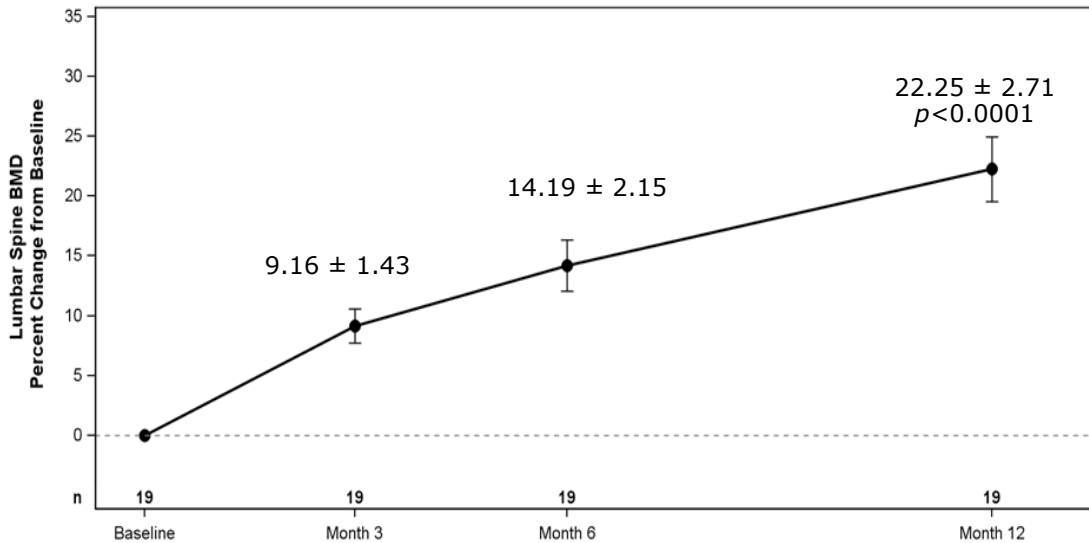


\* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$  vs baseline based on an ANCOVA model with baseline values, treatment group and OI type as covariates. ANCOVA, analysis of covariance; BMD, bone mineral density; DXA, dual-energy X-ray absorptiometry; OI, osteogenesis imperfecta; SEM, standard error 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).

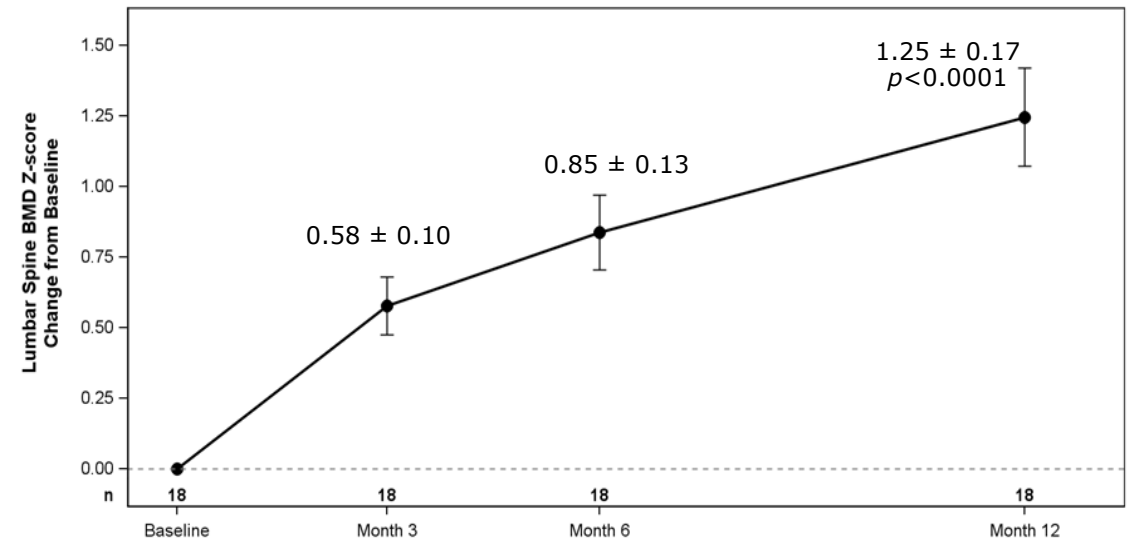
# Orbit Phase 2 – BMD and Z-score mean increase through month 12<sup>1</sup>

## Improvements consistent across all OI Types studied

### Lumbar Spine BMD<sup>1</sup> % Change from Baseline

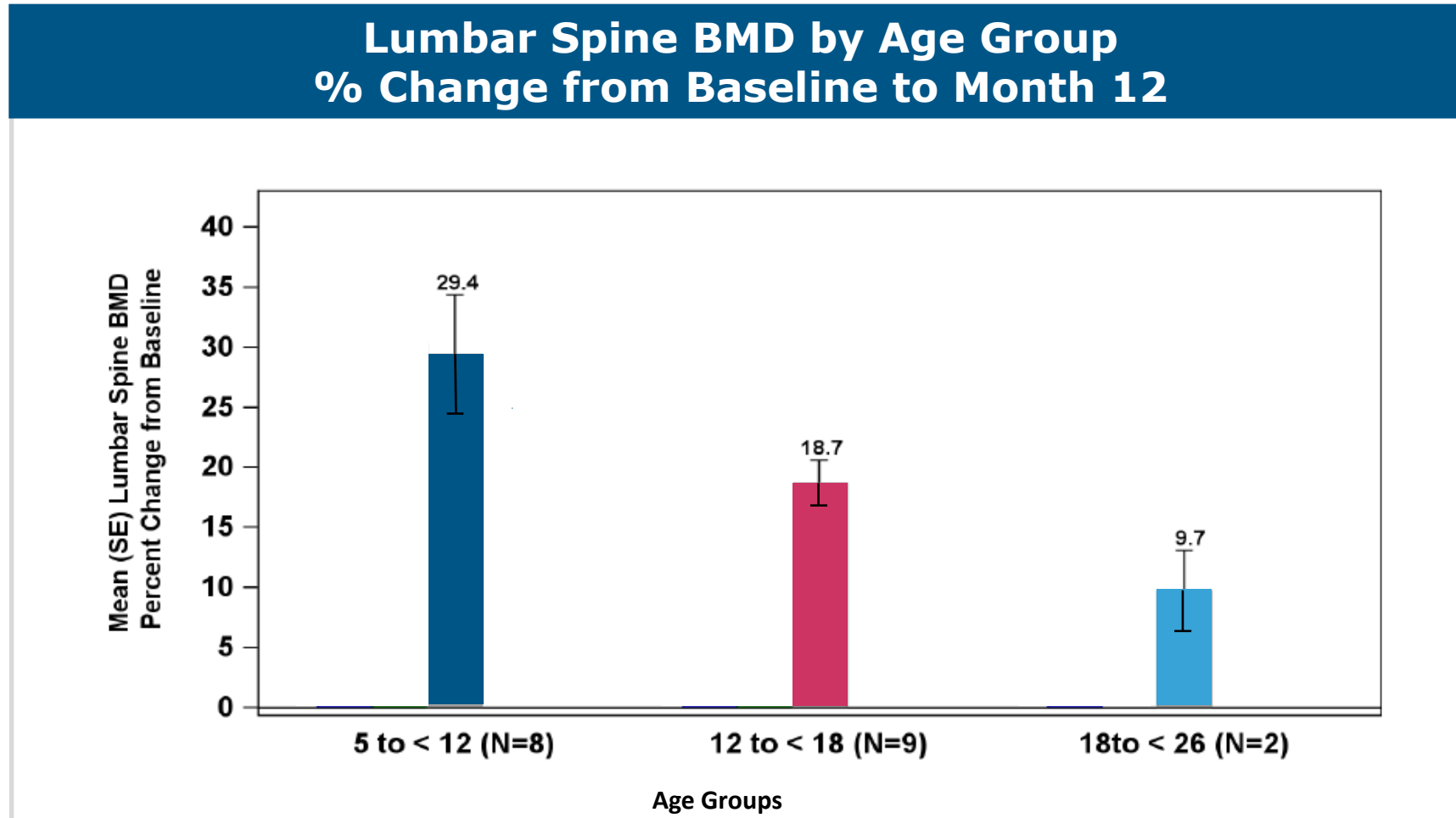


### Lumbar Spine BMD<sup>1</sup> Z-Score Change from Baseline



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)

