Mereo BioPharma

J.P. Morgan Conference

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Our vision

We are working toward a future where people and families living with rare diseases, especially those with few or no treatment options, have access to therapies that can transform their lives.

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Two pivotal rare disease programs and a capital efficient model

Achievements and fundamentals

- Two rare disease programs in-licensed and progressed to pivotal stage:
  - **Setrusumab** for Osteogenesis Imperfecta (OI) Phase 3 results reported around the end of 2025, partnered with rare disease leader, Ultragenyx - determining path forward
  - **Alvelestat** for Alpha-1 Antitrypsin Deficiency-associated Lung Disease (AATD-LD) activities to support initiation of the Phase 3 ongoing, following agreement in principle of the primary endpoints
- Additional clinical stage program – out-licensed to āshibio with EU rights retained
  - **Vantictumab** for osteopetrosis – clinical stage program with IND planned H2 2026
- Financial discipline delivers cash runway into mid-2027
  - ~$41 million of cash and cash equivalents as of December 31, 2025
- Management team with a proven track record in corporate development

Addressing patient populations with high unmet needs and significant market opportunities

	Osteogenesis Imperfecta	Alpha-1 Antitrypsin Deficiency	Osteopetrosis
Disease Background	**Rare genetic bone condition** leading to problems including frequent fractures and skeletal deformities	**Rare genetic progressive lung disease** characterized by unregulated NE-driven lung destruction	**Rare genetic bone disease** characterized by dense, brittle bones leading to multiple fractures and significant morbidity
Epidemiology	**~60,000 patients** across the US & Europe[1]	Severe deficiency patient estimates: **~50,000 in North America** and **~60,000 in Europe**[2]	**1 in 20,000 incidence in North America** and **Europe** with onset typically in late childhood[3]
Unmet Need	**No FDA/EMA approved therapy.** Bisphosphonates widely used Orphan drug status EU and US	Augmentation **efficacy not clear**, not reimbursed in all markets Orphan drug status EU and US	**No FDA/EMA approved therapy**
Mereo's Unique Approach	**Setrusumab** A sclerostin-targeting antibody	**Alvelestat** An oral neutrophil elastase inhibitor	**Vantictumab** An anti-FZD antibody

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1. Based on internal forecast; 2. 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; 3. Wu CC, Econs MJ, DiMeglio LA, et al. Diagnosis and management of osteopetrosis: consensus guidelines from the Osteopetrosis Working Group. J Clin Endocrinol Metab. 2017 Sep 1;102(9):3111-3123.

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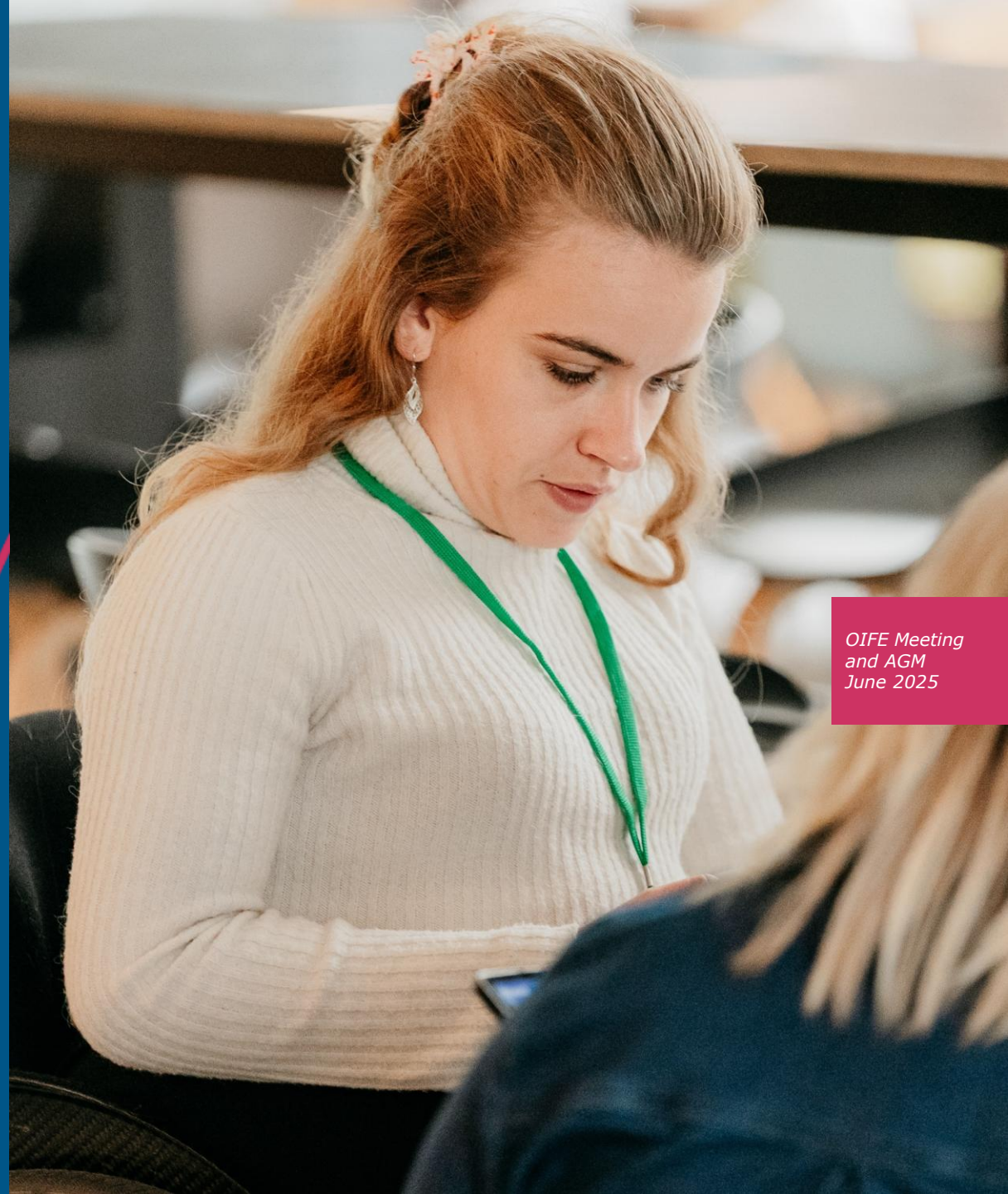
Setrusumab (UX143)

