



December 29, 2025

Dear OI Community,

Ultragenyx announced results from the Phase 3 Orbit and Cosmic studies for setrusumab, an investigational fully human monoclonal antibody for the treatment of osteogenesis imperfecta (OI). Ultragenyx is sharing the below update with key details about this announcement, in response to the community's request for timely information about setrusumab.

- Neither study achieved statistical significance against the primary endpoints of reduction in annualized clinical fracture rate compared to placebo or bisphosphonates, respectively.
- Both studies achieved the secondary endpoints of improvements in bone mineral density (BMD) against comparators with strong statistical significance.
- There was no change in the safety profile observed.

“We are surprised and disappointed by this result given the promising data from our Phase 2 study and the lack of approved treatment options available to patients with OI who live with significant pain and disease burden. We continue to explore the data to gain deeper understanding of the findings,” shared Emil Kakkis, M.D., Ph.D., chief executive officer and president of Ultragenyx.

What happens next?

Ultragenyx is conducting additional analyses on the data across both studies, including on other bone health and clinical endpoints beyond fractures. For individuals enrolled in any setrusumab study, the open-label extension remains active, and participants can continue receiving study drug while the company completes its additional analyses. Specific questions about your individual treatment should be directed to your healthcare provider.

We are grateful to the entire OI community for your support of this program over the past 8 years, as well as to the individuals, parents, and caregivers who contributed to our clinical studies. While we don't yet have a timeline to provide future updates, we are in close contact with patient advocacy groups and will continue to share timely information, as we are able, to ensure that the OI community can stay informed.

On behalf of the Ultragenyx team,

A handwritten signature in black ink that reads "Jenny McCue".

Jenny McCue
Executive Director, Patient Advocacy