

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

FORM 8-K

**Current Report
Pursuant to Section 13 or 15(d) of
the Securities Exchange Act of 1934**

Date of Report (Date of earliest event reported): **January 12, 2026**

MEREO BIOPHARMA GROUP PLC

(Exact name of registrant as specified in its charter)

England and Wales
(State or other jurisdiction of
incorporation)

001-38452
(Commission File Number)

Not Applicable
(IRS Employer Identification No.)

**4th Floor, One Cavendish Place,
London, W1G 0QF
United Kingdom**

(Address of principal executive offices, including zip code)

+44-333-023-7300

(Registrant's telephone number, including area code)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol	Name of each exchange on which registered
American Depositary Shares, each representing five Ordinary Shares, par value £0.003 per share	MREO	The Nasdaq Stock Market LLC
Ordinary Shares, nominal value £0.003 per share*	*	The Nasdaq Stock Market LLC

*Not for trading, but only in connection with the listing of the American Depositary Shares on The Nasdaq Stock Market LLC.

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Item 7.01 Regulation FD Disclosure.

On January 12, 2026, Mereo BioPharma Group plc (the “Company”) issued a press release providing a corporate update. The full text of the press release issued in connection with the announcement is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

The Company has also made available on its website a presentation for use at the J.P. Morgan Healthcare Conference and future conferences and meetings with investors, analysts and others (the “Presentation”). A copy of the Presentation is furnished as Exhibit 99.2 to this Current Report on Form 8-K. The Company undertakes no obligation to update, supplement or amend the materials attached hereto as Exhibit 99.2.

The information contained in this Item 7.01, including Exhibit 99.1 and 99.2 shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), or otherwise subject to the liability of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended (the “Securities Act”) or the Exchange Act, except as shall be expressly set forth by reference in such a filing.

Item 8.01 Other Events.

On January 12, 2026, the Company updated its previous cash runway guidance. As of December 31, 2025, cash and cash equivalents were approximately \$41 million, which are expected to fund operations to mid-2027.

Forward Looking Statements

This Current Report on Form 8-K contains “forward-looking statements.” All statements other than statements of historical fact contained herein are forward-looking statements within the meaning of Section 27A of the Securities Act, and Section 21E of the Exchange Act. Forward-looking statements usually relate to future events and anticipated revenues, earnings, cash flows or other aspects of the Company’s operations or operating results. Forward-looking statements are often identified by the words “believe,” “expect,” “anticipate,” “plan,” “intend,” “foresee,” “should,” “would,” “could,” “may,” “estimate,” “outlook” and similar expressions, including the negative thereof. The absence of these words, however, does not mean that the statements are not forward-looking. These forward-looking statements are based on Mereo’s current expectations, beliefs and assumptions concerning future developments and business conditions and their potential effect on Mereo. While management believes that these forward-looking statements are reasonable as and when made, there can be no assurance that future developments affecting Mereo will be those that it anticipates. All of Mereo’s forward-looking statements involve known and unknown risks and uncertainties some of which are significant or beyond its control and assumptions that could cause actual results to differ materially from Mereo’s historical experience and its present expectations or projections. Such risks and uncertainties include, among others, the uncertainties inherent in the clinical development process; Mereo’s reliance on third parties to conduct and provide funding for its clinical trials; Mereo’s dependence on enrollment of patients in its clinical trials; and Mereo’s dependence on its key executives. You should carefully consider the foregoing factors and the other risks and uncertainties that affect Mereo’s business, including those described in the “Risk Factors” section of its latest Annual Report on Form 10-K, as well as discussions of potential risks, uncertainties, and other important factors in Mereo’s subsequent filings with the Securities and Exchange Commission. Mereo wishes to caution you not to place undue reliance on any forward-looking statements, which speak only as of the date hereof. Mereo undertakes no obligation to publicly update or revise any of our forward-looking statements after the date they are made, whether as a result of new information, future events or otherwise, except to the extent required by law.

Item 9.01 Financial Statements and Exhibits.

The following exhibit relating to Item 7.01 shall be deemed to be furnished, and not filed:

(d) Exhibits

<u>Exhibit No.</u>	<u>Description of Exhibit</u>
99.1	Press Release, dated January 12, 2026.
99.2	Presentation, dated January 12, 2026.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, hereunto duly authorized.