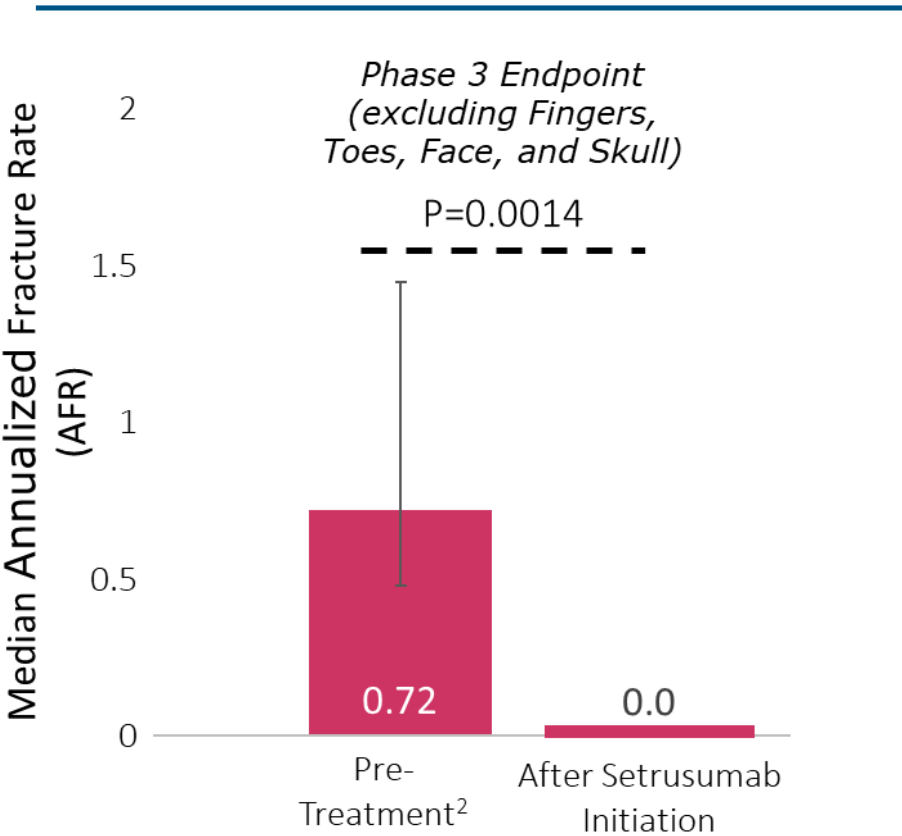
# Orbit Phase 2 – increase in BMD observed in all age groups,<sup>1,2</sup> Greatest increase in patients 5-12 years of age



Data consistent with  
ASTEROID Phase 2  
data in adults<sup>2</sup>

# 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<sup>1</sup>



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

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\*<sup>1</sup>

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

\*All related adverse events were mild to moderate in severity



# Orbit 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 ( $\leq 3$  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** (excludes fingers, toes, face and skull).

# 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 ( $\leq 3$  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.

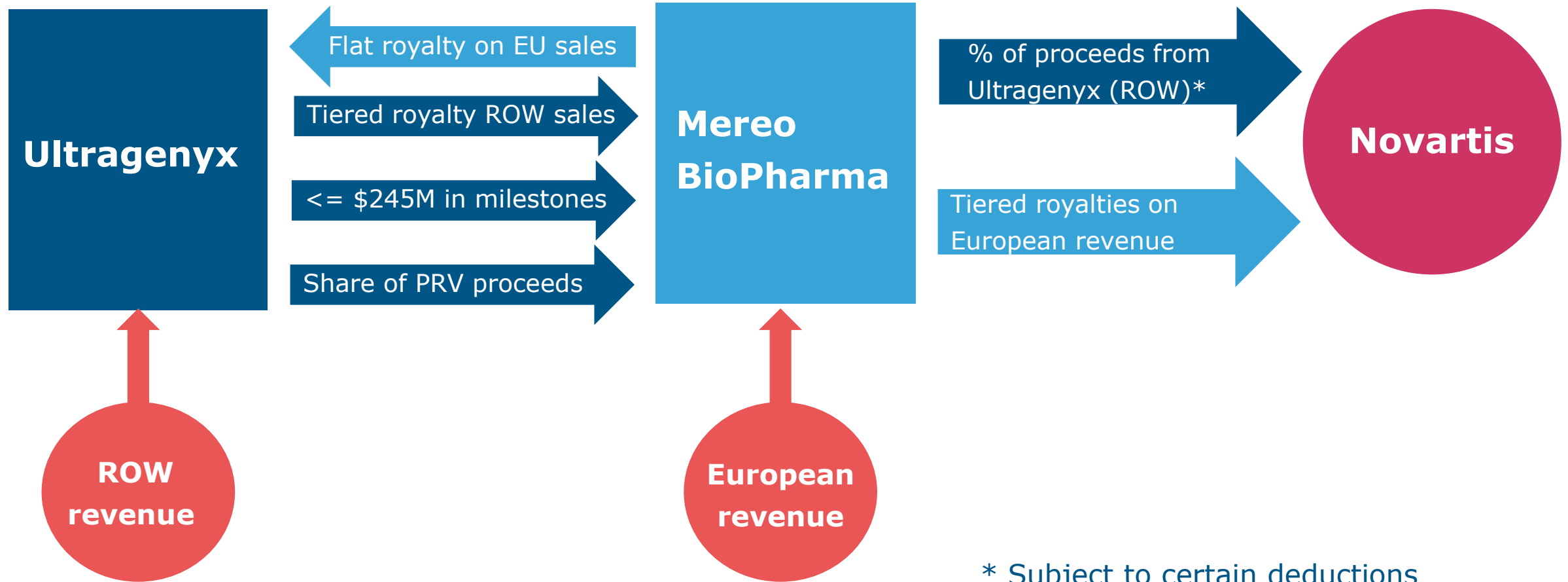
Primary efficacy endpoint of **annualized clinical fracture rate** (including morphometric fractures).

# 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

# 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](http://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), Crysvida 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).<sup>1</sup>



## 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<sup>1</sup>
- 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<sup>4</sup>
  - US patients (weekly I.V.) \$100-150k/year<sup>4</sup>
  - AATD products forecast to reach \$3.2bn by 2031<sup>5</sup>
- 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

# 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<sub>1</sub> observed in bronchitic subset (n~200, p< 0.01)<sup>1</sup>
- **Bronchiectasis** (n=38): >100ml increase in FEV<sub>1</sub> (p= 0.006); numerical improvement St. George’s Respiratory Questionnaire (SGRQ)<sup>2</sup>
- **Cystic Fibrosis** (n=55): Reduction markers of lung damage (desmosine) p<0.05)<sup>3</sup>
- **Hospitalized COVID-19** (n=15): Faster 5-day clinical improvement in WHO severity scale<sup>4</sup>
- **Bronchiolitis Obliterans Syndrome** (ongoing, n=13): Improvement biomarkers of lung damage and fibrosis, with signal of FEV1 stabilization)<sup>5</sup>

