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**UNITED STATES DISTRICT COURT  
NORTHERN DISTRICT OF CALIFORNIA**

STEVEN BAILEY, Individually and on Behalf  
of All Others Similarly Situated,

Plaintiff,

v.

ULTRAGENYX PHARMACEUTICAL INC.,  
EMIL D. KAKKIS, and ERIC CROMBEZ,

Defendants.

Case No. 26-cv-1097

CLASS ACTION

**COMPLAINT FOR VIOLATIONS OF  
THE FEDERAL SECURITIES LAWS**

DEMAND FOR JURY TRIAL

1 Plaintiff Steven Bailey (“Plaintiff”), individually and on behalf of all other persons  
2 similarly situated, by his undersigned attorneys, alleges in this Complaint for violations of the  
3 federal securities laws (the “Complaint”) the following based upon knowledge with respect to his  
4 own acts, and upon facts obtained through an investigation conducted by his counsel, which  
5 included, *inter alia*: (a) review and analysis of relevant filings made by Ultragenyx Pharmaceutical  
6 Inc. (“Ultragenyx” or the “Company”) with the United States Securities and Exchange  
7 Commission (the “SEC”); (b) review and analysis of Ultragenyx’s public documents, conference  
8 calls, press releases, and stock chart; (c) review and analysis of securities analysts’ reports and  
9 advisories concerning the Company; and (d) information readily obtainable on the internet.

10 Plaintiff believes that further substantial evidentiary support will exist for the allegations  
11 set forth herein after a reasonable opportunity for discovery. Most of the facts supporting the  
12 allegations contained herein are known only to the defendants or are exclusively within their  
13 control.

#### 14 NATURE OF THE ACTION

15 1. This is a federal securities class action on behalf of all investors who purchased or  
16 otherwise acquired Ultragenyx common stock between August 3, 2023, to December 26, 2025,  
17 inclusive (the “Class Period”), seeking to recover damages caused by Defendants’ violations of  
18 the federal securities laws (the “Class”).

19 2. Defendants provided investors with material information concerning Ultragenyx’s  
20 expected results for its Phase III Orbit and Cosmic Studies, which tested setrusumab (UX 143) in  
21 patients with Osteogenesis Imperfecta (“OI”). Defendants’ statements included, among other  
22 things, confidence in setrusumab’s ability to ultimately trigger a decrease in the OI patients’  
23 annualized fracture rate, alongside confidence in the study designs to demonstrate such ability and  
24 reduce testing variability that could interfere with such a result.

25 3. Defendants provided these overwhelmingly positive statements to investors while,  
26 at the same time, disseminating materially false and misleading statements and/or concealing  
27 material adverse facts concerning the true state of setrusumab’s potential and the true risk inherent  
28 in the study protocols put forth; notably, that, while setrusumab does increase material bone

1 density, this increase does not correlate to a decrease in annualized fracture rates or otherwise the  
2 Phase III Orbit and Cosmic studies were much less likely to be able to demonstrate such a link  
3 than management claimed. Such statements absent these material facts caused Plaintiff and other  
4 shareholders to purchase Ultragenyx's securities at artificially inflated prices.

5 4. Investors began to question the veracity of Defendants' public statements on July  
6 9, 2025, following Ultragenyx's press release which informed investors that the Phase III Orbit  
7 study failed to achieve statistical significance for the second interim analysis. In pertinent part,  
8 Defendants announced the Phase III Orbit and Cosmic studies would now be "progressing toward  
9 final analysis."

10 5. Investors and analysts reacted immediately to Ultragenyx's revelation. The price of  
11 Ultragenyx's common stock declined dramatically. From a closing market price of \$41.44 per  
12 share on July 9, 2025, Ultragenyx's stock price fell to \$31.03 per share on July 10, 2025, a decline  
13 of about 25.12% in the span of just a single day.

14 6. Notwithstanding the July 9 disclosures, Ultragenyx and the Individual Defendants  
15 continued to mislead investors. Defendants continued to create the false impression that they  
16 possessed reliable information pertaining to the success of the Phase III Orbit and Cosmic Studies,  
17 while also minimizing the risk from study variability. Defendants repeatedly insisted they were  
18 confident that setrusumab's ability to increase material bone density would necessarily translate  
19 to a reduction in the annualized fracture rate of the type 1, 3, or 4 OI patients and, further, remained  
20 confident in the study design created to facilitate the ability to detect the difference in fracture rate  
21 between the treatment and control populations.

22 7. On December 29, 2025, the full truth emerged. Ultragenyx announced that both its  
23 Phase III Orbit and Cosmic Studies had not "achieved statistical significance against the primary  
24 endpoints of reduction in annualized clinical fracture rate compared to placebo or bisphosphonates,  
25 respectively." The Company attributed the study failure to a "low fracture rate in the placebo  
26 group" of Orbit and a trend that fell shy of statistical significance in Cosmic.

27 8. Investors and analysts reacted immediately to Ultragenyx's revelation. The price of  
28 Ultragenyx's common stock declined dramatically. From a closing market price of \$34.19 per

1 share on December 26, 2025, Ultragenyx’s stock price fell to \$19.72 per share on December 29,  
2 2025, a decline of about 42.32% in the span of just a single day.

3 **JURISDICTION AND VENUE**

4 9. Plaintiff brings this action, on behalf of himself and other similarly situated  
5 investors, to recover losses sustained in connection with Defendants’ fraud.

6 10. The claims asserted herein arise under and pursuant to §§10(b) and 20(a) of the  
7 Exchange Act (15 U.S.C. §§ 78j(b) and 78t(a)) and Rule 10b-5 promulgated thereunder by the  
8 SEC (17 C.F.R. §240.10b-5).

9 11. This Court has jurisdiction over the subject matter of this action pursuant to 28  
10 U.S.C. §§1331 and 1337, and Section 27 of the Exchange Act, 15 U.S.C. §78aa.

11 12. Venue is proper in this District pursuant to §27 of the Exchange Act and 28 U.S.C.  
12 §1391(b), as Defendant Ultragenyx is headquartered in this District and a significant portion of its  
13 business, actions, and the subsequent damages to Plaintiff and the Class, took place within this  
14 District.

15 13. In connection with the acts, conduct and other wrongs alleged in this Complaint,  
16 Defendants, directly or indirectly, used the means and instrumentalities of interstate commerce,  
17 including but not limited to, the United States mail, interstate telephone communications and the  
18 facilities of the national securities exchange.

19 **THE PARTIES**

20 14. Plaintiff purchased Ultragenyx common stock at artificially inflated prices during  
21 the Class Period and was damaged upon the revelation of the Defendants’ fraud. Plaintiff’s  
22 certification evidencing his transaction(s) in Ultragenyx is attached hereto.

23 15. Ultragenyx Pharmaceutical Inc. is a California corporation with its principal  
24 executive offices located at 60 Leveroni Court, Novato, CA 94949. During the Class Period, the  
25 Company’s common stock traded on the NASDAQ Stock Market (the “NASDAQ”) under the  
26 symbol “RARE.”

27 16. Defendant Emil D. Kakkis (“Kakkis”) was, at all relevant times, the Founder,  
28 President, Chief Executive Officer, and Director of Ultragenyx.

1 17. Defendant Eric Crombez (“Crombez”) was, at all relevant times, the Chief Medical  
2 Officer and Executive Vice President of Ultragenyx.

3 18. Defendants Kakkis and Crombez are sometimes referred to herein as the  
4 “Individual Defendants.” Ultragenyx together with the Individual Defendants are referred to herein  
5 as the “Defendants.”

6 19. The Individual Defendants, because of their positions with the Company, possessed  
7 the power and authority to control the contents of Ultragenyx’s reports to the SEC, press releases,  
8 and presentations to securities analysts, money and portfolio managers, and institutional investors,  
9 *i.e.*, the market. Each Individual Defendant was provided with copies of the Company’s reports  
10 and press releases alleged herein to be misleading prior to, or shortly after, their issuance and had  
11 the ability and opportunity to prevent their issuance or cause them to be corrected. Because of their  
12 positions and access to material non-public information available to them, each of these Individual  
13 Defendants knew that the adverse facts specified herein had not been disclosed to, and were being  
14 concealed from, the public, and that the positive representations which were being made were then  
15 materially false and/or misleading. The Individual Defendants are liable for the false statements  
16 pleaded herein, as those statements were each “group-published” information, the result of the  
17 collective actions of the Individual Defendants.

18 20. Ultragenyx is liable for the acts of the Individual Defendants, and its employees  
19 under the doctrine of respondeat superior and common law principles of agency as all the wrongful  
20 acts complained of herein were carried out within the scope of their employment with  
21 authorization.

22 21. The scienter of the Individual Defendants, and other employees and agents of the  
23 Company are similarly imputed to Ultragenyx under respondeat superior and agency principles.

24 **SUBSTANTIVE ALLEGATIONS**

25 **A. Company Background**

26 22. Ultragenyx is a biopharmaceutical company focused on rare and ultrarare genetic  
27 disorders. The Company’s product candidates are typically in-licensed from partnerships or  
28 academic institutions.