Date: January 12, 2026

MEREO BIOPHARMA GROUP PLC

By: /s/ Christine Fox

Name: Christine Fox
Title: Chief Financial Officer

Mereo BioPharma Provides Corporate Update

Additional data analyses from Orbit and Cosmic Phase 3 studies of setrusumab (UX143) in osteogenesis imperfecta ongoing to determine potential path forward for the program

*Cash balance of approximately \$41 million as of December 31, 2025;
runway guidance updated to mid-2027*

London, January 12, 2026 - Mereo BioPharma Group plc (NASDAQ: MREO) ("Mereo" or the "Company"), a clinical-stage biopharmaceutical company focused on rare diseases, today provided an update on its programs, setrusumab for the treatment of osteogenesis imperfecta (OI) and alvelestat, which is being studied for the treatment of alpha-1 antitrypsin deficiency-associated lung disease (AATD-LD), and revised its cash runway guidance.

Data from the Phase 3 Orbit and Cosmic studies of setrusumab in osteogenesis imperfecta, including data on bone mineral density, vertebral fractures, and patient reported outcomes on pain and physical function, will be presented at the J.P. Morgan Healthcare Conference.

The Company is also updating its previous cash runway guidance. As of December 31, 2025, cash and cash equivalents were approximately \$41 million, which are expected to fund operations to mid-2027.

"The reductions and delays in pre-commercial and manufacturing activities related to setrusumab that we implemented following the recent top-line data from the Phase 3 Orbit and Cosmic studies have extended our cash runway to mid-2027 and we will continue to tightly manage our resources as we assess potential next steps for the program, alongside our partner, Ultragenyx," said Dr. Denise Scots-Knight, Chief Executive Officer of Mereo. "There are no FDA or EMA approved treatments for people living with OI. Although bisphosphonates are used to improve bone mineral density, OI remains a high unmet need. We will continue to assess the totality of the Phase 3 trial data to determine next steps, including potential interactions with the regulators. In parallel, we are advancing partnering discussions for our Phase 3 ready program, alvelestat in AATD-LD."

Dr. Scots-Knight is scheduled to present at the 44th Annual J.P. Morgan Healthcare Conference on Wednesday, January 14, 2026 at 1:30pm PT (9:30pm GMT). A live audio webcast of the presentation can be accessed through the news and events section of the Company's website at www.mereobiopharma.com/news. Following the conclusion of the live event, an archived replay will be available on the Company's website.

Setrusumab (UX143)

As announced on December 29, 2025, the Phase 3 Orbit and Cosmic studies of setrusumab in OI did not achieve statistical significance against the primary endpoints of reduction in annualized clinical fracture rate compared to placebo or bisphosphonates, respectively. Both studies achieved strong statistical significance against the key secondary endpoint of improvement in bone mineral density versus comparator. The improvement in bone mineral density in the Cosmic study was associated with a decreased rate of fracture in this younger more highly fracturing patient population, although this was not statistically significant. The safety profile of setrusumab was consistent with that observed in prior studies.

Further analyses of the data from both studies are ongoing to determine the path forward, including potential regulatory interactions.

There is a high unmet medical need in OI, which is associated with a substantial clinical, humanistic and economic burden of illness due to the complexity of the condition and necessary medical care and support. As well as fractures, people living with OI present with a broad spectrum of skeletal features including bone

deformity, scoliosis and growth impairment. Pain is the most common and impactful sign, symptom or clinical event reported in children and adolescents.

There are no EMA or FDA approved treatments for OI (except for neridronate, which is approved nationally in Italy). Bisphosphonates are used off-label in children in Europe and the U.S., despite the lack of clinical evidence to support their effectiveness in reducing fractures.

Alvelestat (MPH-966)

The Company is continuing to advance key activities to support the planned initiation of the global Phase 3 pivotal study. Based on previous discussions with the FDA and EMA, Mereo anticipates a single Phase 3 trial enrolling approximately 220 early- and late-stage AATD-LD patients evaluating alvelestat over an 18-month treatment period will support regulatory submissions in both the U.S. and Europe. The primary efficacy endpoint for U.S. approval will be the St. George's Respiratory Questionnaire (SGRQ) Total Score, with lung density measured by CT scan serving as the primary endpoint for potential European regulatory approval.

Mereo continues to be in active discussions with potential partners for the Phase 3 development and commercialization of alvelestat.

Vantictumab (OMP18R5)

The Company out-licensed vantictumab for autosomal dominant osteopetrosis Type 2 (ADO2) to āshibio, Inc. whilst retaining European rights. āshibio, Inc. is responsible for funding the global program and following regulatory discussions, plans to initiate a Phase 2 study in 2H 2026. Vantictumab was previously investigated in Phase 1a/b oncology trials in around 100 patients with biomarker evidence of potential impact on osteoclast function and high bone turnover which led to fragility fractures in some patients. āshibio, Inc. reported promising pre-clinical data at ASBMR 2025 in ADO2 mouse model. Vantictumab significantly decreased areal bone mineral density and rescued the bone phenotype in the ADO2 mouse model.