## 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 <sub>1</sub>	100 mls (34.0)	0.006
SVC	130 mls (74.0)	0.079

### SGRQ at week 4

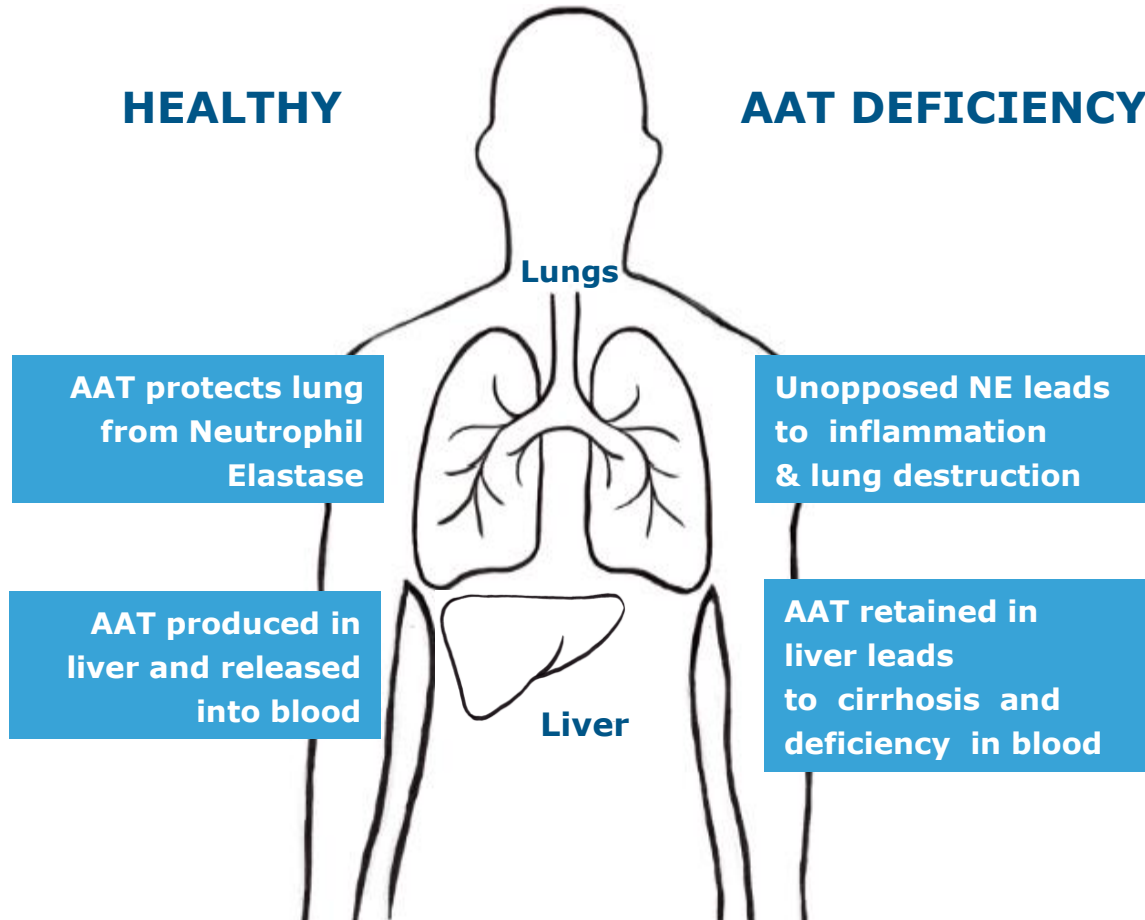
	Improvement over placebo LSM(SEM)*	P Value
Total SGRQ	-5.64 (4.65) <sup>#</sup>	0.236

\*Negative value is improvement for SGRQ

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



# 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**

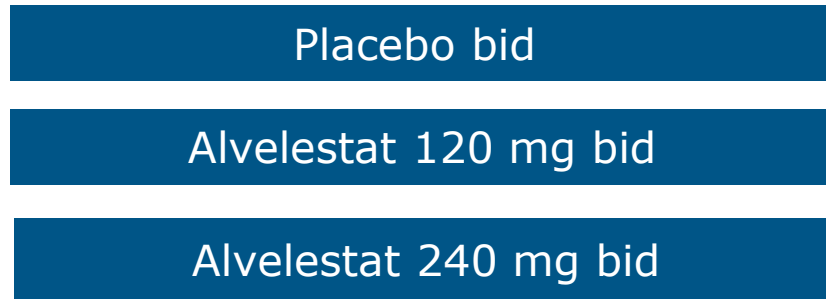
- Sustained NE suppression and effective lung penetration<sup>1</sup>
- Inhibits NE on cell sites inaccessible to AAT<sup>2</sup>

### **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

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

**ASTRAEUS**  
NCT03636347  
12 weeks  
N=99

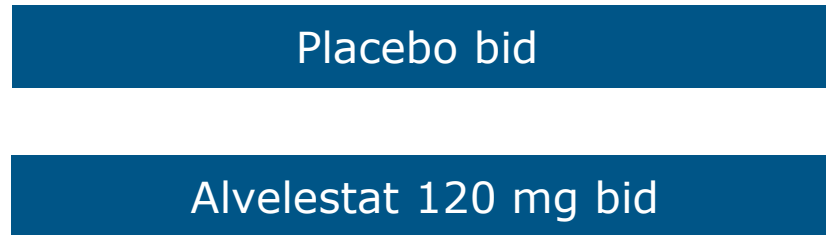


Enrolled PI\*ZZ patients

No subjects on augmentation  
Patients with established disease  
Baseline scores (median):  
FEV<sub>1</sub> - 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



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<sub>1</sub> - 89%  
SGRQ total score - 19.6  
SGRQ activity - 25.5