23. Pertinently, Ultragenyx is testing setrusumab a.k.a. UX143 for the treatment of Osteogenesis Imperfecta (“OI”). Ultragenyx has proceeded to Phase III analysis through its Orbit and Cosmic studies, evaluating setrusumab’s ability to reduce patients’ annualized fracture rate (“AFR”).

**B. The Defendants Materially Misled Investors Concerning the Phase III Orbit and Cosmic Studies for Setrusumab in Patients with Osteogenesis Imperfecta.**

August 3, 2023

24. On August 3, 2023, Defendants conducted an earnings call corresponding to the release of their second quarter fiscal 2023 results. In pertinent part, Defendant Kakkis confidently claimed that if their drug, setrusumab or UX143, could continue to show bone density growth, it would resultantly correlate to reduced AFR, stating:

I'll spend a few minutes discussing the osteogenesis imperfecta . . . program . . . In June, we reported exciting data from the Phase II dose-finding portion of the pivotal Orbit study, showing statistically significant increase in levels of serum PINP, a sensitive marker bone formation.

The bone production response to these patients was extraordinary. This led to a rapid bone-building effect following just 3 months of treatment with setrusumab, resulting in nearly 10% in lumbar bone mineral density. At baseline, these patients had very limited bone mineral density, with an average Z-score in the 20 mg cohort of minus 2.12, which means the bone mineral density were 2 standard deviations below the mean of normal patients for their age.

After 3 months on therapy, the mean Z-score increased by plus 0.65 points, resolving nearly 1/3 of the deficit from normal in a relatively short period of time. As we've said before, **patients are showing meaningful improvements in bone health**, and we are highly encouraged with how they're doing. **Improved bone health refers to the instance of fractures**, bone pain and relative global health and activity of the patients.

...

In July, we announced that we initiated dosing patients in 2 Phase III studies evaluating setrusumab in 2 different age groups. **The Phase III portion of the pivotal Orbit study is evaluating the effect of setrusumab compared to placebo on annualized clinical fracture rate in patients 5 to 25 years old.**

**The newly initiated Phase III Cosmic study is an active controlled study evaluating setrusumab compared to IV bisphosphonate therapy on annualized total fractured patients aged 2 to 5 years old.** Enrollment in both of these studies

1 is going well so far in part because the Phase II data has generated a lot of  
2 excitement for the potential setrusumab for both the clinical sites and from the  
3 patient community.

4 (Emphasis added).

5 25. During the question-and-answer segment of the call, Defendant Kakkis spoke  
6 directly to Ultragenyx's confidence in the Phase III Orbit and Cosmic studies (the "Phase III OI  
7 Studies") during the following pertinent exchange:

8 <Q: Liisa Ann Bayko – Evercore ISI Institutional Equities – Managing Director &  
9 Fundamental Research Analyst> Can you just give us a sense of kind of your level  
10 of confidence about what you're seeing in the OI program and how the changes in  
11 bone mineral density relate to potential changes you might see in fracture?

12 <A: Emil D. Kakkis> We have a **high level of confidence that the magnitude of**  
13 **bone mineral density we saw at 3 months was already sufficient enough to**  
14 **improve the strength of bones and probably reduce fractures at that level we saw**  
15 **at 3 months in.** So we have high confidence in the fact that bone mineral density  
16 will be improved by this mechanism, anti-sclerostin mechanism, where you're  
17 getting anabolism or production of new bone will translate into fracture  
18 improvements.

19 And we've talked about the nonclinical data in the past, but we'll be able to talk  
20 more about this at the October Analyst Day to provide that support, **but we have a**  
21 **high level of confidence that the BMD produced by an anti-sclerostin like**  
22 **setrusumab will translate into fracture reduction.**

23 <Q: Liisa Ann Bayko> Just as a follow-up on that. Can you explain to me the  
24 amount of sort of the bone mineral density levels of OI patients? How do they relate  
25 to those of osteoporosis patients? Because I'm just trying to kind of relate the 2  
26 changes, and the amount of changes you're seeing to what we -- outcomes we've  
27 seen in osteoporosis. It seems to me maybe that bone mineral density levels are  
28 slightly different. Can you expand on that at all?

<A: Emil D. Kakkis> Well, sure, Liisa. What we said for this population, this study,  
is that the mean bone mineral density was minus 2.12, which means 2 standard  
relatable mean of normal people. Now osteoporosis patients have reduced bone  
mineral density. I don't have for you exact comparisons to put forth.

But I would say the mean of minus 2 standard deviations is pretty low on the bone  
scale. And if you look at the range, we had patients as low as minus 4 standard  
deviation. So these patients have, I think, a more severe on average bone mineral  
density problem than an average osteoporosis patient would, and therefore, have  
more need of bone production.

1 *What has been the misunderstanding is everyone thought that the defect in the*  
2 *collagen was why the bones are fracturing. What we're kind of trying to say is*  
3 *actually, while that may be a factor, it's in fact the effect of that mutation on bone*  
4 *production appears to be a bigger factor. And that's something we can change*  
*with setrusumab, and that's why we think we're going to have an important effect*  
*on OI.*

5 (Emphasis added).

6 November 2, 2023

7 26. On November 2, 2023, Defendants conducted an earnings call corresponding to  
8 their third quarter fiscal 2023 results. During the call, Defendant Crombez discussed Ultragenyx's  
9 ORBIT Phase II results and how such learnings could impact Phase III, stating, in pertinent part:

10 Importantly, a subset of 5- to 12-year olds saw nearly a 20% increase in bone  
11 mineral density with a Z-score change of 1.19. *These improvements in bone*  
12 *mineral density across the 24 patients treated in the ORBIT Phase II translated*  
13 *to a 67% reduction in the annualized fracture rate following treatment with*  
*setrusumab for at least 6 months.* 20 of the 24 patients did not experience any new  
fractures in the 6 months following treatment with setrusumab.

14 For the 4 who did have a radiographically confirmed fracture, many of them  
15 occurred early on in treatment or had a traumatic precipitating event. The data is all  
16 the more compelling because many of the patients in this study were previously  
17 treated with phosphonates over the 2 years prior to dosing with setrusumab. During  
18 this time, these patients continued to see a high annualized fracture rate with many  
fractures occurring with very minimal activity. These types of fractures are referred  
to as fragility fractures and examples include fractures occurring during sleep or  
when transferring out of a chair.

19 What we heard from 2 principal investigators who joined us at Analyst Day is that  
20 *they are not seeing fragility fractures in these studies, patients treated with*  
21 *setrusumab and that many of these kids are now feeling strong enough to engage*  
*in more physical activities with friends and family.*

22 (Emphasis added).

23 27. A question-and-answer segment again followed the Company's prepared remarks,  
24 during which Defendant Kakkis highlighted the lack of concern investors should have over  
25 increased activity during and post-treatment on the analysis of setrusumab during the following  
26 pertinent exchange:

27 <Q: Dae Gon Ha – Stifel, Nicolaus & Company, Inc. – Research Analyst> Two,  
28 maybe on GTX-102 and the setrusumab. Just wanted to clarify on setrusumab,

1 Emil, did you say enrollment completion in 1Q '24? Is that for both ORBIT as well  
2 as COSMIC? And are you placing any protocol restrictions on strenuous activity?  
3 I mean it's encouraging their being more active and fearless but in terms of  
endpoints, I wonder if that could kind of create a confounder . . .

4 <A: Emil D. Kakkis> Very good, Dae Gon. So for setrusumab, we're talking about  
5 both ORBIT and COSMIC in terms of finishing enrollment. I think we're likely.  
6 But the main one we're talking about is ORBIT, which is the main driver. And I  
7 believe both of them should get done in that time frame. And in terms of this control  
8 of excise [sic] or the hazard risk, if someone is feeling better and exercising, well,  
9 that's already what's happening in Phase II. ***People were a lot more active and what  
was, actually, on the plus side is that they were active and a lot of them where  
they were falling and had fractures unnecessarily. So while there is some risk  
that they might be doing more, there was one person who played volleyball, that  
they hadn't been playing.***

10 We're actually -- ***overall feeling is that the pattern of having falls and fractures  
seems to be better.*** And so our ***net effect overall, as we think even with increased  
activity, there will be a reduction in fractures,*** which is really the best thing  
11 possible, that is, a kid is going to be active and to have a reduction of fractures while  
12 being active. So ***we're not so worried about the, let's say, the noise of having more  
fracture risk at this point. It looks like you still see the effect well, even if there is  
some risk there.***

13  
14  
15 (Emphasis added).

16 May 2, 2024

17 28. On May 2, 2024, Defendants published their first quarter fiscal 2024 results. During  
18 the corresponding earnings call, Defendant Kakkis briefly discussed the planned interim analysis  
19 for the Orbit and Cosmic studies, noting, in pertinent part, the following:

20 For the UX143 Phase 3 portion of the Orbit study, there are 2 interim analyses  
21 planned with the first anticipated by the year-end or early 2025. The first analysis  
22 will have a stringent threshold of p less than or equal to 001. If the threshold is not  
met, a second interim analyses will occur a few months later, followed by a final  
analysis at 18 months.

23 Interim analyses will not report to the company by the Data Monitoring Committee  
24 unless they are positive. In the event of a positive interim analyses, we would share  
25 that outcome, but top line results will not be announced immediately as the study  
26 would require patients to complete a final visit and time to collect and prepare the  
data for a formal analysis.