About Mereo BioPharma

Mereo BioPharma is a biopharmaceutical company focused on the development of innovative therapeutics for rare diseases. The Company has three rare disease product candidates: setrusumab for the treatment of osteogenesis imperfecta (OI); alvelestat for the treatment of alpha-1 antitrypsin deficiency-associated lung disease (AATD-LD) and vantictumab for the treatment of autosomal dominant osteopetrosis type 2 (ADO2). The Company's partner for setrusumab, Ultragenyx Pharmaceutical Inc., has reported results from the Phase 3 portion of a pivotal Phase 2/3 study in pediatrics and young adults (5 to 25 years old) for setrusumab in OI and in the Phase 3 study in pediatric patients (2 to <7 years old). The partnership with Ultragenyx includes potential additional milestone payments of up to \$245 million and royalties to Mereo on commercial sales in Ultragenyx territories. Mereo has retained EU and UK commercial rights and will pay Ultragenyx royalties on commercial sales in those territories. Setrusumab has received orphan designation for osteogenesis imperfecta from the European Commission ("EC") and the FDA, PRIME designation from the EMA, and has Breakthrough Therapy designation and rare pediatric disease designation from the FDA. Alvelestat has received Orphan Designation for AATD from the EC and the FDA, and Fast Track designation from the FDA for AATD-LD. Following results from ASTRAEUS and ATALANTa in AATD-lung disease, the Company has aligned with the FDA and the EMA on the primary endpoints for a Phase 3 pivotal study which, if successful, could enable full approval in both the U.S. and Europe. The Company's partner for vantictumab, āshibio, Inc., is funding the global development program. Mereo has retained EU and UK commercial rights. Mereo has also entered into an exclusive global license agreement with ReproNovo SA, a reproductive medicine company, for the development and commercialization of leflutroazole, a non-steroidal aromatase inhibitor for the treatment of infertility in men with low testosterone. In addition, Mereo has two oncology product candidates, etigilimab, an anti-TIGIT; and navicixizumab for the potential treatment of late-line ovarian cancer. Navicixizumab has been partnered with Feng Biosciences, Inc. in a global licensing agreement that includes milestone payments and royalties.

Forward-Looking Statements

This press release contains "forward-looking statements" that involve substantial risks and uncertainties. All statements other than statements of historical fact contained herein are forward-looking statements within the meaning of Section 27A of the United States Securities Act of 1933, as amended, and Section 21E of the United States Securities Exchange Act of 1934, as amended. Forward-looking statements usually relate to future events and anticipated revenues, earnings, cash flows or other aspects of our operations or operating results. Forward-looking statements are often identified by the words "believe," "expect," "anticipate," "plan," "intend," "foresee," "should," "would," "could," "may," "estimate," "outlook" and similar expressions, including the negative thereof. The absence of these words, however, does not mean that the statements are not forward-looking. These forward-looking statements are based on the Company's current expectations, beliefs and assumptions concerning future developments and business conditions and their potential effect on the Company. While management believes that these forward-looking statements are reasonable as and when made, there can be no assurance that future developments affecting the Company will be those that it anticipates.

All of the Company's forward-looking statements involve known and unknown risks and uncertainties some of which are significant or beyond its control and assumptions that could cause actual results to differ materially from the Company's historical experience and its present expectations or projections. Such risks and uncertainties include, among others, the uncertainties inherent in the clinical development process; the Company's reliance on third parties to conduct and provide funding for its clinical trials; the Company's dependence on enrollment of patients in its clinical trials; and the Company's dependence on its key executives. You should carefully consider the foregoing factors and the other risks and uncertainties that affect the Company's business, including those described in the "Risk Factors" section of its Annual Report on Form 10-K, as well as discussions of potential risks, uncertainties, and other important factors in the Company's subsequent filings with the Securities and Exchange Commission. The Company wishes to caution you not to place undue reliance on any forward-looking statements, which speak only as of the date hereof. The Company undertakes no obligation to publicly update or revise any of our forward-looking statements after the date they are made, whether as a result of new information, future events or otherwise, except to the extent required by law.

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Mereo BioPharma
J.P. Morgan Conference



Disclaimer

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

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Forward-Looking Statements

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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.