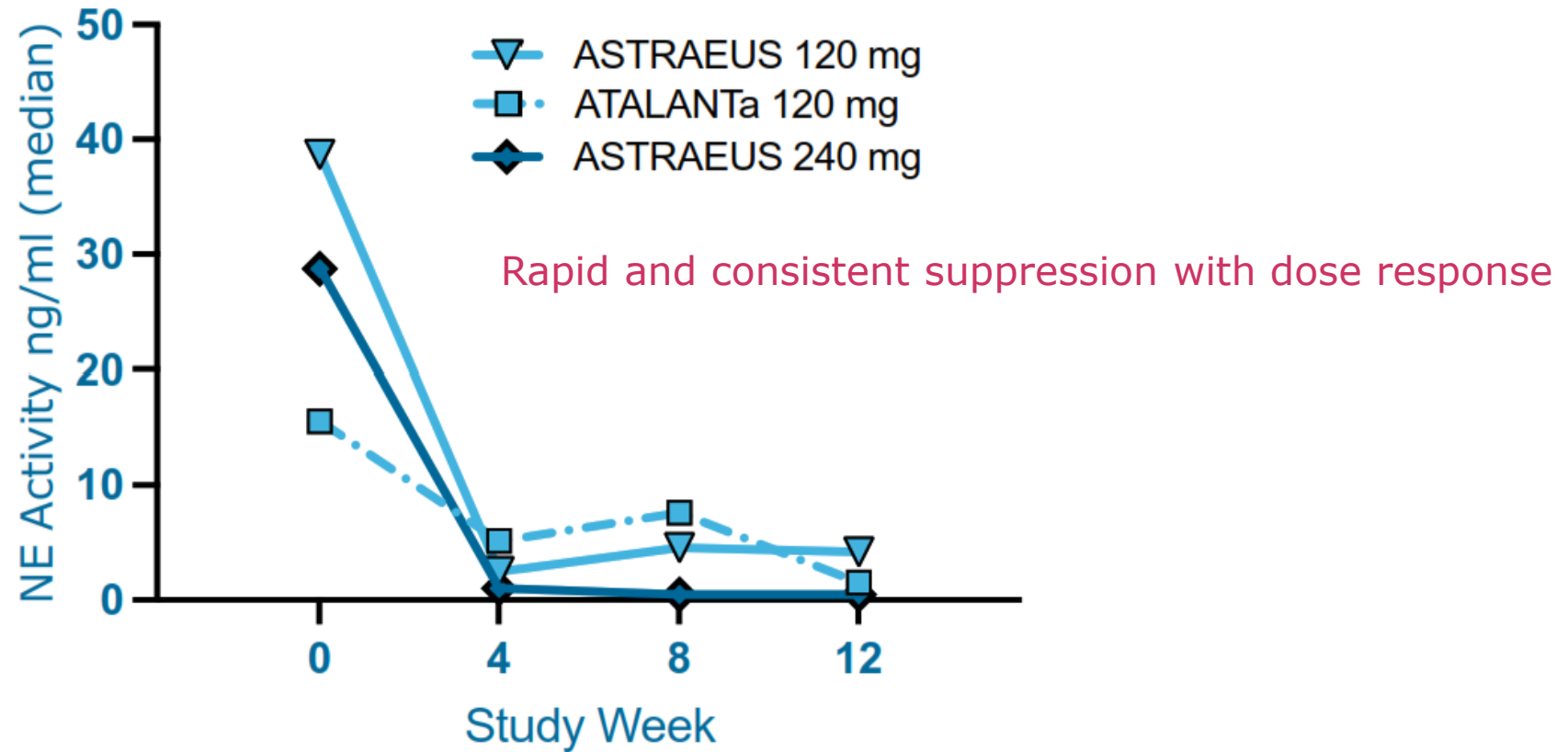


Funded by  
**NCATS**



\*SGRQ scores out of 100, lower SGRQ scores equate to better status

# Alvelestat suppression of Blood Neutrophil Elastase Activity



- 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

# Biomarkers and PK modelling confirm 240 mg dose for progression

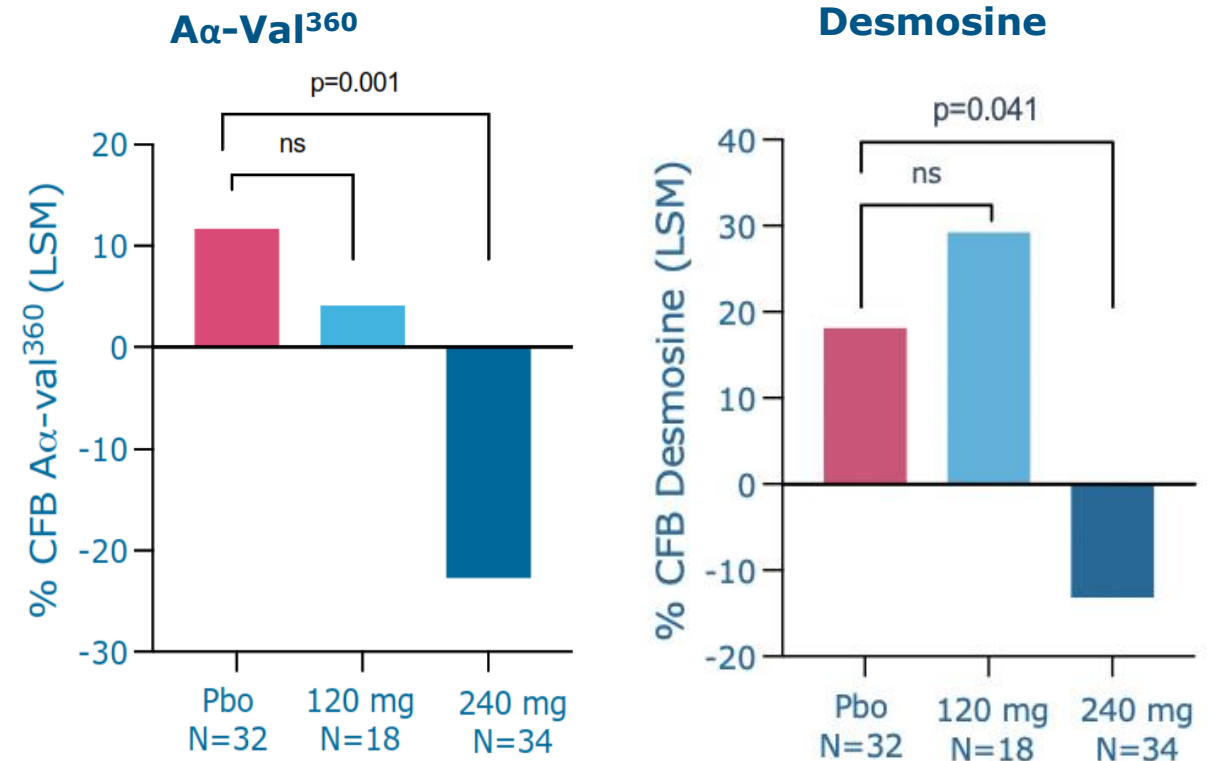
## ASTRAEUS

- 240 mg – progressive reduction in biomarkers of NE-driven protein breakdown ( $A\alpha$ -val<sup>360</sup>) 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  $A\alpha$ -Val<sup>360</sup> ( $p=0.03$ ), but not significant compared to placebo

## ASTRAEUS (Primary Endpoints)



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

# 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 (%)
<b>SAE</b>	3 (7.5)	1 (1.9)	0 (0)
<b>Adverse Events of Special Interest</b>	11 (27.5)	10 (18.5)	18 (26.9)
<b>Infections requiring antimicrobial therapy</b>	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

# 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

# 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<sup>1</sup>
- Phase 2 studies demonstrated a consistent association between the effects of alvelestat (biomarker reductions) and improvement in SGRQ (Total score and Activity Domain)<sup>2,3</sup>
- 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<sub>1</sub>)

# Earlier stage lung disease patients show greater SGRQ response

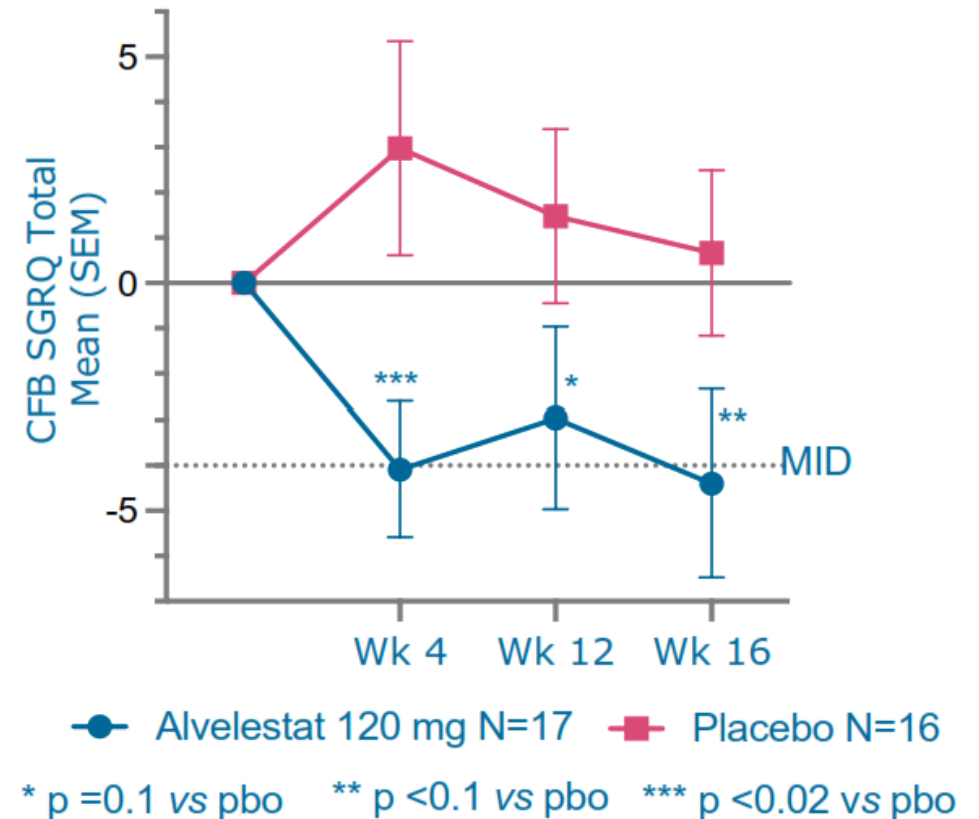
- ATALANTa study – Non-augmentation subgroup (median FEV<sub>1</sub> 89.3%). Between group changes at week 12:
  - **SGRQ Total** = 4.7-point improvement (p=0.10)
  - **SGRQ Activity** = 10.0-point improvement (p=0.01)
- Post hoc analysis of ASTRAEUS and **SGRQ Total** change shows earlier stage patients 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