27 29. Following the Company's prepared remarks, Defendants Kakkis and Crombez  
28 fielded a question concerning the risk factors of the Phase III OI Studies. Pertinently, Defendants

1 addressed how they planned the study to control for fracture rate in order to give the studies the  
2 optimal chance to achieve the designated AFR end points:

3 <Q: Kristen Brianne Klusta – Cantor Fitzgerald & Co. – Analyst> We often get  
4 asked about setting expectations for the first interim readouts for setrusumab. Could  
5 you please help us frame what are some of the factors that are controllable that we  
6 can kind of help to predict in advance? And then some of the items where we're  
7 less sure about. And again, how to help frame these 2 expectations?

8 <A: Emil D. Kakkis> Well, I think our Phase 2 data kind of lay down what I think  
9 we're going to expect. I would expect it to be -- **that a reduction would be very**  
10 **similar to what we've seen, if not better.** So we found there with only a minimum  
11 of 6 months, an average of 9 months exposure, 67% reduction. The patients we're  
12 enrolling are very comfortable with that. **If anything, enrolled patients might have**  
13 **a higher fracture rate, I think. And so we would expect that reduction to be**  
14 **something that you'd expect to see.** Those are -- I don't know if you consider --  
15 when you enroll patients with fractures, it's not exactly controllable. They are who  
16 they are. **But because we have a threshold requirement to get in the trial, we're**  
17 **essentially eliminating patients who would have very low fracture rates and**  
18 **wouldn't necessarily be able to demonstrate benefit in that period of time.**

19 I think with the type of patients enrolled, the number of which type, **I think we've**  
20 **set ourselves up to replicate what we saw before. And I really don't see any**  
21 **uncontrolled factors.** I don't know, Eric, if you have anything.

22 <A: Eric Crombez> Yes, definitely. I mean, **I think the biggest controllable factor**  
23 **was really enrollment rate and the studies are fully enrolled.** Yes, we know the  
24 types of patients, and it was good to get a good mix of 1, 3 and 4 in there. I would  
25 say, yes, I would agree, **the uncontrollable factor may be,** especially when you're  
26 first initiating treatment **in the first couple of months, you may have some patients**  
27 **arriving with fractures before, setrusumab really takes effect there.** But there is a  
28 degree of unpredictability with fractures.

<A: Emil D. Kakkis> It's probably also the fact that some people -- **some of the**  
**kids like feel really good and are getting more active. People are worried maybe**  
**that caused more fractures, but it didn't look like that was true or that they felt**  
**they didn't fracture.** So we actually are not concerned about the fact that his [sic]  
**might feel good and start being more active. It doesn't look like it's going to cause**  
**a problem that looks like their bones are stronger and they're doing great.**

So the **truth is that more activity probably strengthens the bone faster because the**  
**action actually puts strain in the bone, the bone actually are strengthened by that**  
**actual action.** So thank you for the question.

(Emphasis added).

August 1, 2024

1  
2 30. On August 1, 2024, Defendants presented their second quarter results for the year  
3 and again spoke to the issue of being able to show a reduction of AFR in their Phase III OI Studies.  
4 In pertinent part, the following exchanges occurred during the question-and-answer segment of the  
5 call:

6 <Q: Salveen Jaswal Richter – Goldman Sachs Group, Inc. – Vice President> Could  
7 you help us understand how you look on OI with regard -- how you look at OI with  
8 regard to the Phase II data translating to Phase III here? And particularly, as the  
9 patients see improvements, how that kind of impacts the rate of fractures here for  
10 the population, and your assumptions around that in the Phase III trial?

11 <A: Emil D. Kakkis> Well, I think what we've shown at the 14-month data was, in  
12 fact, that the bone marrow density continues to increase dramatically. And the p-  
13 value got much smaller. So remember, that's looking at all the patients, not just the  
14 median, but it tells you -- ***the p-value declining substantially tells you that all the***  
15 ***patients are moving toward a reduction in fractures. So we feel that the effect is***  
16 ***very large.***

17 In terms of translating to Phase III, we know from the data we had in a few placebos  
18 that they do not see bone marrow density improvement during this period of time.  
19 So there will be no placebo effect from that.

20 With regard to fractures, ***fractures are dependent on both disease severity and also***  
21 ***environmental factors like what the patient is doing. Our expectation is that***  
22 ***patients, when they feel better, could start doing more work, but what we have***  
23 ***seen is patients that have gotten stronger and have been on treatment for a longer***  
24 ***period of time will have falls and not have fractures. So we feel pretty confident***  
25 ***that the strength of bones as such to even compensate for any change might occur***  
26 ***because patients are more active.*** But we do think that the way patients feel their  
27 activity will bode well for supportive clinical data and how the patients are doing,  
28 which I think will support the value of the product and its clinical meaning for this.

...

23 <Q: Kristen Brianne Klusta – Cantor Fitzgerald & Co. – Analyst> Congrats on a  
24 great quarter. On setrusumab, I wanted to ask if you think that there are any benefits  
25 this drug could potentially show as it relates to the pain these patients experience.  
26 Is there a reason to think that both reducing those fractures and putting down better  
27 bone has the potential to have an impact on pain?

28 <A: Emil D. Kakkis> Yes. Our impression from the Phase II patients, particularly  
with their increased activity, they're feeling better. They're having less pain. And  
while we look -- talk about fractures all the time, OI patients have weak bones. And  
what that means is lots of microfractures. So if they do some heavily strong activity,

1 they'll feel terrible the next day because they probably have induced a bunch of  
2 microfractures. So it's not a single point fracture.

3 ***What we can see from the patients treated at the 1-year point or beyond? Patients***  
4 ***are having much more activity, not needing wheelchairs, not being as afraid of***  
5 ***physical activity. So we have confidence that stronger bones will reduce***  
6 ***microfractures and will improve pain.*** And so we are evaluating both pain, quality  
7 of life and other measures in the study. ***And it's a large enough study that it should***  
8 ***help us power those endpoints.*** So we think it's one of the ways that will make, I  
9 think, setrusumab a really important therapy for OI.

10 <Q: Kristen Brianne Klusta> And then just on that point, I know people sometimes  
11 ask, if you're feeling better and you're doing more activities, does that open the door  
12 for any potential fractures? But maybe on the other end of that spectrum, if people  
13 are exercising and doing more activity, could that help even further slowdown any  
14 type of bone loss or density loss?

15 <A: Emil D. Kakkis> Yes, it's a very good point. ***I think it certainly could increase***  
16 ***fracture risk.*** We did have a patient who started doing sports again and did have a  
17 fracture, but I'm not the one to tell a patient, you feel great now, now don't do  
18 anything with that, right? It's just not rational to think that. ***What I will say is these***  
19 ***patients, if you're sedentary, you or I sit in our bed and we don't do enough, our***  
20 ***bones get weaker. So the exercise they do will actually stimulate their bones to***  
21 ***lay down the bone where their bone is weakest. It will actually enhance their bone***  
22 ***strength further.*** So I think ***it'll have a beneficial effect*** for them to be more active  
23 and -- with sports or anything else. ***So we're not worried about the moral risk of***  
24 ***getting more fractures. We think it's part of a healthy pattern towards more***  
25 ***activity, stronger bone and better lives for these OI patients.***

26 (Emphasis added).

27 31. Further into the question-and-answer portion of the call, Defendant Kakkis  
28 discussed the potential for the varying types of OI, highlighting that Ultragenyx believed  
setrusumab to be able to reduce AFR regardless of OI subtype:

<Q: Michael H. Riad – Morgan Stanley – Research Associate> This is Michael  
Riad on for Jeff Hung. Going back to setrusumab and thinking about that cycle of  
fractures leading to bone deformation and then loss of activity. What factors do you  
think play a role -- bigger role in the treatment course? Is it age or OI type? I mean,  
if you think about like the profile of setrusumab, do you view it as like a broadly  
better option for most pediatric patients regardless of type, whereas for adults you'd  
expect more OI-type-dependent penetration?

<A: Emil D. Kakkis> Well, I think each patient is going to have a reason to be  
treated. It may be different. If you're a Type 3 patient or Type 4 with a really severe  
bone disease, and you're treated when you're 1 or 2 years old, our hope, and we will  
see what the Phase III data show, is that we could be transformed in terms of

1 stopping fracture, stopping vertebral compression and not basically destroying your  
2 skeleton before you're 3 or 4 years of age and ending up in a wheelchair. So that  
3 would be what you could do when you're treating kids that are young.

4 However, when they're old, like even if you're in a wheelchair because you have  
5 deformed bones, you're still fracturing, you're still in pain all the time. **Being able  
6 to stop being in pain by stopping fracturing**, even if you can't change deformation,  
7 it's still highly valuable in an adult with Type 3 or 4.

8 **For Type 1, probably the superior half of that population will have enough  
9 fractures where at any age, young or old, it's going to be beneficial.** They don't  
10 have as much deformation, but being able to be comfortable, participating in sports  
11 or activities you might not have been doing before, I think will get Type 1s treated.