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

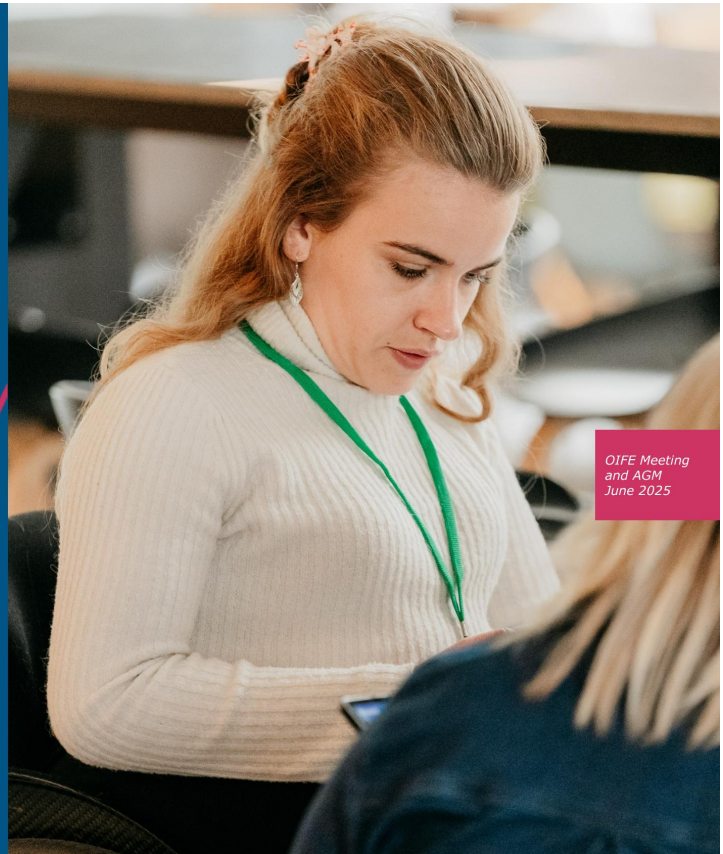


1. Based on internal forecast; 2. Blanco I et al. 2017. alpha-1 antitrypsin Pi*Z gene frequency and Pi*ZZ genotype numbers worldwide: an update. Int J COPD: 12 561-569; 3. Wu CC, Econs MJ, DiMeglio LA, et al. Diagnosis and management of osteopetrosis: consensus guidelines from the Osteopetrosis Working Group. J Clin Endocrinol Metab. 2017 Sep 1;102(9):3111-3123.



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 AFR¹ 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



1. Annualized fracture rate

Data presented at JP Morgan Healthcare Conference 2026

Two randomized Phase 3 studies provide large data set



	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	
Objective				
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)		
◆ Type I	43 (40.2)	21 (40.4)	Type I	12 (35.5)
◆ Type III	43 (40.2)	10 (19.2)	Type III	15 (44.1)
◆ Type IV	21 (19.6)	21 (40.4)	Type IV	7 (20.6)
◆ Peds 5 to <12 yo	44 (41.1)	23 (44.2)	Peds 2 to 7 yo	34 (49.3)
◆ Teens 12 to <18 yo	47 (43.9)	21 (40.4)		35 (50.7)
◆ Adults 18 to 26 yo	16 (15.0)	8 (15.4)		



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	
	Setrusumab	Placebo	Setrusumab	IV-BP
Baseline Fractures¹				
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

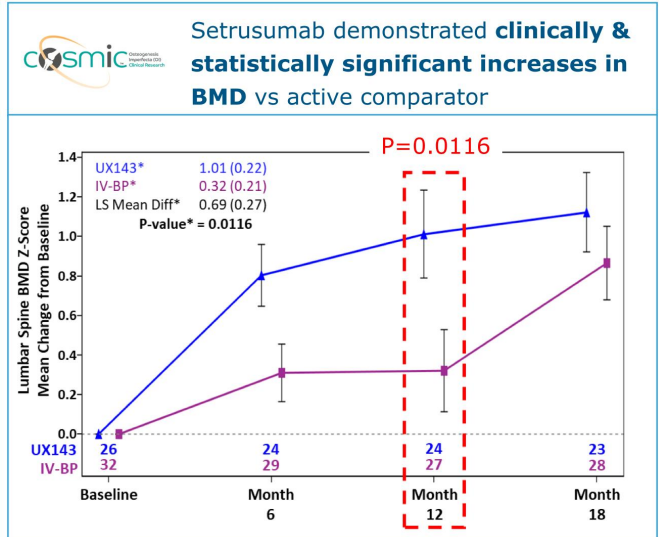
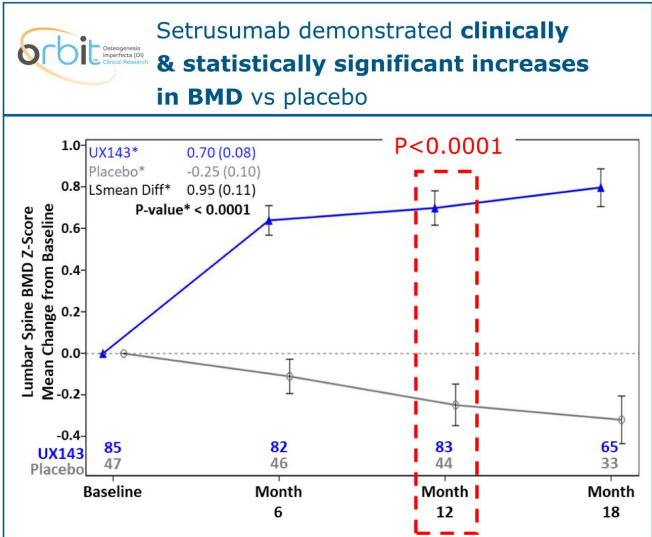
Cosmic had no rescue criteria since it was active treatment controlled