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



OIFE Meeting and AGM June 2025

Setrusumab for osteogenesis imperfecta Phase 3 results

Neither study achieved primary endpoint of reduction in AFR[1] compared to placebo (*Orbit*) or bisphosphonates (*Cosmic*)

Both studies demonstrated statistically significant increases in bone mineral density (BMD)

Additional data shows reduction in vertebral fractures and improvements in patient reported outcomes of disease severity, pain/comfort, and daily activities

Further understanding will help determine if there is a potential path forward

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1. Annualized fracture rate

Two randomized Phase 3 studies provide large data set

orbit Osteogenesis Imperfecta (OI) Clinical Research

cosmic Osteogenesis Imperfecta (OI) Clinical Research

Objective	**Setrusumab vs. placebo** 2:1 randomization, Double blind Follow-up 18-24 months	**Setrusumab vs. bisphosphonates** 1:1 randomization, Open label Follow-up 18-24 months
Enrolment	**159** subjects (with ≥1 AFR) ages **5 to 25 years** with OI Types **I, III, or IV**	**69** subjects (with ≥1 AFR) ages **2 to 7 years** with OI Types **I, III, or IV**

Patient Demographics	Setrusumab (%)	Placebo (%)		Setrusumab (%)	IV-BP (%)
Total N	**107 (67.3)**	**52 (32.7)**		**34 (49.3)**	**35 (50.7)**
Type I	43 (40.2)	21 (40.4)	Type I	12 (35.5)	16 (45.7)
Type III	43 (40.2)	10 (19.2)	Type III	15 (44.1)	13 (37.1)
Type IV	21 (19.6)	21 (40.4)	Type IV	7 (20.6)	6 (17.1)
Peds *5 to <12 yo*	**44** (41.1)	**23** (44.2)	**Peds** *2 to 7 yo*	**34** (49.3)	**35** (50.7)
Teens *12 to <18 yo*	47 (43.9)	21 (40.4)			
Adults *18 to 26 yo*	16 (15.0)	8 (15.4)			

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Baseline fractures are comparable between groups in both studies

Orbit: more severe type III/IV patients exited placebo via rescue criteria

Objective	Setrusumab vs. placebo 2:1 randomization, Double blind Follow-up 18-24 months		Setrusumab vs. bisphosphonates 1:1 randomization, Open label Follow-up 18-24 months		
Baseline Fractures[1]	**Setrusumab**	**Placebo**		**Setrusumab**	**IV-BP**
Mean / Median number of fractures	**3.2 /2.0**	**3.3 / 2.0**		**4.1 / 4.0**	**4.3 / 3.0**
Fracture ≤3 Pt number (%)	71 (66.4)	35 (67.3)	Fracture ≤4 & no FTH	4 (11.8)	4 (11.4)
Fracture >3 Pt number (%)	36 (33.6)	17 (32.7)	Fracture >4 or ≥1 FTH	30 (88.2)	31 (88.6)

In Orbit, 31 (19.5%) patients met rescue criteria at 12 months primarily due to fractures

- 28 of 31 were more severe Type 3/4 patients
  - Setrusumab 15/64 **(23%)**
  - Placebo 13/31 **(42%)**

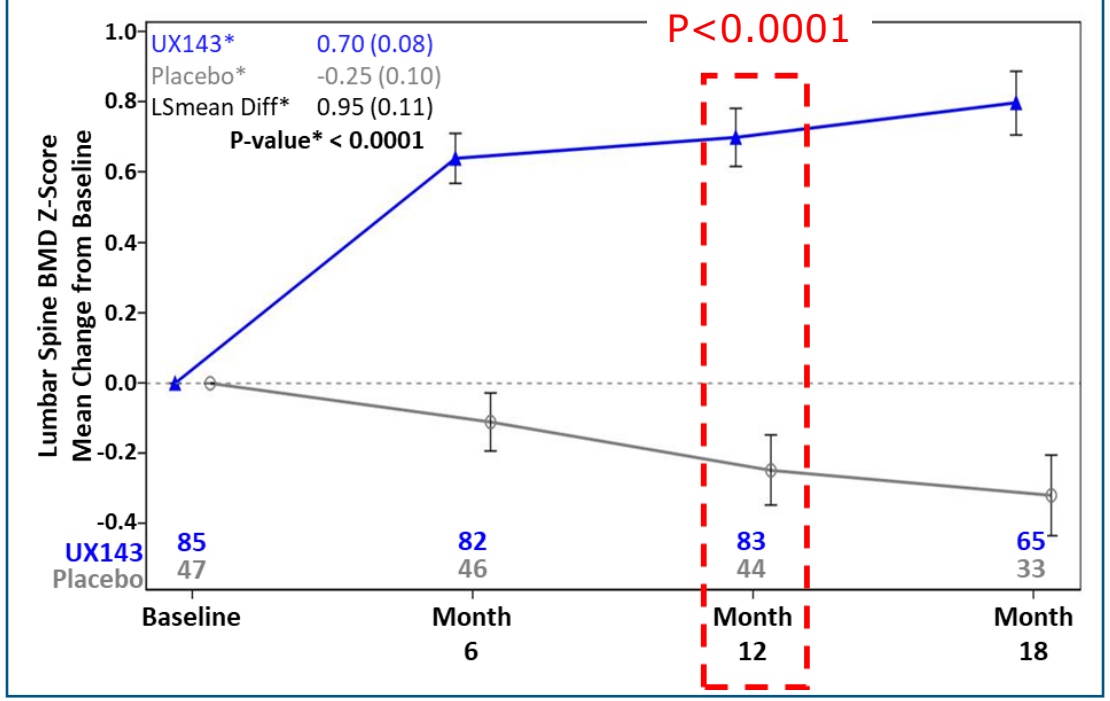
A substantially larger number of Placebo patients exited Orbit