12 There may be some Type 1s who are milder, don't have as many fractures, and there  
13 might not be as an addressable -- as much addressable need in those patients. So we  
14 wouldn't expect all the Type 1s. **What I can say from the data we've shown you  
15 though, the Type 1s do really well on the treatment as do the Type 3s and 4s. So  
16 we expect that we'd have a good penetration of all 3 types as well as in all ages  
17 because we think there's a reason to treat at any point in life in almost any of  
18 these diseases.**

19 (Emphasis added).

20 32. Defendant Kakkis additionally fielded a question related to potential competition in  
21 the OI space, again highlighting how Ultragenyx will be able to differentiate itself by being  
22 “superior” in reducing fracture rates:

23 <Q: Jingming Chen – Evercore ISI Institutional Equities – Research Analyst> This  
24 is Jingming on for Liisa. So we noticed that Amgen is running an open-label Phase  
25 III study for romosozumab in OI, and they have indicated that if the Phase III study  
26 is positive, they may have an opportunity to pursue approval and launch in OI. So  
27 I'm just wondering what implications do you think it would have for setrusumab if  
28 Amgen decides to pursue approval in OI?

<A: Emil D. Kakkis> Well, that's news to us. They've already given us the  
intellectual property access. So I don't think they've had that much interest in it.  
They -- it's a biologic for them. Osteoporosis is a huge indication. It's growing.  
There's a big shift toward anabolic agents in osteoporosis. I really think that's their  
focus.

With regard to OI, we've seen their Phase II data. We understand their dosing from  
the published comments in the clinicaltrials.gov, or the European version of it.  
Right now, they're getting substantially less bone mineral density at the dose levels  
they're using. **So we're a superior treatment in terms of our bone mineral density  
improvement, and we will then be superior in fracture reduction.**

1 So I think you should look at this as an unclear story. What they've done in their  
2 Phase III is not optimize the drug nor the presentation for OI. And so I really don't  
3 have concerns right now because we know our data. It's far superior for them to get  
4 to our data. They would have to change their dosing dramatically from Phase III,  
which is not likely to happen at this point. ***So at this point, I think they will be  
inferior to us, and I think that will be a factor.***

5 (Emphasis added).

6 November 5, 2024

7 33. On November 5, 2024, Defendants unveiled third quarter fiscal year 2024 results.  
8 During the earnings call that followed, Defendants engaged with analysts during the question-and-  
9 answer segment, providing further assurances of the rigor and methodology of the ongoing Phase  
10 III OI Studies, in pertinent part as follows:

11 <Q: Christopher Josphe Raymond – Piper Sandler & Co. – MD & Senior Research  
12 Analyst> . . . And then maybe also a follow-up on setrusumab. Can you give a little  
13 bit more color on this negative binomial regression model that you're using just to  
explain a little bit about what that means, what you're doing there?

14 <A: Emil D. Kakkis> . . . With regard to setrusumab, P. K. Tandon, our Head of  
15 Biometrics, a highly experienced biometric statistician who was at Genzyme for 20  
16 years and has done probably more rare disease programs than anyone, believes ***a  
negative binomial model is the best way to do an event-driven analysis, and it's a  
basic model that the FDA has agreed to.*** We are -- for me to go through the math  
17 would be probably pretty difficult, but we probably can provide some explanation  
18 for investors on that model. ***But it's the best way to look at events and looking at  
event rates and being able to control in the model for things like baseline fracture  
rate or age or other factors that will be different between different patients.*** So  
19 ***while I can't explain it, what I can say is the study is very well powered to succeed  
in the setrusumab Orbit study.***

20 . . .

21 . . .  
22 <Q: Joseph Patrick Schwartz – Leerink Partners LLC – Senior MD of Rare Diseases  
23 & Senior Research Analyst> Great. I also have a couple of questions on setrusumab.  
24 I was wondering, first, on Orbit, if you could talk a little bit more about how you're  
25 calculating the effect size in Orbit, how that compares to how you did in Phase II  
and then the range of effect size separations that might be needed in order to hit stat  
26 sig at different interim analyses would be very helpful. And then I have a follow-  
up on Cosmic.

27 <A: Emil D. Kakkis> Well, we assumed a 50% reduction in fracture rate and a  
28 fracture rate of 0.7 for the powering estimate. However, for the interims and the  
choice of doing interims, that was based on the concept there could be more

1 fractures events happening, not a higher fracture rate reduction. *And so if there are*  
2 *more fractures, it improves the power to detect that result earlier, right, just*  
3 *because more events defined.*

4 So the effect size of 50% and the fracture rate, 0.7, was what was used in both the  
5 power and design. Given that the fracture rate reduction was closer to 67%, which  
6 could be similar or higher with the binomial, *I think we feel pretty comfortable*  
7 *that we're in good position in how we've designed the study.* So that's sort of what  
8 happened there with regard to the effect size.

9 ...

10 <Q: Joseph Patrick Schwartz> Okay. So in terms of Cosmic, what kind of a  
11 treatment effect do you assume in your powering relative to bisphosphonates? What  
12 do you hope to see for the setrusumab arm? Are there any nuances in terms of how  
13 the end points in Cosmic are calculated versus Orbit?

14 <A: Emil D. Kakkis> Well, keep in mind something about Orbit and the Phase II  
15 part Orbit is those patients were -- the vast majority of those patients had been on  
16 bisphosphonates. The bisphosphonates are in their bones. *So when we're looking*  
17 *at the 67% reduction, that's really like setrusumab on top of bisphosphonates, just*  
18 *to be clear, right? That's not -- so we'd expect that a similar differential occur even*  
19 *head to head with bisphosphonates, right? It is really like an add-on, if you will,*  
20 *in Orbit because they already have them in their bones.*

21 There might be some tailing off of the bisphosphonate effect in Orbit. But in  
22 Cosmic, everyone had to be on bisphosphonates upfront, so our expectation is  
23 actually similar in terms of we went with the 50% reduction in fracture rate.

24 *Now the fracture rate in little kids can be much higher. It could be several fold*  
25 *higher, which is partly why the study is in the 60- to 70-patient range rather than*  
26 *150. But that's our assumptions right now.*

27 (Emphasis added).

28 34. Defendant Kakkis, in fielding questions on the timing and potential interim analysis  
outcomes, further discussed the breakdown of patients in the Phase III OI Studies during the  
following exchanges:

<Q: Huidong Wang – Barclays Bank PLC – Research Analyst> I have one question  
regarding setrusumab Phase III study. I mean you did actually provide a little bit  
more clarity regarding the time line. I remember last time was more likely  
beginning of 2025. Now is at year-end '24, beginning of 2025. And second interim,  
very definitive, is 1Q '25. Is that because the event's already picking up and you  
have more clarity regarding when this will happen?

1 And then also, will you share the baseline characteristics of Phase III trial at some  
2 point? If not, could you comment on patient baseline attack rate range and also the  
3 breakdown of the patients, specifically between age 5 to 12, 12 to 18 and 18 to 25?

4 <A: Emil D. Kakkis> With regard to the first interim timing, the clarity on the  
5 timing is not based on data we're collecting, so it's not based on fractures. We said  
6 from the beginning that would be end of the year, early 2025. And then a few  
7 months later, we're being a little more specific saying middle for 2025, but it was  
8 always a few months. ***So we weren't intending to change anything. It was just  
where the time line is.*** But we did change -- a long time ago, we talked about having  
fracture number as being the trigger, but because it was so operationally challenged,  
***we just estimated when we hit a certain number of fractures. But none of the  
change in timings were related to the fractures.***

9 We haven't put out baseline characteristics yet, but we will at the appropriate time.  
10 Usually when we bring out the Phase III data, we'll bring in the characteristics, but  
11 we would not expect to put out that data until we're releasing our Phase III data.  
12 ***What we have said to date is that the population has more type III and type IV  
patients, closer to half or more as opposed to what was in Phase II where there  
was about 1/3, and so that's 1 difference. We'd expect those patients to have more  
fractures. We expect then the Phase III trend -- study to have a higher fracture  
rate than what we saw before.***

14 But right now, ***we haven't put in the breakout for age groups that are enrolled in  
the study either. It is spread across the age groups. It is primarily ped study with  
the majority of the patients in the peds age range.*** We are stratifying in the  
15 randomization to make sure that we're -- we have similar populations in both  
16 groups. That's where we stand. Thanks for the good questions.

17 ...  
18

19 <Q: Maurice Thomas Raycroft – Jefferies LLC – Equity Analyst> Congrats on the  
20 progress. For setrusumab, just wondering what are key learnings from the Phase II  
21 14-month data update at ASBMR that help you triangulate around fracture rates  
22 and chances of success for the first interim or second interim updates. And maybe  
just a quick follow-up, if you can clarify if you'll have new patients with less follow-  
up in the Angelman data updates that you have.

23 <A: Emil D. Kakkis> Okay. So I think what we learned from the 14-month update  
24 on setrusumab was, in fact, that ***these patients can have a very profound degree of  
separation, and that separation can lead to the majority of patients having no  
fractures over a significant period of time.***

25  
26 The other thing we learned is that particularly ***the younger patients have a dramatic  
improvement in bone mineral density. So I think what we learned is that how  
strong the effect could be, and that gave us more confidence in putting in the  
interim in the first place*** because if they are separating very quickly within 2 or 3  
27 months and if that effect size is large, then we would expect the groups could  
28

1 separate early. We just don't know for sure. We set a stringent threshold for the first  
2 one. The second one, less so.