- 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



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



*Based on Month 12 timepoint

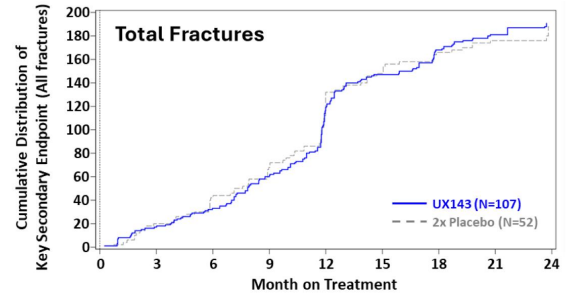
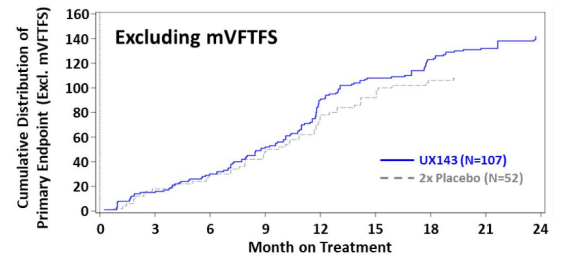
Data presented at JP Morgan Healthcare Conference 2026

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)
<i>P-value</i> ²		<i>0.305</i>	<i>0.865</i>



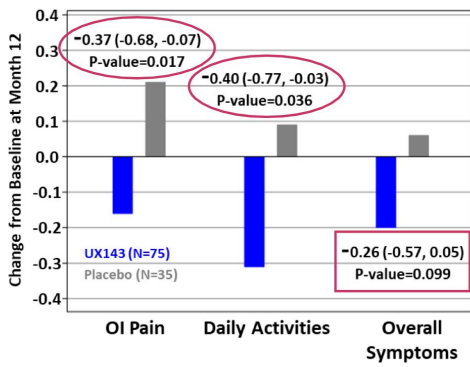
1. Radiographically confirmed fractures, excluding morphometric vertebral fractures and fingers, toes, face, and skull;
2. Negative Binomial model

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

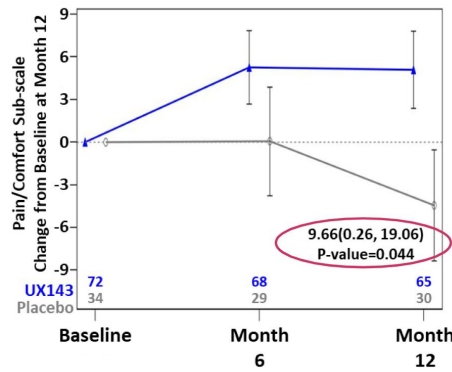


Peds/Teens patients constitute 85% of subjects in Orbit Ph3 study (135/159)

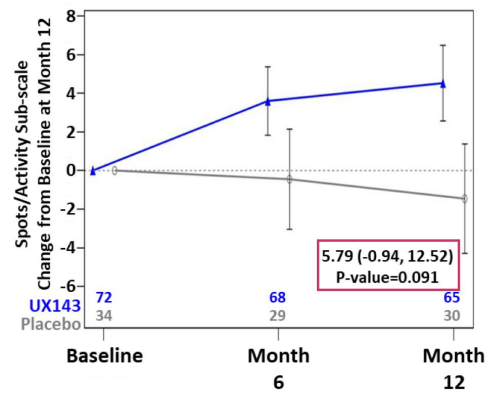
Patient Global Impression Scale of Severity (PGIS)