Cosmic had no rescue criteria since it was active treatment controlled

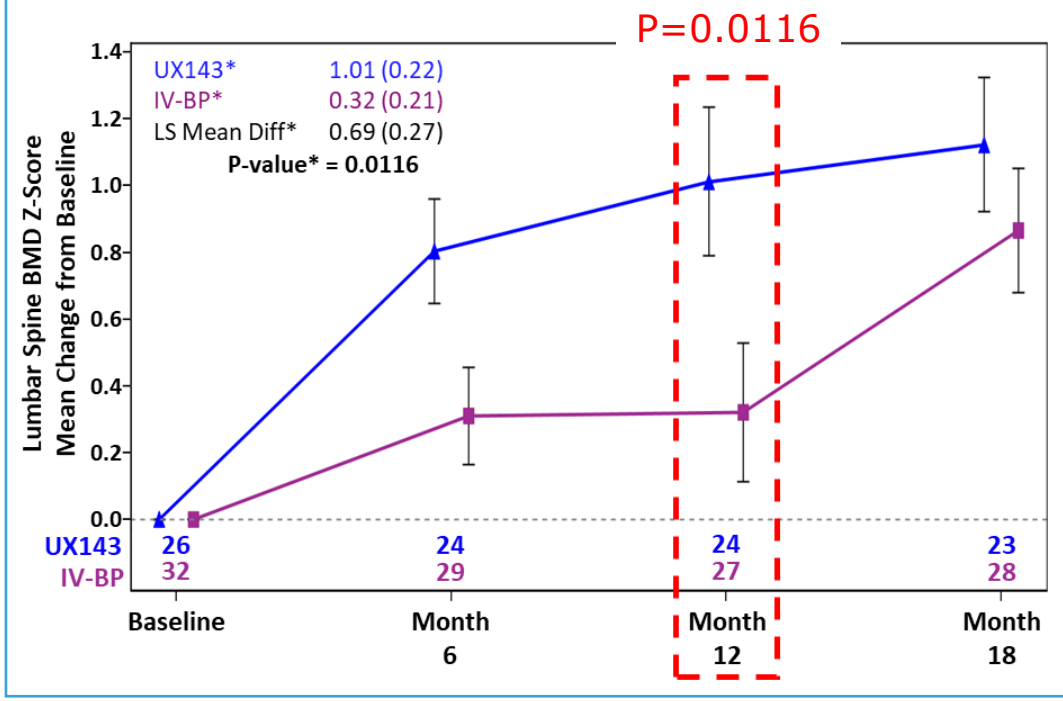
1. All suspected and radiographically confirmed fractures over prior 2 years; Abbreviations: FTH: Femur, Tibia or Humerus

Setrusumab is substantially more effective in increasing BMD

Setrusumab demonstrated **clinically & statistically significant increases in BMD** vs placebo



Setrusumab demonstrated **clinically & statistically significant increases in BMD** vs active comparator



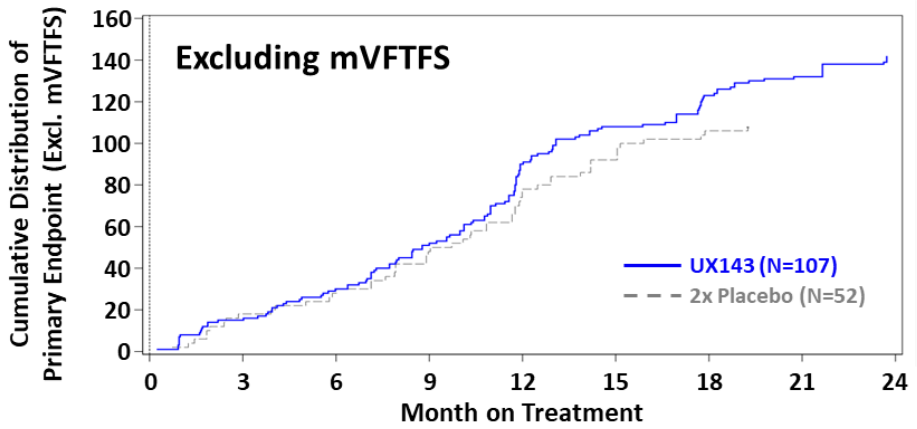
*Based on Month 12 timepoint

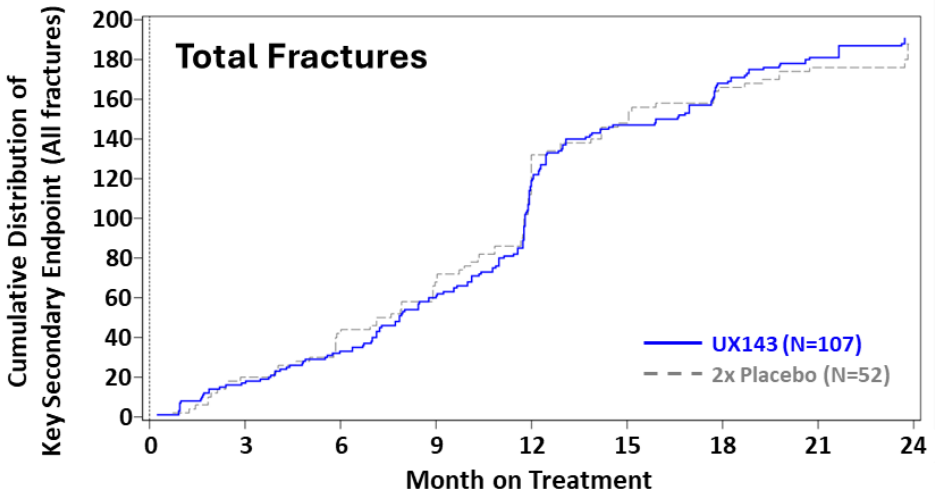
Data presented at JP Morgan Healthcare Conference 2026

Orbit: Setrusumab patients showed an increase in fractures over a low placebo rate, but were the same as placebo when all fractures were considered (p=ns)