3 But that data gave us confidence that we can do that. ***It also gave us confidence we***  
4 ***can lower the number of patients modestly and shorten the time line then to finish***  
5 ***enrollment.*** So those are the things we learned and what we expect to know. And  
6 everything that we've seen so far tells us that we have a strong effect going on, and  
7 we want to reach that as promptly as we can.

8 (Emphasis added).

9 35. Defendant Kakkis went on to discuss in detail why Ultragenyx is confident in being  
10 able to demonstrate an improved fracture rate in the fragile population being studied during the  
11 following pertinent exchange:

12 <Q: Kristen Brianne Klusta – Cantor Fitzgerald & Co – Analyst> On setrusumab,  
13 I was hoping to get a little bit more color around thoughts about the placebo arm.  
14 We know that the 5 bisphosphonate studies had diverse readouts. So can you give  
15 us some context about how you developed that 20% figure? And then is there any  
16 possibility in this trial that because patients are used to being quite inactive that we  
17 could see more fractures on placebo if the protocol requires them to go to the clinic?

18 <A: Emil D. Kakkis> Yes. So there were -- we're aware of 5 randomized studies to  
19 look at bisphosphonates. Three of them failed and 2 of them were successful. And  
20 the 2 that were successful, there was an estimate that they had a reduction of 20%  
21 in fracture reduction. And they did make patients feel better, too, which is one of  
22 the reasons why people are using it, less about fracture reduction than feeling better,  
23 which is probably dealing with like micro fractures and something of that kind. So  
24 the data are not really that compelling, ***but if you look at our own Phase II data,***  
25 ***the 67% reduction was on top of bisphosphonates, which were on the majority of***  
26 ***those patients. So it's pretty clear what -- we should be able to see a substantial***  
27 ***difference between the 2.***

28 Now if you talk about the placebo arm in the study, ***they're not getting the***  
***bisphosphonates anymore during the study, so they will be weaning,*** which might  
have some impact on their bones over the period of the year. But in addition, ***most***  
***of them would be normally staying at home.*** And we know that by ***coming in the***  
***clinic alone, the incident of accidents and fractures goes up. It's one of the***  
***reasons patients are elected to come in a placebo-controlled study.***

***They know going back and forth the clinic every month opens them up to having***  
***fractures. So we'd expect actually the clinical activity to actually increase their***  
***fractures, which would give us more opportunity to detect the difference between***  
***them.*** So -- but because the data in the Phase II were so strong, the doctors, the  
patient decided they want to get in even if they got placebo because they realized  
they would cross over on the drug before anyone else, and they want that  
opportunity. ***So that's why we suddenly were able to get enrollment to crank up***

1 *and go real well as people felt like this is going to be too big a difference to not*  
2 *want to be part of it.*

3 (Emphasis added).

4 January 13, 2025

5 36. On January 13, 2025, Defendants issued a press release announcing preliminary  
6 fiscal 2024 results, guidance for fiscal 2025, and pertinently announced that “UX143 (setrusumab)  
7 Phase 3 Orbit study for osteogenesis imperfecta [would be] progressing to secondary interim  
8 analysis in mid-2025.”

9 37. The same day, Ultragenyx presented at the 43<sup>rd</sup> Annual J.P. Morgan Healthcare  
10 Conference 2025 and provided additional clarity on the interim results. In pertinent part,  
11 Defendant Kakkis responded to an inquiry on the matter as follows:

12 <Q: Anupam Rama – J.P. Morgan Chase & Co – Vice President and Analyst> . . .  
13 There's this thesis out there now that you've gone past the first interim to the second  
14 interim that somehow the probability of technical success is now different for the  
15 Orbit study. Do you agree with this? Where would you push back on that?

16 <A: Emil D. Kakkis> No, no, I completely disagree. The idea of the first interim  
17 was simply try to see if we can accelerate further had nothing to do with that. I think  
18 the time frame and how much time of exposure was the question, how fast they can  
19 separate. They need a very extreme rapid separation. ***But the truth is that we know  
20 what will happens between 6 months and 1 year of exposure, we already have  
21 that data and we present it to people. So we feel really comfortable that this is  
22 going to be a successful product.***

23 ***The question is how fast we can accelerate.*** Remember, it was originally a 2-year  
24 type design, and we've been pulling it up. ***So it's really more about -- not about  
25 PTS, it's about how fast we can get to the success point.***

26 ***So we feel very comfortable that either the mid or the end of the year, we'll be  
27 hitting the trial. We know the drug works very well. And so we're confident in it.***

28 (Emphasis added).

February 13, 2025

38. On February 13, 2025, Defendants provided their full year fiscal 2024 results and  
provided further points of confidence in the construction and ultimate success of their Phase III OI  
Studies.

1 39. In pertinent part, Defendant Kakkis discussed the decision and ramifications of  
2 increasing the prevalence of higher severity types of OI during the following exchanges:

3 <Q: Yaron Benjamin Werber – TD Cowen – MD & Senior Biotechnology Analyst>  
4 Right. So I also, shockingly, have a 143 question. In the Orbit study, are you  
5 stratifying, just remind us, Type I, III and IV between the two arms? And then  
6 secondly, when you look at the primary of fracture rates, do you have a secondary  
7 looking fracture rates by type, underlying type?

8 <A: Emil D. Kakkis> Yes. So in general, we do stratify, but it's mainly for -- it's  
9 overall fractures and its age. I'll let Eric talk about the way we're approaching.

10 <A: Eric Crombez> Yes. So because the primary endpoint is annualized fracture  
11 rate, you want to stratify by fracture rate. *So while that definitely will kind of*  
12 *encompass the different types there, the strict stratification is based on fracture*  
13 *rate coming into the study.*

14 <A: Emil D. Kakkis> *So Type [ III and IVs ] may have a higher fracture, but*  
15 *we're focusing on that -- doing it by the IIIs and IVs and Is, it didn't look like*  
16 *that was going to be the right way to go, as fracture rate was a better way.* So we  
17 are also looking at ages so there's an age balance between the groups. And regarding  
18 the other endpoints, *we are looking at total fractures, not just the fractures minus*  
19 *fingers, toes, skull. Those total fractures are our endpoint.* And the subset between  
20 subtypes, I'm sure we'll do analysis sensitivities on that in there, but it's not a formal  
21 secondary endpoint.

22 ...

23 <Q: Jeff Hung – Morgan Stanley – Equity Analyst> I just wanted to clarify, make  
24 sure I understood correctly. You talked about how the Phase II data and the 0.014.  
25 But just for setrusumab, would the Orbit Phase II portion have hit with the second  
26 interim analysis criteria, and if not, how were the baseline fracture rates different  
27 from the Phase II portion?

28 <A: Emil D. Kakkis> Yes. So what I said was the Phase II data at 6 months, last  
patient in, we had 0.04, and then with the 14-month data we had 0.0014, right? So  
that was the difference. You're asking how close does that reflect what's going on?  
*Well, the Phase II patients are fairly similar in terms of the entry criteria for*  
*fractures are the same.* They're made up of Type Is, IIIs, 4. *Their Phase III has*  
*somewhat more 3s and IVs, but not a dramatic difference. So it's a very*  
*comparable population, age range, types included and baseline fracture*  
*requirements. So I think that those are reasonable ways to look at what Phase III*  
*should be happening.* And so the only question has to do with how -- the variation  
in the population, how big is it and how much it moves in the timeframe. But I think  
the data from Phase II are a reasonable model for what's happening. Is that helpful?

(Emphasis added).

1 40. Further, Defendant Kakkis again spoke to Ultragenyx's ability to meet the interim  
2 analysis and why the inability to do so should not reduce investor confidence in the ultimate  
3 outcome of the studies during the following pertinent exchanges:

4 <Q: Salveen Jaswal Richter – Goldman Sachs Group, Inc. – Vice President> Maybe  
5 help us understand, if it doesn't hit on the second interim, what would those reasons  
6 be, or what are the risks to that? And then how long would we have to wait for the  
7 final analysis?

8 <A: Emil D. Kakkis> Well, we said the second interim will be midyear. ***For it not  
9 to hit at 12 months, it's usually in rare disease it would have to do with the amount  
10 of variation and the number of fractures.*** If there's a lot of variation, there's a wide  
11 range of patient baseline fracture rates because we have some Type III, IV and then  
12 Type I patients. A large variation could create some -- a challenge. But I think that  
13 ***so far, we feel like the trial is proceeding as expected.*** So if it doesn't hit in the  
14 second interim, we'd expect to release data by the end of the year on the final  
15 assessment for the trial.

16 <Q: Joon So Lee – Truist Securities, Inc. – Vice President> If the OI study goes to  
17 completion in 4Q, does that imply that the magnitude of effect may not be as great  
18 as expected? And in that case, how competitive would setrusumab be compared to  
19 bisphosphonate?