Pain/Comfort POSNA-PODCI



Sports/Activity POSNA-PODCI



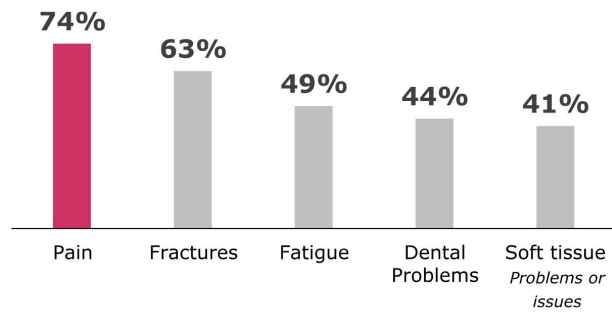
12-month assessment is as randomized and most important as no patients had exited due to rescue criteria



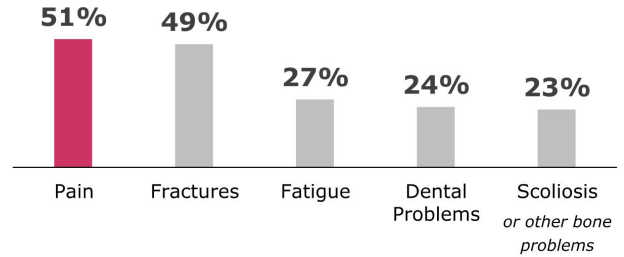
Pain is the most common & impactful sign, symptom or clinical event amongst peds and teens with OI



Top 5 clinical events, signs and symptoms in proxy peds & adolescents with OI by prevalence¹



Top 5 clinical events, signs and symptoms in proxy peds & adolescents ranked as mod-to-severe impact¹



Impact of OI on areas of QoL in children, % of proxy children responding as activity mod-to-severely impacted²



70%
Leisure Activities



52%
Social Life



50%
School attendance



49%
Daily tasks



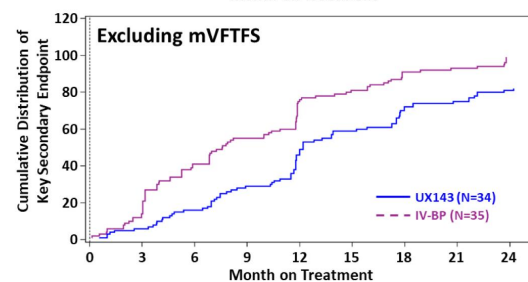
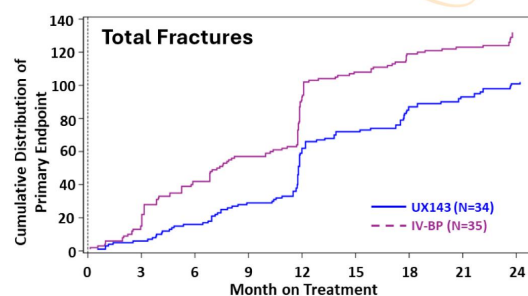
1. Adapted from Westerheim et al, 2024.; 2. Data on file, light red portion reflects "Mild or very mildly impacted"

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)
<i>P-value</i> 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 mV¹)	84	104	1	18
All fractures (Excluding mVFTFS²)	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*

	Est. Setrusumab AFR (95% CI)	All Vertebral Fractures
Negative Binomial Model (95% CI)	0.14 (0.04, 0.51)	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)

	Est. Setrusumab AFR (95% CI)	Only Morphometric Vertebral Fractures
Negative Binomial Model (95% CI)	0.15 (0.04, 0.51)	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