Confirmed fractures by x-ray & skeletal survey

		Primary Endpoint[1] Excl. mVFTFS	Key Secondary All Fractures
Setrusumab AFR (n=107)	# of fractures	142	191
	Mean (SD, SE)	0.92 (1.16, 0.11)	1.22 (1.29, 0.12)
	Median (Q1, Q3)	**0.58** (0.00, 1.53)	0.68 (0.00, 1.82)
Placebo AFR (n=52)	# of fractures	54	94
	Mean (SD, SE)	0.80 (1.48, 0.21)	1.27 (1.96, 0.27)
	Median (Q1, Q3)	**0.00** (0.00, 0.93)	0.61 (0.00, 2.02)
Est.[2] Setrusumab AFR (95% CI)		**0.71** (0.50, 0.99)	1.16 (0.90, 1.50)
Est.[2] Placebo AFR (95% CI)		**0.55** (0.35, 0.86)	1.12 (0.80, 1.57)
Rate Ratio[2] Setrusumab/Placebo (95% CI)		1.28 (0.80, 2.06)	1.03 (0.71, 1.52)
Rate Change[2] Setrusumab Placebo (95% CI)		**28.14** (-20.21, 105.79)	**3.38** (-29.48, 51.54)
	P-value[2]	*0.305*	*0.865*





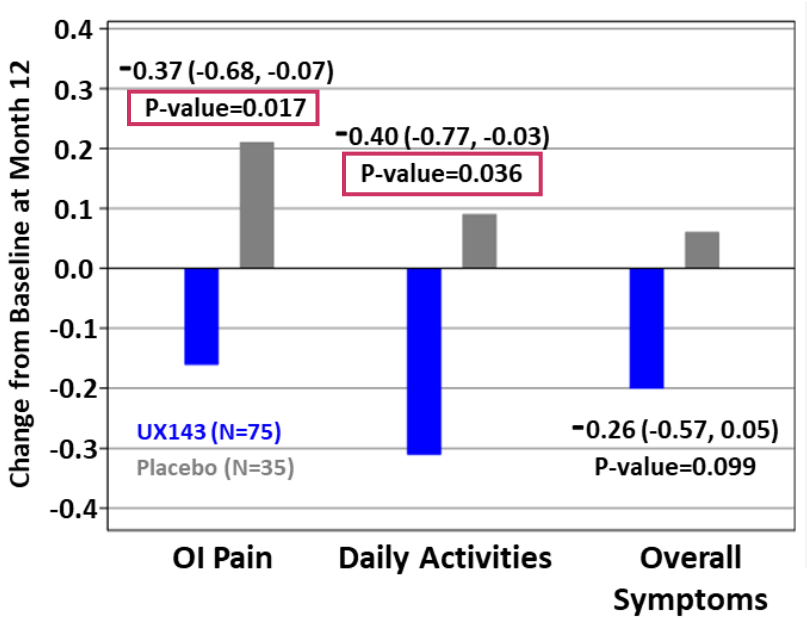
1. Radiographically confirmed fractures, excluding morphometric vertebral fractures and fingers, toes, face, and skull;
2. Negative Binomial model

Data presented at JP Morgan Healthcare Conference 2026

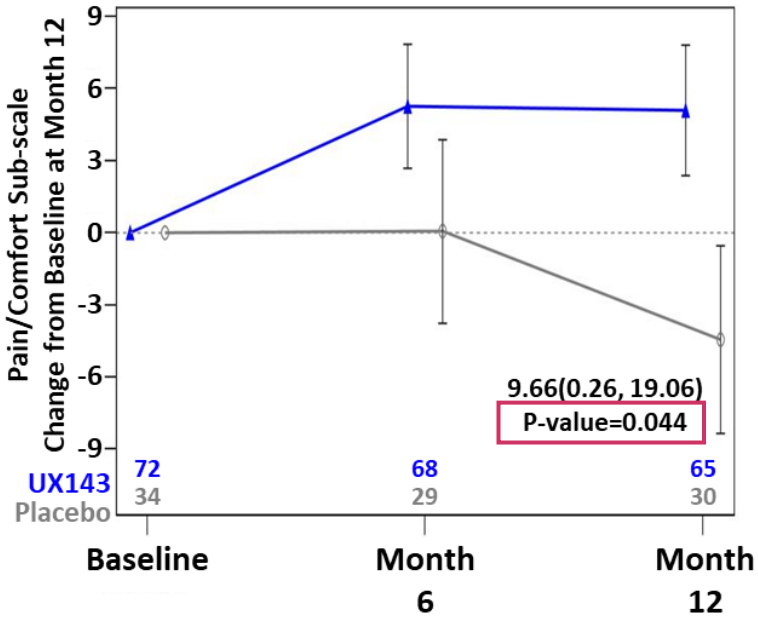
Orbit: In setrusumab patients, disease severity (PGIS) in peds/teens reduced and pain/comfort & sports/activity improved

Peds/Teens patients constitute 85% of subjects in Orbit Ph3 study (135/159)

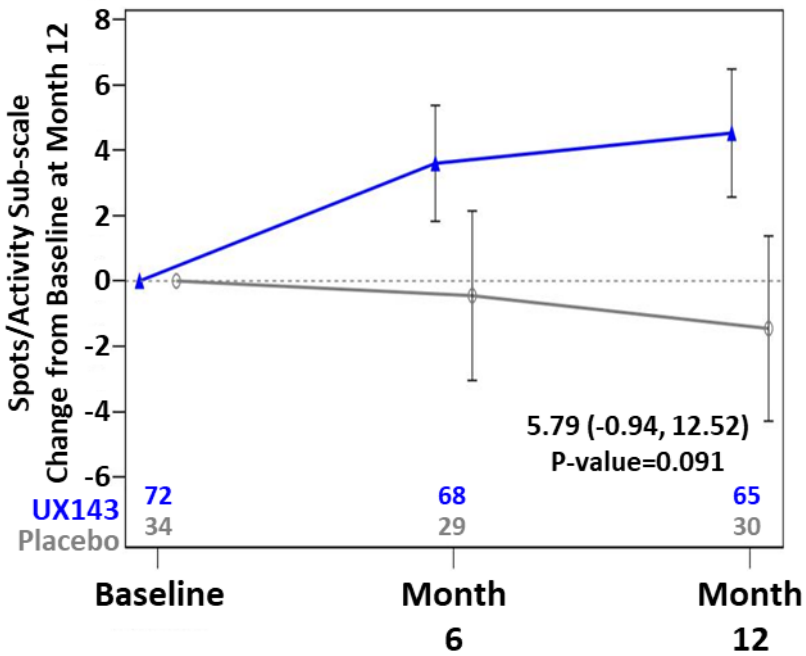
Patient Global Impression Scale of Severity (PGIS)