20 <A: Emil D. Kakkis> Actually, it would not mean it's not as great. If you remember,  
21 earlier when we had 6-month data and 14 months in Phase II, they both had 67%  
22 reduction in fractures. What it has to do with is the two lines have to separate. So  
23 the biggest [ creation ] if there's too much variation and those variations might cause  
24 a delay. But the actual rate separation could very well be 67%. ***It's just you have a  
25 lot of patients that may have 10 fractures a year or one fracture a year in the  
26 same study, and some of the ones may not have fractured, for example, and then  
27 -- for whatever reason. And so it's really more about separating the two groups.***  
28 But I don't think it necessarily tells you what the percent reduction is.

29 We think if you listen to some of the KOLs, that 50% or greater reduction in fracture  
30 is considered really important. ***And frankly, when we look at patients after a year,  
31 15, 16 months of therapy, we've had some -- or longer -- many of them are not  
32 fracturing at all at some point. So we feel very comfortable that the long-term  
33 outcome here is greatly reduced fractures,*** whatever the number is. But I think the  
34 biggest issue is the variation in how much fractures are occurring in each group and  
35 that wide range that probably exists that will impact how the study reads out. ***We  
36 are using covariables to manage that variation, but that would be the #1 reason.  
37 So I don't think you can conclude the drug is not working well if we go to the  
38 end.***

Remember, the original plan here was to do a 2-year study. ***The only reason we felt  
we could go sooner is because the percent reduction was higher than we thought  
and that the speed of response was faster.*** Those are the things that give us

1 confidence that we can go earlier. But we've been moving this up from 18 months  
2 to 2-year study, right, down to what we're talking about now to the 12- to 18-month  
3 time frame. ***So 18 months is still a win, and I feel confident, whichever one  
4 happens, that we have a drug that will be far better than bisphosphonate and  
5 certainly the best treatment for OI that's available.***

6 (Emphasis added).

7 May 6, 2025

8 41. On May 6, 2025, Defendant Crombez reiterated their plans for an interim  
9 announcement on positive results at the midyear point, stating, in pertinent part:

10 The Orbit and Cosmic studies will both have an interim analysis midyear after all  
11 patients have been on therapy for at least 12 months. The data readouts will be led  
12 by Orbit, meaning that if Orbit clears the p-value threshold of less than 0.01, we  
13 will look to see if Cosmic has cleared the same p-value threshold of less than 0.01.  
14 If Orbit progresses to full study completion in the fourth quarter of this year,  
15 Cosmic will also continue to a data readout to align with the Orbit data readout  
16 without spending alpha at this interim assessment.

17 42. During the question-and-answer segment, Defendant Kakkis fielded a question on  
18 the likelihood of success should the Phase III OI Studies fail to reach the second interim date  
19 benchmark during the following exchange:

20 <Q: Tazeen Ahmad – BofA Securities – MD in Equity Research & Research  
21 Analyst> . . . if the study moves to a third interim read, what's your view of the  
22 likelihood of success? You've talked now multiple times about confidence in the  
23 molecule overall, and we would agree that the drug is active. But if the study moves  
24 to the third interim, what would be a reason to be concerned that it would not work  
25 at the third interim?

26 <A: Emil D. Kakkis> Right. Well, it won't be -- the next assessment is the final  
27 assessment for the study, and that p-value threshold will be 0.04. So it would be a  
28 lot easier to hit 0.04. ***So we think that we will hit one or the other based on our  
experience, what we've seen. I don't think we could miss the 0.04 at that point  
with 18 months of time.*** But as always in rare disease programs, the other -- the  
thing you always are battling us is variation, variability in patients. ***But based on  
the profound difference in bone mineral density change that we see that happens  
within 2 to 3 months and the fracture rate effect happens within 2 to 3 months,  
we feel pretty good about IA2 hitting, but confident about overall the study hitting  
even at the end, if not at the IA2.***

So I can't tell you a reason why, but variation is always the thing that can create  
complexities. But given that the patients -- ***the program is 159 patients, that's a  
pretty large study. And we were -- the data we're talking about before was 24. So  
I think we've got a lot of power in there,*** but -- ***and we've done everything we can***

1 *to manage variations. So I feel good about we'll hit it this year, either at 0.01 or*  
2 *0.04 after 18 months.*

3 (Emphasis added).

4 43. Defendant Kakkis further spoke to the prevalence and impact of increased severe  
5 OI subtypes in the Phase III studies during the following pertinent exchanges:

6 <Q: Yigal Dov Nochomovitz – Citigroup Inc. – Director and Smid Cap Biotech  
7 Analyst> Have you commented at all on the distribution of the types for OI for 1,  
8 3 and 4 for the Phase II versus the Orbit trial?

9 ...

10 <A: Emil D. Kakkis> So on the OI types, I think we've disclosed before that in the  
11 *Phase II study, there were 7 type 3s and 4s and 17 type 1s.* And then because the  
12 doctors were then impressed with the results, then they were interested in bringing  
13 in their more severe 3 and 4 patients. *So we ended up with more type 3s and about*  
14 *half the patients are type 3 and 4 approximately there in the study. So it's*  
15 *definitely an increase in Type 3s and 4s in the Phase III study than they were in*  
16 *the Phase II study, all right?*

17 ...

18 <Q: Mahdi Goudarzi – Truist Securities, Inc. – Biotech Equity Research Associate>  
19 This is Mahdi on for Joon. So I go on OI and follow up Yigal's question on  
20 composition of OI types. So do you agree that setrusumab's MOA benefits the type  
21 1 patients more than Type 4 and 3. This is the question.

22 <A: Emil D. Kakkis> *Well, I know there's been some academics saying that,* but  
23 -- and I know some of them very good academics, *but they're actually incorrect*  
24 *because we already have data.* So it's not -- the theory would be that in type 1  
25 patients have deficient collagen, don't have abnormal collagen. *Therefore, if we*  
26 *just make more bone, it will be okay.* And the type 3s and 4s have abnormal  
27 collagen, therefore, it's not improved, but that's not actually what we saw. We see  
28 both of them have improved reduction in fractures. And in fact, the ones fractures  
we did see were in type 1 patients, I think were some of the ones not type 3s and  
4s.

So the truth is all of them are improved because while one is a deficiency collagen  
and one is abnormal collagen, whether deficient or abnormal, the net benefit of  
making more bone is bone, greater bone strength and reduced fractures. So it  
actually works in all three. *And historical clinical view of OI is going to change*  
*because the truth is that even with abnormal collagen, the bones can be*  
*strengthened,* we believe, in these patients, and that's what we've seen, and that's  
in the data from Phase II. *And so we're confident that the type will not matter.* You  
get the same bone mineral density effect and the strength improvement will be the  
same regardless of the collagen mutation.

1 (Emphasis added).

2  
3 44. The above statements in Paragraphs 24 to 43 were false and/or materially  
4 misleading. Defendants created the false impression that they possessed reliable information  
5 pertaining to the effects of setrusumab on patients with variable types of OI, while also minimizing  
6 risk that patients in the Phase III Orbit study would fail to achieve a statistically significant  
7 reduction in AFR, such that the second interim analysis could be performed and presented to the  
8 investing public. In truth, Ultragenyx's optimism in the Phase III Orbit study's results and interim  
9 analysis benchmark were misplaced; Ultragenyx failed to convey the risk associated with basing  
10 such threshold figures on Phase II results that had no placebo control group for appropriate  
11 comparison and thus had not ruled out that the reduction in AFR from that study could merely be  
12 triggered by an increased standard of care and the placebo effect of being provided a novel  
13 treatment.

14 **C. Ultragenyx Reveals the Phase III ORBIT Study Failed To Achieve the Second Interim**  
15 **Output**

16 July 9, 2025

17 45. On July 9, 2025, Ultragenyx issued a press release and "announced that the  
18 randomized, placebo-controlled Phase 3 portion of the *Orbit* study evaluating UX143  
19 (setrusumabg) in pediatric and young adult patients with [OI] is progressing toward a final analysis  
20 consistent with the original plan, around the end of the year."

21 46. The release further reminded investors of the easier-to-achieve threshold for the  
22 final analysis due at years end:

23 Patients will continue dosing in the ongoing Phase 3 Orbit and Cosmic clinical  
24 studies with the final analyses to be conducted after patients have been on therapy  
25 for at least 18 months. The threshold for the Phase 3 Orbit final analysis is  $p < 0.04$   
and for the Phase 3 Cosmic final analysis is  $p < 0.05$ .

26 47. The aforementioned press releases and statements made by the Individual  
27 Defendants are in direct contrast to statements they made during the above-referenced earnings  
28 calls and shareholder presentations. On those calls, Defendants continually expressed confidence

1 in the ability of its Phase III Orbit study to achieve the second interim results threshold necessary  
2 to present results to the investing public, while also minimizing the risk that the study could fail to  
3 demonstrate that setrusumab results in a reduction in AFR for the OI patients tested.

4 48. Investors and analysts reacted immediately to Ultragenyx's revelation. The price of  
5 Ultragenyx's common stock declined dramatically. From a closing market price of \$41.44 per  
6 share on July 9, 2025, Ultragenyx's stock price fell to \$31.03 per share on July 10, 2025, a decline  
7 of about 25.12% in the span of just a single day.

8 49. A number of well-known analysts who had been following Ultragenyx lowered  
9 their price targets in response to Ultragenyx's disclosures. For example, Wells Fargo, while  
10 slashing their price target more than 26%, justified their cut on the failure to meet the second  
11 interim analysis thresholds. In pertinent part, the analyst highlighted that "most of our inbounds  
12 suggested high expectations that the study would hit this interim analysis; management  
13 commentary had also been bullish on IA2, with even recent comments around commercial  
14 readiness planning."