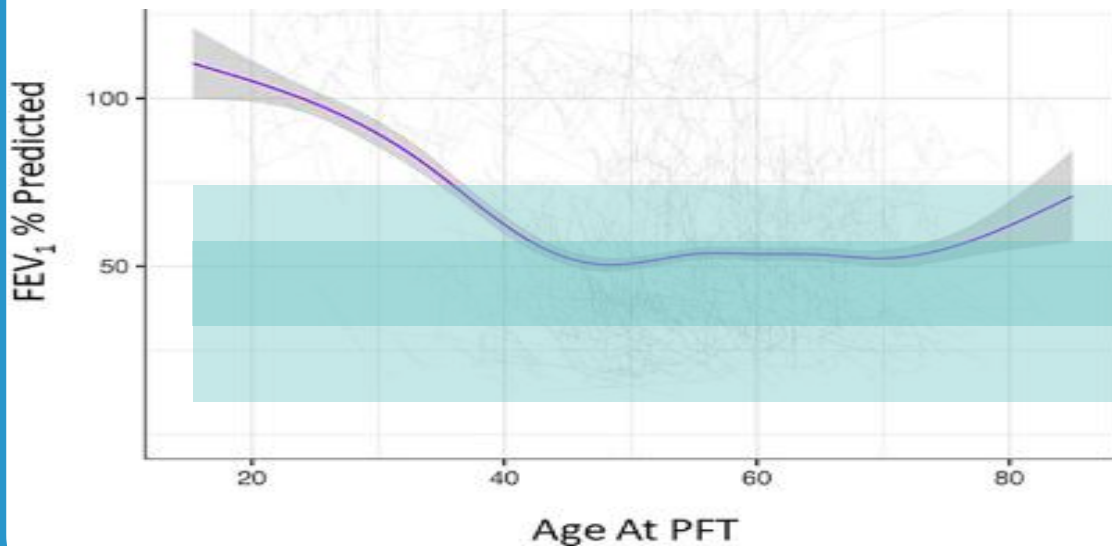




## Historical augmentation studies

**Limited to FEV<sub>1</sub> <70% or <80%**  
(Average FEV<sub>1</sub> in RAPID, EXACTLE ~50%)

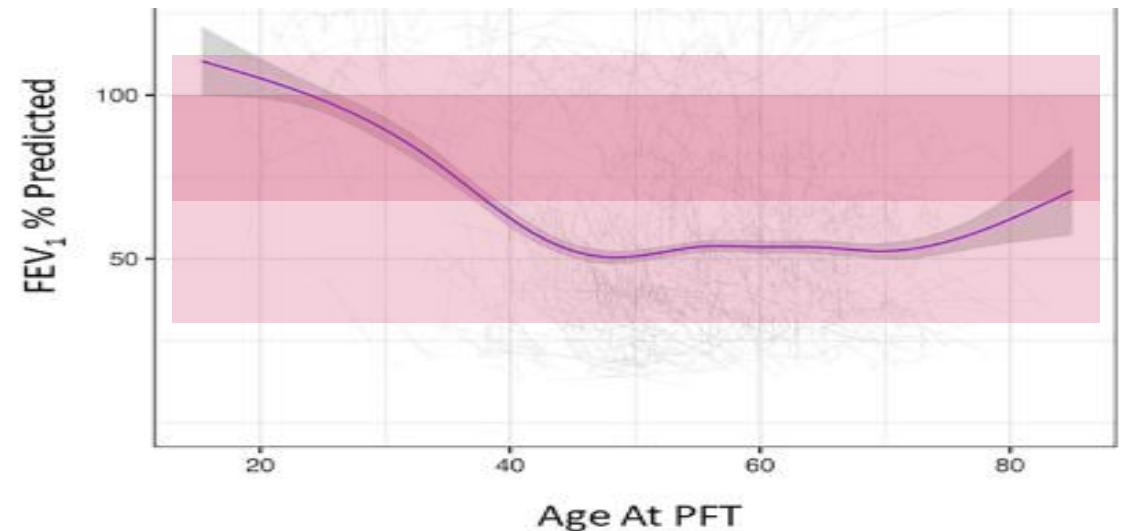
- Patients earlier in their disease not eligible
- Intervening later may limit impact



## Mereo's approach to Phase 3

**No upper FEV<sub>1</sub> limit**

- FEV<sub>1</sub> – weighting towards patients >75%
- More patients eligible, including those not eligible for augmentation therapy
- Intervening earlier may have greater impact



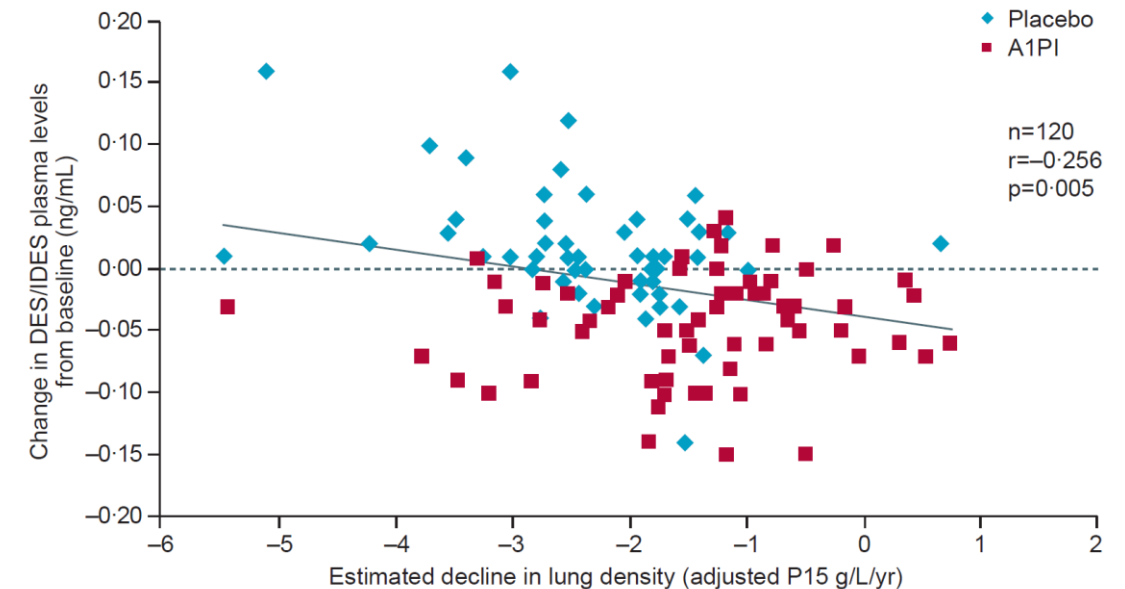
# Translating desmosine changes (elastin) to CT efficacy endpoint

		Augmentation therapy <sup>1</sup>	Alvelestat (240 mg, ASTRAEUS)
Desmosine (absolute reduction from baseline, mean)	Month 3	-0.013 ng/ml	<b>-0.028 ng/ml<sup>†</sup></b>
	Month 12	-0.031 ng/ml	Study duration 12 weeks

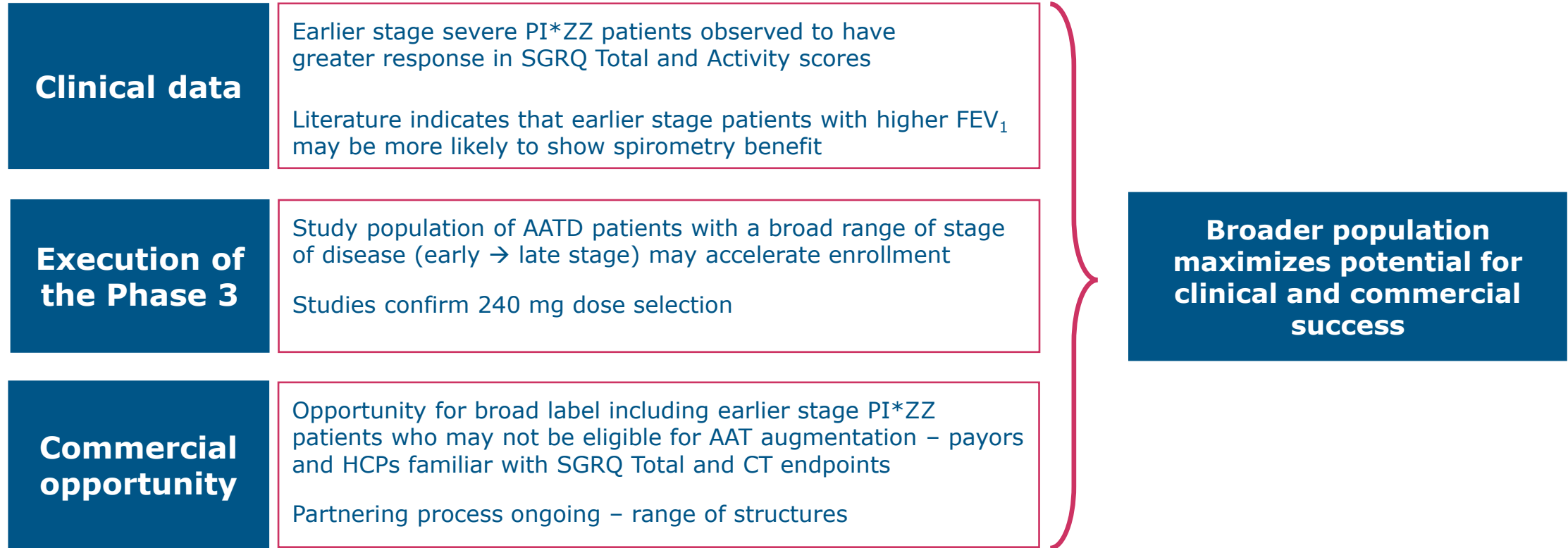
**Effects progressive over 12 weeks and from augmentation experience expected to continue over the course of 2-4 years<sup>1</sup>**