Pain/Comfort POSNA-PODCI



Sports/Activity POSNA-PODCI

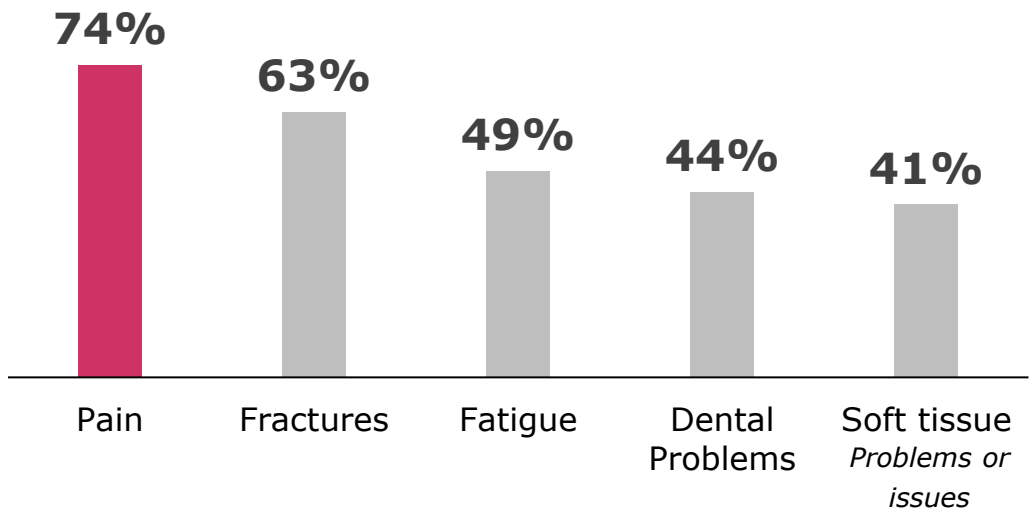


12-month assessment is as randomized and most important as no patients had exited due to rescue criteria

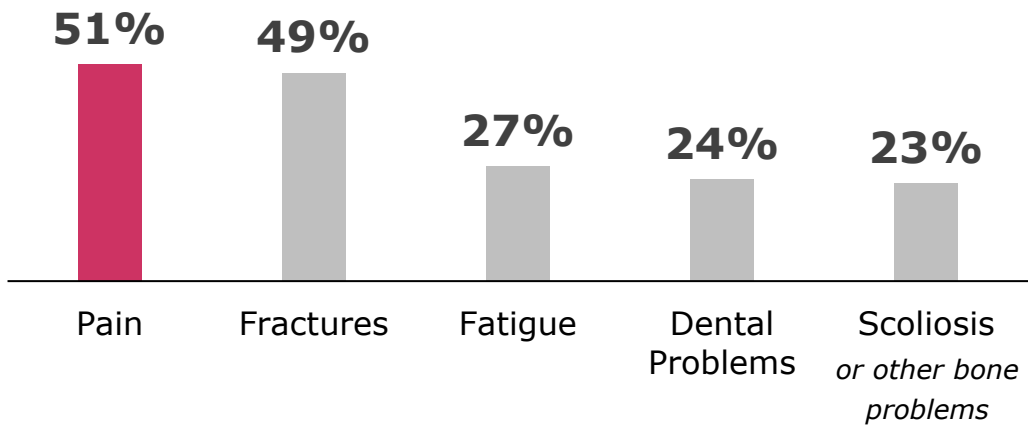
Pain is the most common & impactful sign, symptom or clinical event amongst peds and teens with OI

THE iMPACT SURVEY

Top 5 clinical events, signs and symptoms in proxy peds & adolescents with OI by prevalence[1]

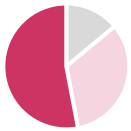


Top 5 clinical events, signs and symptoms in proxy peds & adolescents ranked as mod-to-severe impact[1]



Impact of OI on areas of QoL in children, % of proxy children responding as activity mod-to-severely impacted[2]