15 50. The fact that this analyst, and others, discussed both Ultragenyx's "bullish"  
16 commentary on the second interim readout and the failure to achieve the threshold requirements  
17 for the analysis suggest the public placed significant weight on Ultragenyx's prior optimistic and  
18 confident statements regarding the Phase III OI Studies. The frequent, in-depth discussion of such  
19 statements confirms that Defendants' statements during the Class Period were material.

20 51. Notwithstanding Defendants' disclosures, they continued to mislead investors by  
21 misrepresenting their understanding of the risk that the Phase III OI Studies would be unable to  
22 achieve their respect endpoints of reduced AFR. In doing so, the Defendants deceptively claimed  
23 confidence in the studies achieving positive results.

24 August 5, 2025

25 52. On August 5, 2025, Defendants issued a press release announcing their financial  
26 results for the second quarter of fiscal year 2025 and a "Corporate Update" on its existing studies.

27 53. Pertinently, the release reminded investors that the "randomized, placebo-  
28 controlled Phase 3 portion of the Orbit study was evaluated by the Data Monitoring Committee at

1 an interim analysis in July 2025 and they informed the company that UX143 demonstrated an  
2 acceptable safety profile and that the study should continue to the final analysis.”

3 54. During the same-day earnings call, and despite missing the second interim window,  
4 Defendant Kakkis reiterated Ultragenyx’s confidence in setrusumab’s ability to demonstrate a  
5 statistically reduced fracture rate in the Phase III OI Studies, stating, in pertinent part:

6 ***The Orbit and Cosmic studies are continuing to the final analysis that will occur***  
7 ***around the end of the year.*** While I hope the studies might have stopped early at  
8 the interim time point last month, ***we remain confident in completing a successful***  
9 ***study.*** We're pleased the safety profile is as expected and that after looking at the  
10 data, the DMC recommended we continue to the final analysis. ***As we head to the***  
11 ***final analysis, the continued treatment of Phase III should further strengthen***  
12 ***bones of the treated patients. The additional 6 months of treatment for the treated***  
13 ***subjects, along with the larger p-value threshold at 0.04, will help power the final***  
14 ***assessment.*** We look forward to unblinding the Phase III datasets and sharing  
15 results around the end of the year.

16 Now based on all the data we've seen in Phase II, ***we are confident UX143 will be***  
17 ***a transformational treatment for pediatric and adult patients with osteogenesis***  
18 ***imperfecta.*** The ***combination mechanism of building bone and reducing excess***  
19 ***resorption is at exactly the sites in their body where they need more bone will***  
20 ***increase bone strength and reduce fractures, while at the same time improving***  
21 ***overall bone health.*** In addition to reducing fractures, we are encouraged by the  
22 functional effect we are seeing on increasing physical activity and ability that  
23 speaks to the long-term potential for this treatment.

24 (Emphasis added).

25 55. Defendants Kakkis and Crombez further fielded several question pertaining to why  
26 the study was unable to meet its interim thresholds and why the Defendants remained confident in  
27 the study, pertinently as follows:

28 <Q: Kristen Brianne Kluska – Cantor Fitzgerald & Co. – Analyst> For the Orbit  
study reading out later this year, I know you still have very high conviction in the  
trial being successful. But I wanted to talk about a hypothetical scenario where  
maybe the fracture data falls slightly under what you were hoping for, but you see  
really strong benefits on pain. Do you still think that there is a strong case to make  
for the FDA here? And could you argue that this will drive higher adoption for  
patients since they deal with this on a daily basis over the fracture aspects?

<A: Emil D. Kakkis> Well, I think that your point is maybe there's some variation  
in fractures and you just missed that and you have other supportive data. I think the  
FDA will always look at the total -- totality of the data in our rare disease program.  
We've had that many times in many programs. ***Our sense here is that we're seeing***

1 *a fundamental mechanistic effect on bone mineral density, the effect it has on*  
2 *fractures depends on how many fractures that patient have in their particular*  
3 *condition.*

4 *We have a lot more Type IIIs and Type IVs in the study. They have a lot of*  
5 *complex problems.* And so I'm sure that the support of other data would help us in  
6 any situation, whatever the statistical or treatment size is. And so that's just  
7 generally been the case. *We feel confident what the fracture data will be, what it*  
8 *is. We're seeing what's going on in Phase II. We know that as time goes on,*  
9 *there's very few fractures among patients after they've gotten established on the*  
10 *treatment.*

11 So we feel good we'll be able to do that. But hypothetically, I think the data will  
12 always be more than just fractures in this disease state. And the body of data we  
13 have, we think, will support its use however we come out with on fractures.

14 ...

15 <Q: Yigal Dov Nochomovitz – Citigroup Inc. – Director and SMidCap Biotech  
16 Analyst> Okay. I was going to say on OI, given the first 2 interims have passed and  
17 now we're looking at the final one, I'm just curious if you have any updated thoughts  
18 as far as what you believe the expected placebo AFR would be. Obviously, we've  
19 done some work, and there are a number of epidemiologic studies out there, both  
20 in Scandinavia as well as the United States, which point to various ranges for AFR.

21 I'm just wondering if you could comment on what you believe would be the most  
22 likely scenario at this point as well as on some of the more specific aspects of the  
23 statistics again regarding this concept of variance or overdispersion which, as we  
24 know, is a feature of this particular dataset given the way the fractures are  
25 distributed.

26 <A: Eric Crombez> Yes. So yes, we're aware of the annualized fracture rate  
27 available in the literature. And looking at natural history the principal investigators  
28 have on hand, we really use a lot of the data coming on for pretreatment for baseline  
for both Orbit and Cosmic to do our modeling. *And we were really looking at those*  
*patients with the baseline AFR between 0.72 and 1 for our modeling to support*  
*both of the work for the interim analysis and obviously, the powering we did for*  
*the primary efficacy analysis period at 18 months.*

And with the dispersion, yes, I mean, I think while we did not change the entry  
criteria for Orbit Phase II going into Orbit Phase III, on the strength of the Phase II  
data, *we had really what I consider to be a self-enrichment of patients with Type*  
*IIIs and Types IV. I think they needed to see that strong safety and efficacy data*  
*to take the risk to come into clinic because remember, they really are at risk just*  
*from traveling into sites to sign consents and begin studying participation. So I*  
*will say we did -- we have a greater number of patients with Type III and Type*  
*IV OI in the Phase III part of Orbit compared to Phase II.*

1 (Emphasis added).

2 November 4, 2025

3 56. On November 4, 2025, during Ultragenyx's final earnings call before the results  
4 Phase III OI Studies would be released, Defendant Kakkis remained confident they would  
5 demonstrate a reduction in AFR, pertinently stating the following during the call:

6 As we move into the final analyses, we remain confident in setrusumab's  
7 mechanism of action, its ability to make more bone in the places that need more  
8 strength, which should reduce fractures. If successful, this will lead to a  
9 transformational treatment for pediatric and adult patients with osteogenesis  
imperfecta.

10 ...

11 Now with regard to what we expect in Phase III, *we've said that anywhere between*  
12 *40% and 70% reduction in fractures, in that range, is a very good fracture*  
13 *reduction level. And I don't think that the exact percentage within that range*  
14 *matters as much as how patients feel and how they're functioning.* And from the  
Phase II study, it's pretty clear that the way patients are functioning is quite  
important in terms of their ability to take on exercises, to walk better, get out of  
wheelchairs or using walkers, et cetera.

15 *So we think anywhere in that range -- and I think most KOLs have suggested*  
16 *something better than 40%.* We've seen 67% in the Phase II study. I think  
17 anywhere in that range is -- I think, would be a clinically meaningful change for  
these patients

18 ...

19 So I think if we get one or the other study positive, we'll be able to work forward.  
20 And how we solve the issue of the age range and the indication, *I don't expect there*  
21 *to be a difference in how the drug works. I think both studies should show a*  
22 *substantial bone mineral density benefit improvement and should show*  
*improvement in fractures.* So we're confident in the program, but I think we can  
make it work with either combination of results.

23 (Emphasis added).

24 57. The above statements in Paragraphs 52 to 56 were false and/or materially  
25 misleading. Defendants created the false impression that they possessed reliable information  
26 pertaining to the effects of setrusumab on patients with variable types of OI, while also minimizing  
27 risk from study variability and the potential outperformance of the control groups. In truth,  
28

1 Ultragenyx’s claims of changing the “historical clinical view of OI,” increasing the control group’s  
2 fracture rate to “give [Ultragenyx] more opportunity to detect the difference between them,” and  
3 being able to demonstrate a reduction in AFR despite permitting increased activity among tested  
4 patients fell shy of reality as such claims relied far too heavily on assumptions Defendants had  
5 made on a smaller sample size and differing patient pool that populated the Phase II Orbit study.  
6 Ultimately, Defendants failed to convey the associated risk of such assumptions to Ultragenyx’s  
7 investors. Ultragenyx was simply either unable to generate a study that could accurately show  
8 setrusumab’s impact on annualized fracture rates or the drug simply does not have the impact that  
9 Defendants repeatedly and confidently claimed they could demonstrate.