## Significant correlation of desmosine reduction and rate of lung tissue loss by CT density in AATD<sup>1</sup>

Figure 1(b)



# Development strategy for Phase 3 registrational trial





## Other programs, milestones and financials



# Key milestones for core programs

Product candidate	2023		2024		2025		Next milestone
	H1	H2	H1	H2	H1	H2	
<b>Setrusumab</b>  OI							Phase 3 Interim analysis Phase 3 Interim analysis
<b>Alvelestat</b>  AATD-LD  BOS*							Potential partnering, Phase 3 initiation  Medical conferences  BOS: Phase 2 data

# 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

**Leflutrosole** – 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**  
 \$87.5 million as of  
 June 30, 2024

<b>Cap Table</b> <i>(June 2024)</i>	<b>ADSs</b> <i>(in thousands)</i>
Shareholders > 2% holding	79,675
Shareholders < 2% holding	74,089
<b>Share capital – Issued and outstanding as of June 30, 2024<sup>1</sup></b>	<b>153,764</b>
<b>Potential Future Dilution:</b>	
Warrants <sup>2</sup>	1,401
Convertible loan notes	3,421
Employee share schemes <sup>3</sup>	12,349

<sup>1</sup> ADS equivalents of 768,821,274 ordinary shares, with one ADS representing five ordinary shares.

<sup>2</sup> Assumes a market price of \$4.00 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.