70% Leisure Activities



52% Social Life

50% School attendance

49% Daily tasks

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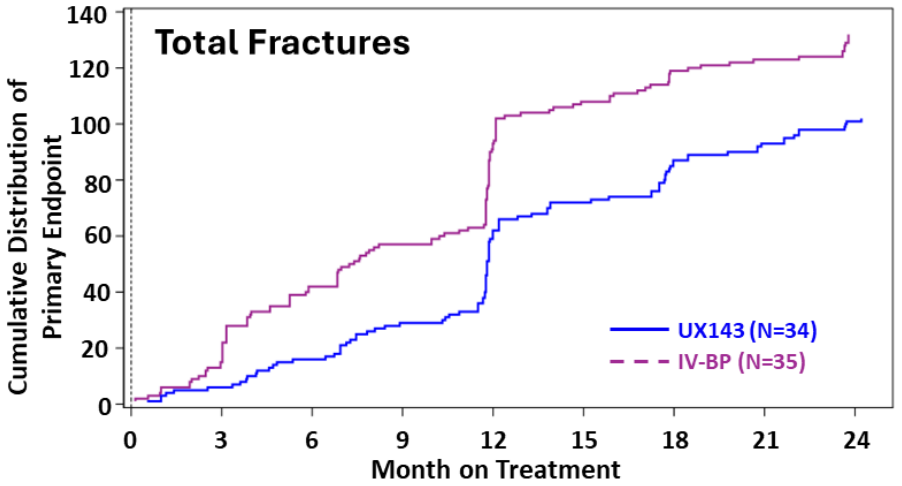
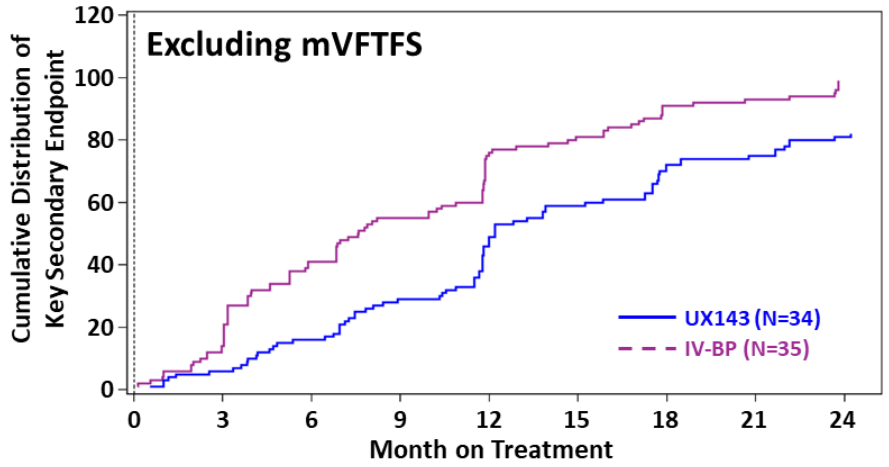
1. Adapted from Westerheim et al, 2024.; 2. Data on file, light red portion reflects "Mild or very mildly impacted"

Cosmic: Setrusumab treatment shows reduced fractures over IV-BP (p=ns)

Confirmed fractures by x-ray & skeletal survey

		Primary Endpoint Total fractures	Key Secondary Excl. mVFTFS
Setrusumab AFR (n=34)	# of fractures	102	82
	Mean (SD, SE)	1.87 (1.69, 0.29)	1.53 (1.53, 0.26)
	Median (Q1, Q3)	2.02 (0.00, 3.04)	1.42 (0.00, 2.53)
IV-BP AFR (n=35)	# of fractures	132	99
	Mean (SD, SE)	2.6 (3.19, 0.54)	1.97 (2.90, 0.49)
	Median (Q1, Q3)	1.38 (0.55, 4.06)	0.67 (0.00, 3.04)
Est.[2] Setrusumab AFR (95% CI)		**0.91** (0.51, 1.60)	0.68 (0.34, 1.35)
Est.[2] IV-BP AFR (95% CI)		**1.15** (0.65, 2.04)	0.79 (0.39, 1.61)
Rate Ratio[2] Setrusumab/IV-BP (95% CI)		0.79 (0.48, 1.28)	0.86 (0.47, 1.57)
Rate Change[2] Favoring setrusumab (95% CI)		**-21.27** (-51.75, 28.47)	**-14.27** (-53.07, 56.61)
	P-value[2]	0.338	0.616





1. Radiographically confirmed fractures, excluding morphometric vertebral fractures and fingers, toes, face, and skull;
2. Negative Binomial model

Cosmic: Large (59%) reduction in vertebral fractures on setrusumab (p=0.081)

Despite more severe type III/IV patients on setrusumab (65% setrusumab vs 54% IV-BP)

Radiographically confirmed fractures

	Total Fractures		Vertebral Fractures	
	Setrusumab	IV-BP	Setrusumab	IV-BP
All fractures	102	132	**19**	**46**
All fractures (Excluding mV[1])	84	104	**1**	**18**
All fractures (Excluding mVFTFS[2])	82	99	1	18
mVertebral fractures (Tertiary endpoint)	18	28	18	28

Setrusumab showed:

- **59%** fewer vertebral fractures of all types
- **94%** fewer non-morphometric vertebral fractures

Comparing 19 vs 46 vertebral fractures*		All Vertebral Fractures
Negative Binomial Model (95% CI)	Est. Setrusumab AFR (95% CI)	0.14 (0.04, 0.51)
	Est. IV-BP AFR (95% CI)	0.33 (0.10, 1.12)
	Ratio UX143/IV-BP (95% CI)	0.44 (0.18, 1.11)
	Rate Change favoring Setrusumab (95% CI)	**-56.00** (-82.48, 10.53)
	P-value	0.081

Comparing 18 vs. 28 mV fractures (Tertiary endpoint)		Only Morphometric Vertebral Fractures
Negative Binomial Model (95% CI)	Est. Setrusumab AFR (95% CI)	0.15 (0.04, 0.51)
	Est. IV-BP AFR (95% CI)	0.24 (0.07, 0.79)
	Ratio UX143/IV-BP (95% CI)	0.64 (0.26, 1.61)
	Rate Change favoring Setrusumab (95% CI)	**-35.87** (-74.43,60.86)
	P-value	0.344

*Post-hoc analysis; 1. Morphometric vertebral fractures; 2. Morphometric vertebral fractures and fingers, toes, face, and skull

Data presented at JP Morgan Healthcare Conference 2026

No new safety concerns identified, reported TEAEs are consistent with the anticipated safety profile for setrusumab

	orbit Osteogenesis Imperfecta (OI) Clinical Research	cosmic Osteogenesis Imperfecta (OI) Clinical Research
Treatment emergent adverse events (TEAE)	• No serious-related TEAEs • Low incidence (<2%) severe-related TEAEs • Low incidence (<3%) TEAE's leading to treatment or study discontinuation	• No serious related TEAEs • Low incidence (<3%) severe-related TEAE • No TEAEs leading to treatment discontinuation or study discontinuation
Adverse events of special interest (AESI)	• No ischemic CV Events • No hypersensitivity reactions related to UX143 • One TEAE in neurologic sequalae due to bony overgrowth ○ Radial nerve injury following a surgical procedure	• No ischemic CV events • No hypersensitivity reactions related to UX143 • No neurologic sequalae due to bony overgrowth
Deaths	**No Deaths**	**No Deaths**