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



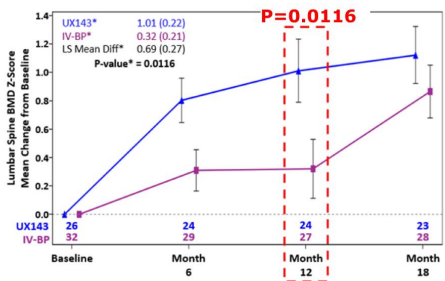
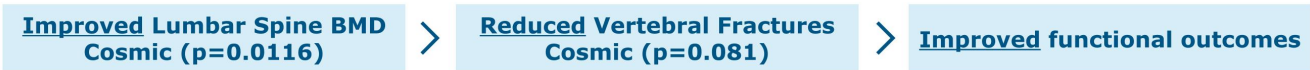
Treatment emergent adverse events (TEAE)	<ul style="list-style-type: none"> • No serious-related TEAEs • Low incidence (<2%) severe-related TEAEs • Low incidence (<3%) TEAE's leading to treatment or study discontinuation 	<ul style="list-style-type: none"> • No serious related TEAEs • Low incidence (<3%) severe-related TEAE • No TEAEs leading to treatment discontinuation or study discontinuation
Adverse events of special interest (AESI)	<ul style="list-style-type: none"> • No ischemic CV Events • No hypersensitivity reactions related to UX143 • One TEAE in neurologic sequelae due to bony overgrowth <ul style="list-style-type: none"> ○ Radial nerve injury following a surgical procedure 	<ul style="list-style-type: none"> • No ischemic CV events • No hypersensitivity reactions related to UX143 • No neurologic sequelae due to bony overgrowth
Deaths	No Deaths	No Deaths



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**



	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





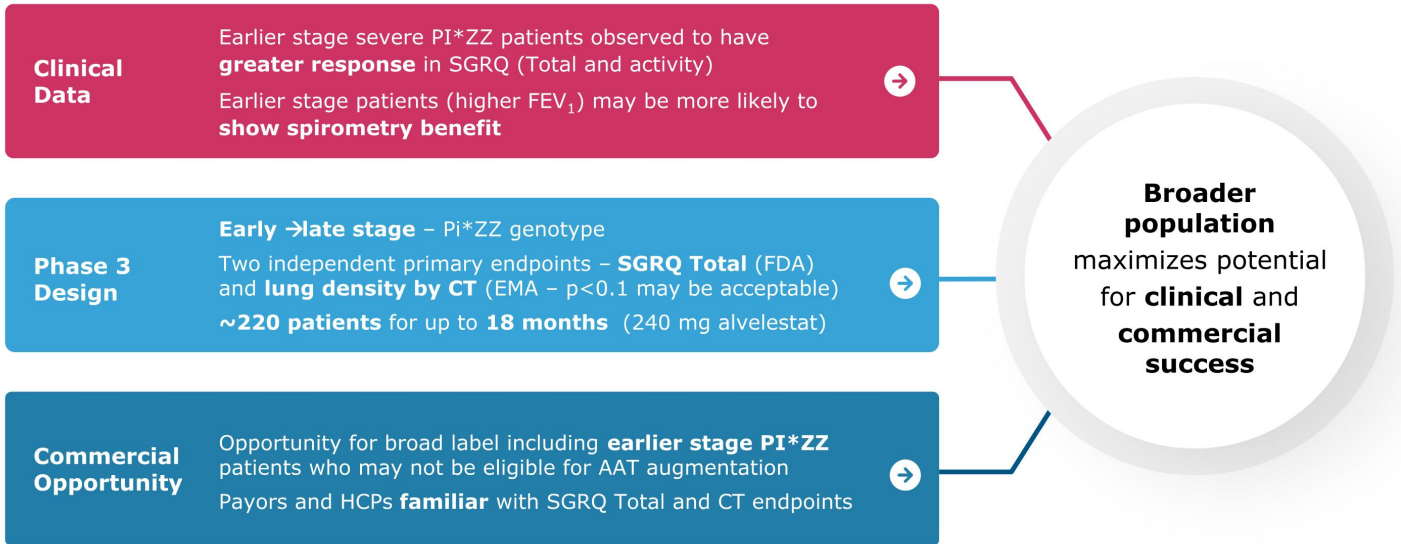
Alvelestat (MPH966)

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



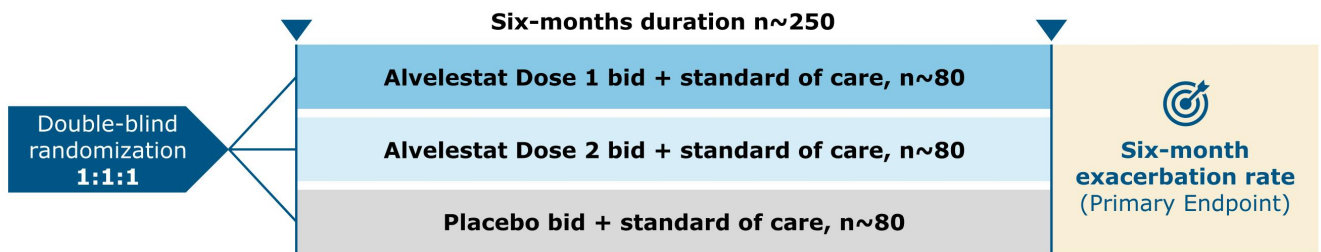
Alpha 1 Support
Group UK
Information Day
September 2023