**APPENDIX**





## Setrusumab (BPS-804)

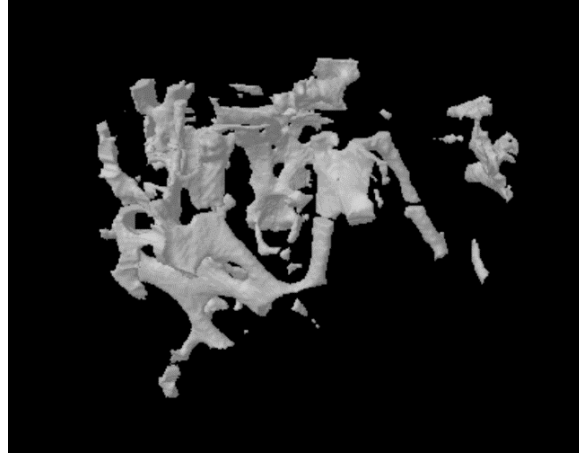
Mouse models and HR-pQCT



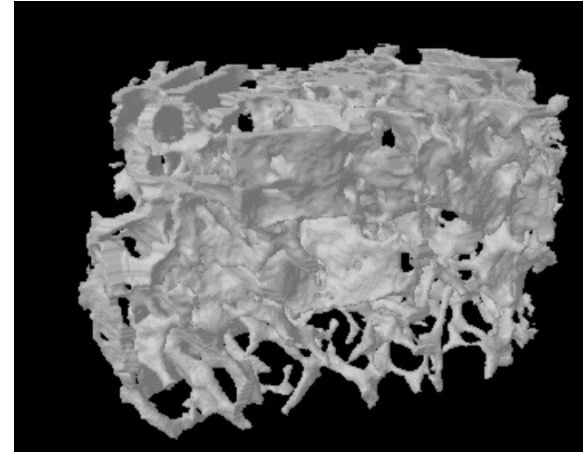
Rare Disease  
Day  
February 2023

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

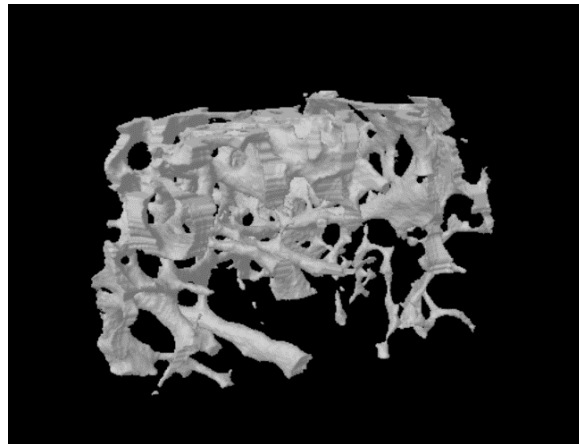
Mature Brtl control



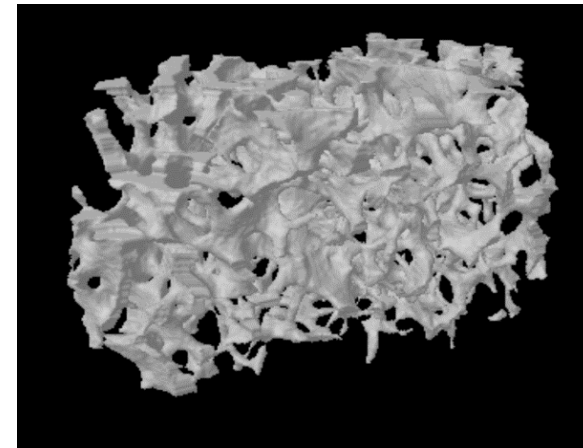
Mature WT Control



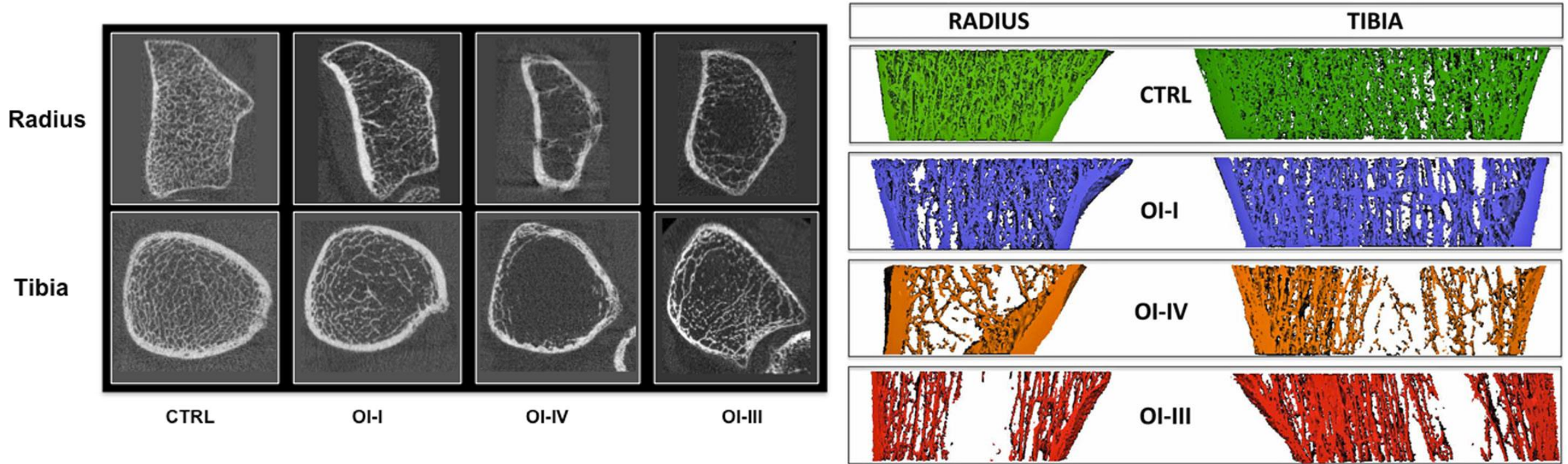
Mature Brtl treated



Mature WT Treated



# HR-pQCT scans of patients with OI and controls



# 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



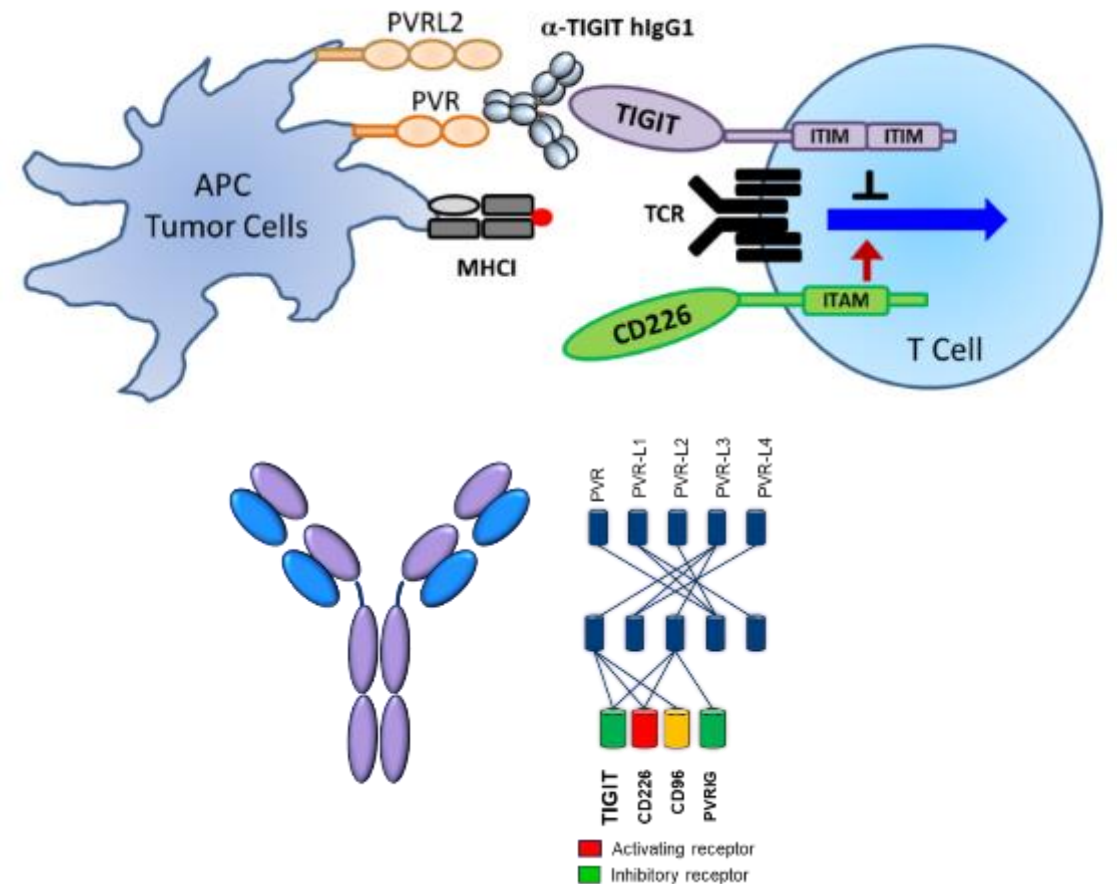
# Etigilimab (MPH313)

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

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

All responses confirmed

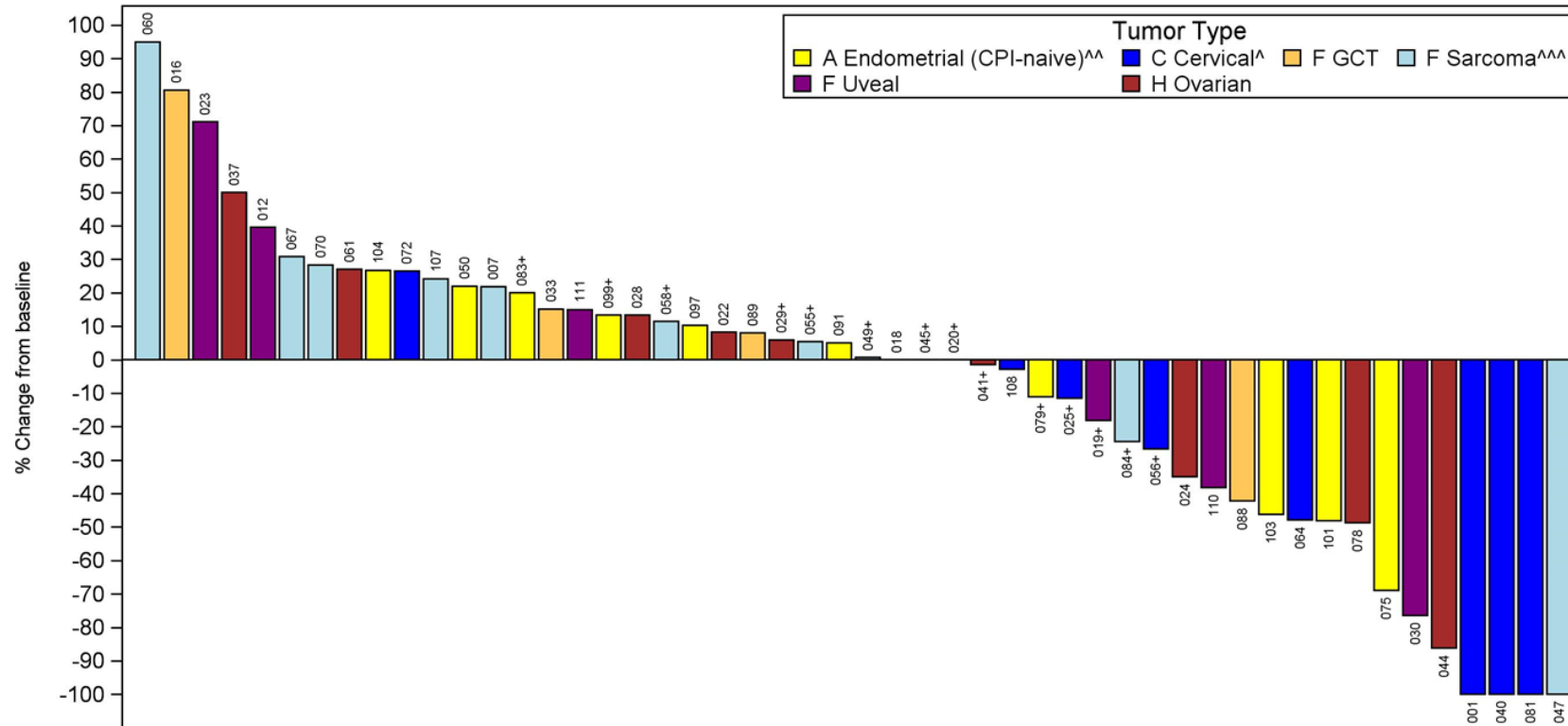
\*Efficacy analysis set: Best Observed Response (BOR) by investigator-assessed response per RECIST 1.1/clinical progression; data cut-off 3/29/2023. <sup>^</sup> Includes 1 TMB-H cervical pt E025 with CPS >1% by central lab.

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)