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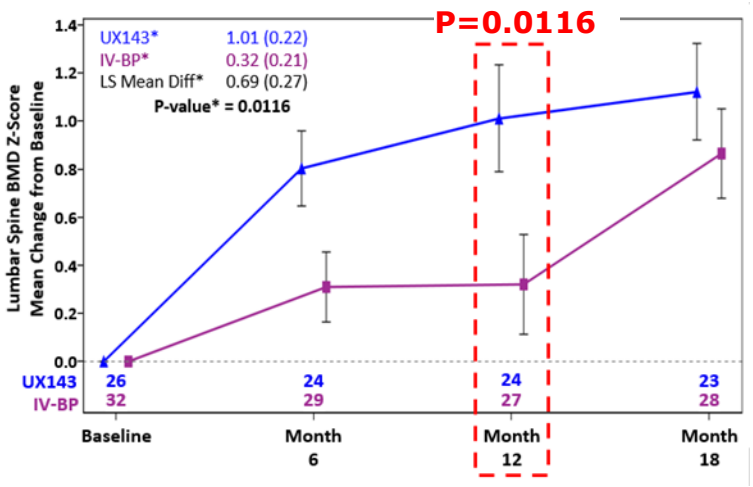
Data presented is representative of the setrusumab arm only

Overall data suggest an impact of setrusumab on OI disease although missed primary AFR endpoints

The largest BMD improvements found in the lumbar spine BMD are associated with **reduced vertebral fractures** and **improved pain and functional outcomes in pediatric patients**

Improved Lumbar Spine BMD Cosmic (p=0.0116) > **Reduced Vertebral Fractures Cosmic (p=0.081)** > **Improved functional outcomes**



Vertebral Fractures

	Setrusumab	IV-BP
All fractures	19	46
All fractures (Excluding mV[1])	1	18

- ✓ **Decreased bone pain**
  - **Orbit** – peds & teens: PGIS OI Pain (**p=0.017**); POSNA/PODCI (**p=0.044**)
- ✓ **Improved functional ability**
  - **Orbit** – peds & teens: PGIS daily activities (**p=0.036**)
- ✓ **Improved walking ability**

Further understanding will help determine if there is a potential path forward

1. Morphometric vertebral fractures

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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

Well-defined plan for Phase 3 registrational trial in AATD-LD

Clinical Data

Earlier stage severe PI*ZZ patients observed to have **greater response** in SGRQ (Total and activity)

Earlier stage patients (higher FEV_1) may be more likely to **show spirometry benefit**

Phase 3 Design

Early → late stage – Pi*ZZ genotype

Two independent primary endpoints – **SGRQ Total** (FDA) and **lung density by CT** (EMA – p<0.1 may be acceptable)

~220 patients for up to **18 months** (240 mg alvelestat)

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

Broader population maximizes potential for **clinical** and **commercial success**

- **EU & US Orphan Designation**
- **Phase 3 feasibility completed**
- **Partnering process ongoing**

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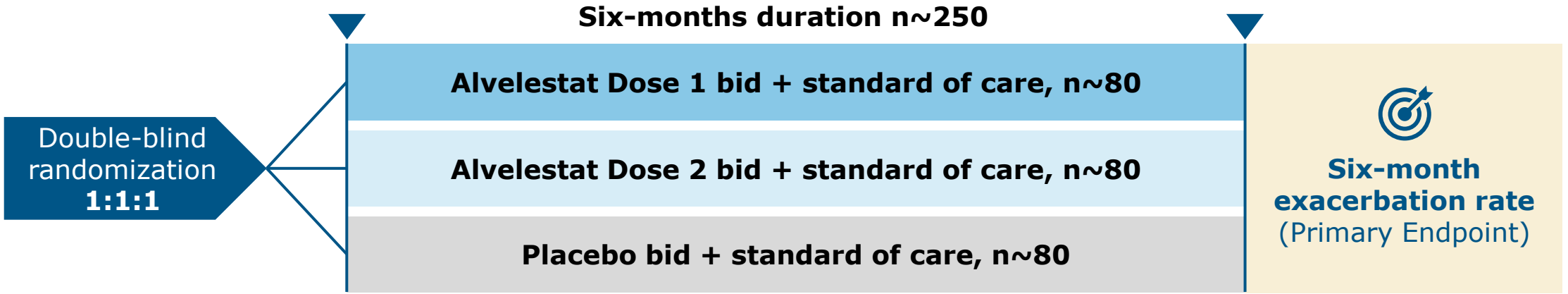
Potential Phase 2b Design for Bronchiectasis to Broaden the Scope of the Partnering Process



- Phase 2b WILLOW study provides **good precedent for 2b design**[1]
- Exacerbations = **required confirmatory endpoint** = **substantially de-risk Phase 3**

Source: 1. Chambers et al, NEJM 2020; 383:22

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Vantictumab

Osteopetrosis: a rare bone disease with high unmet need

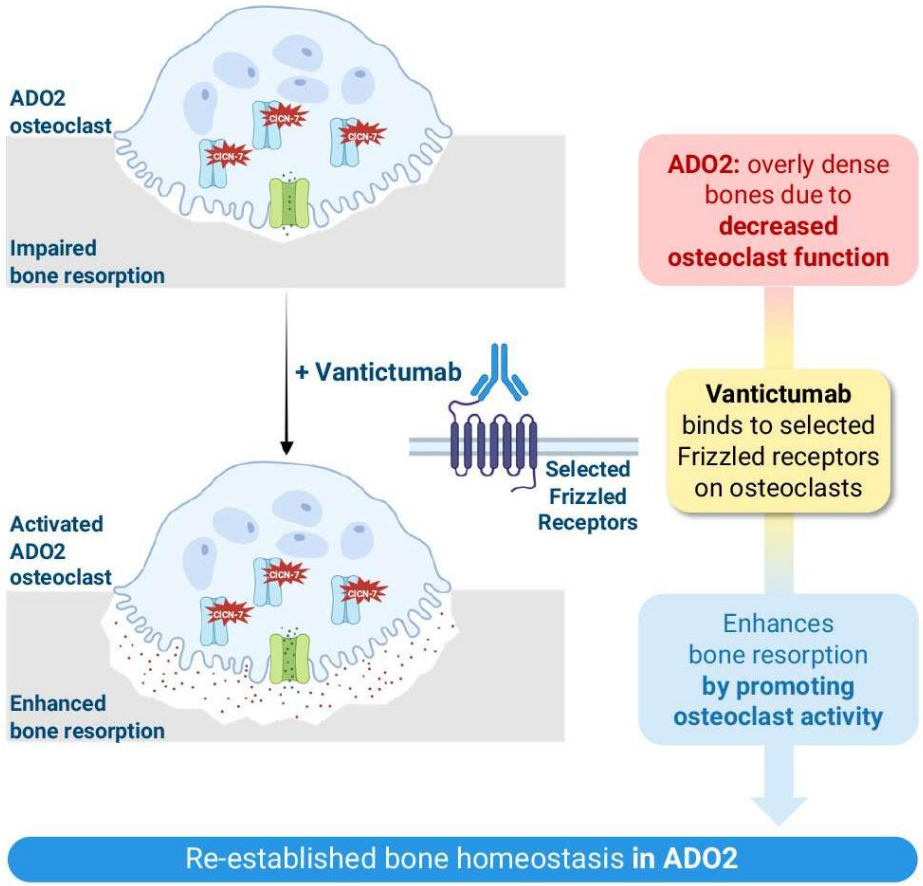
Significant opportunity in underserved rare bone disorder