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



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

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**







Vantictumab

Osteopetrosis: a rare bone disease with high unmet need

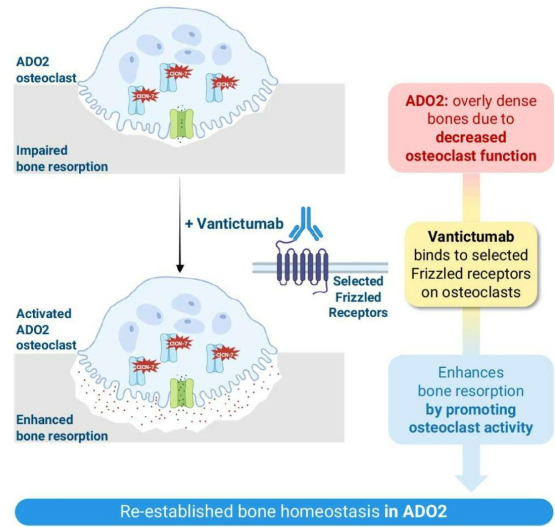


Significant opportunity in underserved rare bone disorder

ADO2 overview¹

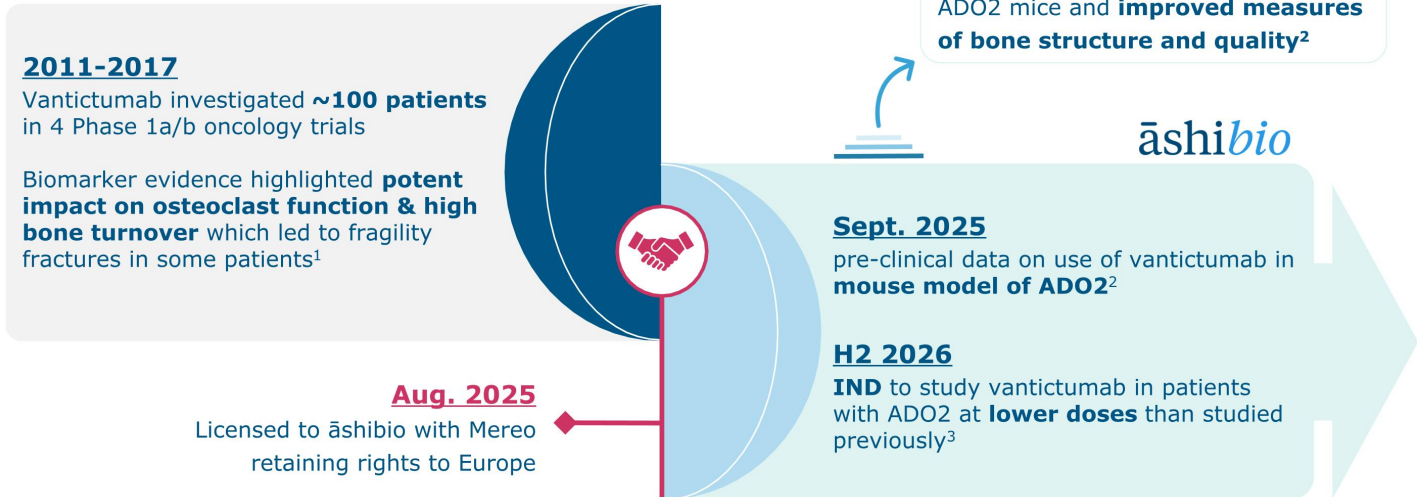
	ADO2 is an inherited metabolic bone disorder characterized by impaired osteoclast function
	Dense, brittle bones lead to multiple fractures, osteomyelitis, bone pain, low blood counts, significant morbidity
	No approved therapy
	1 in 20,000 incidence with onset typically in late childhood
Clear unmet need for a therapy that rescues osteoclast function, improves bone structure, and reduces morbidity	

Vantictumab Mechanism of Action²



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 ashbio's website

Vantictumab development timelines



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



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



Key milestones



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

Candidate	Preclinical	Phase 1	Phase 2	Phase 3	Partner	Next milestone
Setrusumab Osteogenesis Imperfecta	Orbit (5 - 25 yrs old)				ultragenyx <small>pharmaceutical</small>	Potential regulatory interactions
	Cosmic (2 - 6 yrs old)					
Alvelestat AATD-LD					Partnering process ongoing	Potential partnering & Phase 3 initiation
Vantictumab Osteopetrosis					āshibio	IND in H2 2026 ¹

Thank you

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