Waterfall Plot - Percent Change/Subject Number  
Efficacy Analysis Set\*



^Cervical cancer patient (E025) enrolled in IMB-H cohort with PD-L1 CPS>1%

^^ Endometrial cancer – CPI-naïve patient (G101) enrolled in post-CPI cohort

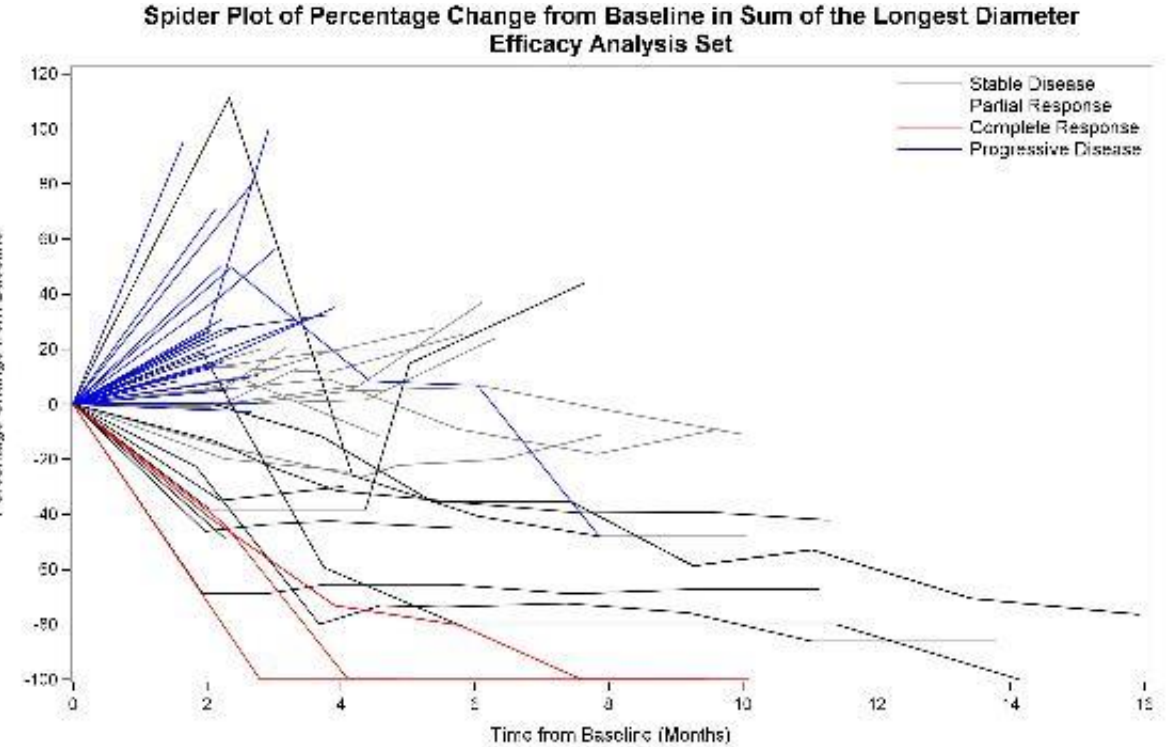
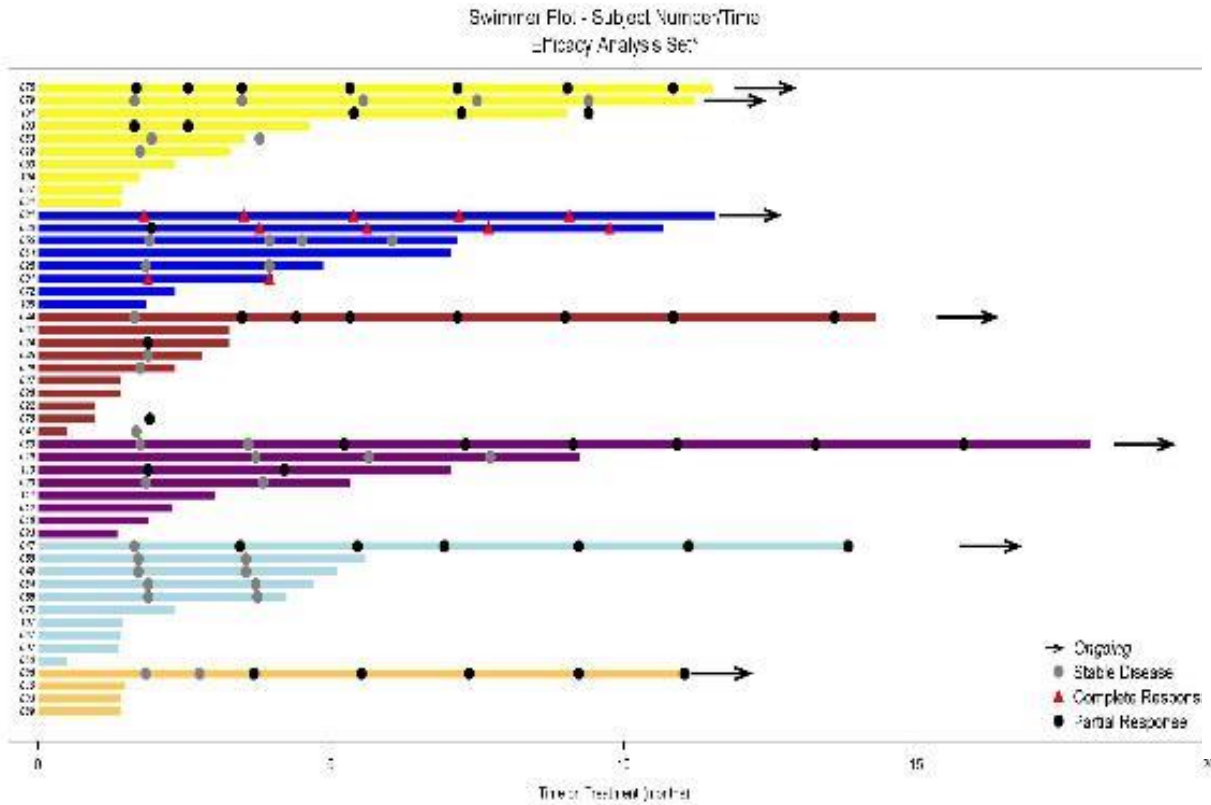
^^ Sarcoma subjects only include those with de-differentiated liposarcoma

+ 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)

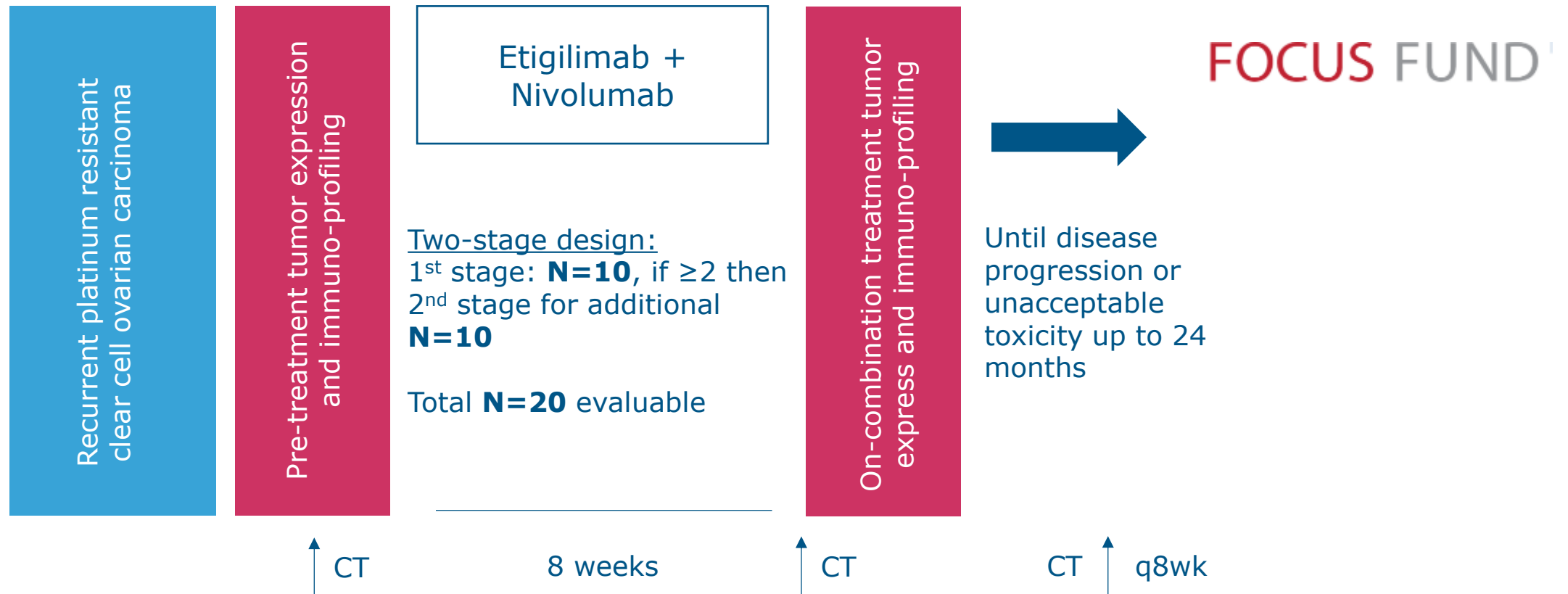


Median time on treatment for EC-N, cervical, GCT, de-differentiated liposarcoma, uveal patients

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

<sup>^</sup> Sarcoma subjects only include those with De-differentiated liposarcoma  
<sup>^</sup> Cervical cancer patient (E025) enrolled in TMB-H cohort with PDL-1 CPS>1%  
<sup>^^</sup> 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 (→)

# 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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