ADO2 overview[1]

- ADO2 is an inherited metabolic bone disorder characterized by impaired osteoclast function
- Dense, brittle bones lead to multiple fractures, osteomyelitis, bone pain, low blood counts, significant morbidity
- No approved therapy
- 1 in 20,000 incidence with onset typically in late childhood

Clear unmet need for a therapy that rescues osteoclast function, improves bone structure, and reduces morbidity

Vantictumab Mechanism of Action[2]



ADO2: Autosomal Dominant Osteopetrosis 2, also known as Albers-Schönberg disease; 1. Wu CC, Econs MJ, DiMeglio LA, et al. Diagnosis and management of osteopetrosis: consensus guidelines from the Osteopetrosis Working Group. J Clin Endocrinol Metab. 2017 Sep 1;102(9):3111-3123. doi: 10.1210/jc.2017-01127; 2. Adapted from āshibio's website

Vantictumab development timelines

2011-2017

Vantictumab investigated **~100 patients** in 4 Phase 1a/b oncology trials

Biomarker evidence highlighted **potent impact on osteoclast function & high bone turnover** which led to fragility fractures in some patients[1]

Aug. 2025

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VAN **sig. decreased areal BMD** in ADO2 mice and **improved measures of bone structure and quality**[2]

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Sept. 2025

pre-clinical data on use of vantictumab in **mouse model of ADO2**[2]

H2 2026

IND to study vantictumab in patients with ADO2 at **lower doses** than studied previously[3]

Existing clinical data de-risks the program allowing **rapid advancement into clinical development** for ADO2

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1. Diamond J, et al. Breast Cancer Res Treat. 2020 Nov;184(1):53-62. doi: 10.1007/s10549-020-05817-w.; 2. Alam I, et al. Vantictumab, an anti-FZD antibody, rescues the osteopetrotic bone phenotype in heterozygous ADO mice. Presented at ASBMR Annual Meeting, September 7, 2025, Presentation number SUN-582; 3. As per āshibio's website

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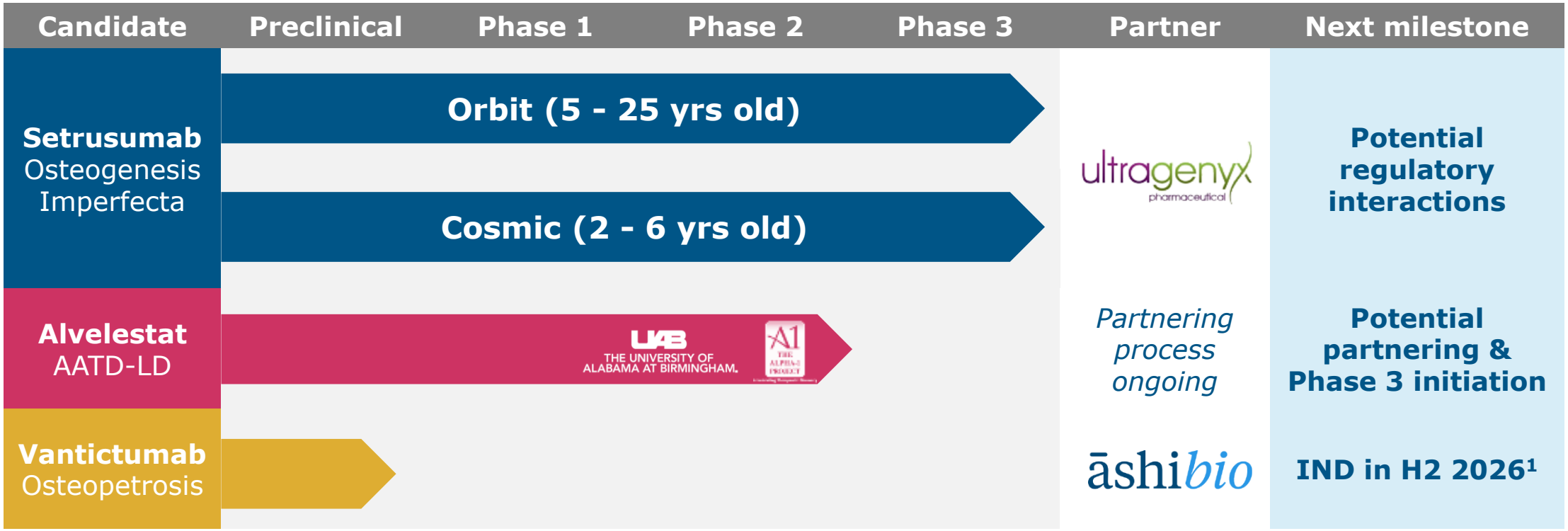
Key milestones

OIFE Meeting and AGM June 2025

Late-stage pipeline with financial discipline to execute into mid-2027



1. Per āshibio's website

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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