10 **D. The Full Truth Emerges When Ultragenyx Reports Results of the Phase III Orbit and**  
11 **Cosmic Studies**

12 December 29, 2025

13 58. On the morning of December 29, 2025, Defendants announced the “results from  
14 the Phase 3 Orbit and Cosmic studies for setrusumab (UX143) in Osteogenesis Imperfecta” in a  
15 form 8-K filing.

16 59. The filing disclosed that both studies failed to achieve statistical significance  
17 “against the primary endpoints of reduction in annualized clinical fracture rate compared to  
18 placebo or bisphosphonates,” respectively, despite achieving “secondary endpoints of  
19 improvements in bone mineral density (‘BMD’).”

20 60. In pertinent part, the release provided the following limited details, adding:

21 In the Orbit study, participants experienced statistically significant and substantial  
22 improvements in BMD compared to placebo, at levels consistent with the treatment  
23 effect observed in the Phase 2 portion of the study. ***These BMD changes were not***  
24 ***accompanied by a corresponding reduction in annualized fracture rates and***  
25 ***there was a low fracture rate in the placebo group.***

26 In the pediatric Cosmic study, ***patients had a substantially higher baseline***  
27 ***fracture rate*** compared to the patients enrolled in Orbit. In this younger patient  
28 population, meaningful improvements in BMD were ***associated with a reduction***  
in annualized fracture rate for setrusumab treated patients compared to  
bisphosphonate treated patients, though ***the reduction did not meet statistical***  
***significance.***

(Emphasis added).

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61. Defendants further announced that, as a result of the failed studies, Ultragenyx “is evaluating its planned operations and *will promptly define and implement significant expense reductions*” (emphasis added).

62. The aforementioned press releases and statements made by the Individual Defendants are in direct contrast to statements they made during the above-referenced earnings calls, shareholder presentations, and interim study updates. In those statements, Defendants continually claimed a high level of confidence that setrusumab’s ability to increase material bone density would necessarily translate to a reduction in the annualized fracture rate of patients with type 1, 3, or 4 osteogenesis imperfecta. Defendants further claimed a lack of concern over whether minimal fractures in the control groups or increased fractures in the treatment groups could ultimately confound the results of the Phase III OI Studies. Indeed, in both instances, Defendants claimed their study design would facilitate the ability to detect the difference in fracture rate between the groups while minimizing the risk of either scenario triggering a significant negative impact on the results.

63. Investors and analysts reacted immediately to Ultragenyx’s revelation. The price of Ultragenyx’s common stock declined dramatically. From a closing market price of \$34.19 per share on December 26, 2025, Ultragenyx’s stock price fell to \$19.72 per share on December 29, 2025, a decline of about 42.32% in the span of just a single day.

64. A number of well-known analysts who had been following Ultragenyx lowered their price targets in response to Ultragenyx’s disclosures. For example, Baird, while slashing their price target by nearly 35%, justified their price cut as, “disappointingly, setrusumab did not show a benefit in AFR in the ~159-patient-placebo-controlled ORBIT study (despite a statistically-significant improvement in BMD, [Bone Mineral Density].” The analyst further highlighted Ultragenyx’s position that a “higher-than-expected placebo response was a key headwind to the study,” and pointed to anticipated “analyses, such as responses in Type 1s vs Type 3/4s.”

65. Similarly, Barclays, while dropping their price target 12% to \$44, noted that “while ORBIT’s miss was *somewhat a surprise*, COSMIC’s failure *was in line with our prediction* ...

1 While both studies showed low nominal p value for BMN improvement, it was not accompanied  
2 by a reduction of AFT in ORBIT and placebo had a low fracture rate” (emphasis added).

3 66. Additionally, Wells Fargo reduced their probability of success for FDA approval  
4 down to only 33%, noting the new difficulties from the Phase III study failure, in pertinent part:

5 FDA’s stance seems to be more about using BMD to avoid the need for large, long  
6 trials required to evaluate AFR. However, RARE has already done this & we think  
7 asking the FDA to ignore an already generated negative AFR result in favor of  
8 BMD will require flexibility beyond the spirit of the osteoporosis guidance.  
Secondly, the FDA explicitly calls out hip BMD as assessed by DXA, and not  
lumbar BMD which is what RARE assessed in ORBIT/COSMIC.

9 Notably, Wells Fargo reduced their price target by an additional \$20 to \$45.00, a reduction of  
10 nearly 49% from the \$88 target leading into the second interim analysis.

#### 11 E. Additional Remarks Following the Class Period

12 January 12, 2026

13 67. On January 12, 2026, Defendant Kakkis presented on behalf of Ultragenyx at the  
14 44<sup>th</sup> Annual J.P. Morgan Healthcare Conference and provided additional color on the ORBIT and  
15 COSMIC results.

16 68. In pertinent part, Defendant Kakkis highlighted the breakdown of the presented  
17 variations of osteogenesis imperfecta in the studies, stating:

18 If you look at the patients that we enrolled in the 2 designs, *in Orbit, they were*  
19 *generally balanced, but there were more type 3s, which are severe in the*  
20 *setrusumab arm and more type 4s in the placebo arm. And if you look at Cosmic,*  
*they’re relatively well balanced. So there were 64% of the more severe type vs 54.*

21 ...

22 Now in Orbit, because it was placebo controlled, we had to include a rescue arm  
23 because patients did not want to enroll in a trial that could go as long as 2 years, be  
24 off their bisphosphonate treatments. So if they hit a certain number of fractures,  
25 they could exit the study; 19%, *19.5% did exit the study. The placebo, though*  
*exited with type 3, type 4 patients, essentially, as you would expect, at nearly twice*  
26 *the rate of what the treated patients. So there’s clearly a differential between*  
*which patients came out.*

27 (Emphasis added).

1 69. Defendant Kakkis went on to highlight and discuss the details behind the failure of  
2 the studies to achieve their annualized fracture rate endpoints, providing, in pertinent part, the  
3 following:

4 Now if we dive in the Orbit fracture story, this is where things started to change. If  
5 you look on the right, you can see the cumulative fracture distribution curves, and  
6 you can see the groups are not really separating whichever way you look at it  
7 without the primary endpoint, without vertebral fractures and fingers and skull and  
8 the others where you look at total fractures, very similar.

9 And because the story comes really -- *if you look at the placebo group, based on*  
10 *the negative binomial model, it was only a 0.55 fracture rate estimated. But the*  
11 *median, if you look above is 0, which means of 52 patients, 26 patients had no*  
12 *fractures in the study. So this gives you very little power now to tell the difference.*  
13 The fracture frequency in the UX143 group was actually fine, 0.71. It was not very  
14 high, considering what the pretreatment fractures were at.

15 *So both study arms were lower. The placebo is slightly favored, but that's only*  
16 *with the primary endpoint, looking at all fractures are about the same.* So the  
17 question is what's going on here in the study with fractures. This was the part that  
18 was a surprise. *Now we know from the Phase II study patients felt better and got*  
19 *more active. So one of the question is did they get more active and cause more*  
20 *fractures, that we won't know for sure, but we did look at how they did, and Orbit*  
21 *is a placebo-controlled trial.*

22 ...

23 So you might wonder, *well, if the fractures aren't better, why are they doing*  
24 *better? I think it could be because they're doing better and they're running*  
25 *around. And we did see that in Phase II that some kids had fractures, but we still*  
26 *should have seen some differentiation, we didn't.* But this is the Orbit story, we  
27 think this shows an activity, but we didn't show the fracture differential.

28 So now let's talk about Cosmic. *In Cosmic, the story is a little different.* The  
fracture rate was higher. If you look at the mean or median, you could see there was  
2.6 was the mean for the bisphosphonate group. So several fold more fractures  
going on in the study. *If you look at the cumulative distribution graphs on the*  
*right, you can see that they're separating quickly, right, after initiation of trial.*  
*There's a little turn up in the graph that happens to be when we do a 12-month*  
*skeletal survey.*

That's why a bunch of fractures are added because we see the fractures on a survey  
that weren't seen before and they're added. But you can see the separation of the 2  
lines gets even greater. *So this is separating in the way we would have thought,*  
*right? This is what we were expecting. When you do the negative binomial model,*  
*it shows a 21% difference, but still not significant,* but it's -- the pattern looks more  
like what we would have expected to see.

1 (Emphasis added).

2 70. During the question-and-answer segment that followed, Defendant Kakkis further  
3 highlighted the Company's current lack of understanding as to the fracture rate results during the  
4 following exchange:

5 <Q: Anupam Rama – JPMorgan Chase & Co – Vice President and Analyst> How  
6 do you think about next regulatory steps now that you have the totality of this data?  
7 Like is there a path forward, you believe, even if it's in a subset of patients such as  
8 pediatrics?

9 <A: Emil D. Kakkis> I think right now, *our most important thing is to really*  
10 *understand more about the data and why it is the way it is. Long bone did not*  
11 *appear better. Is that because kids were more active and they fractured? Or is*  
12 *there something else going on there?* So we need to understand all of that to  
13 understand it better. And then we need to do that before we end up going. If we go  
14 to the agency, we'll want to do that with a firm understanding of what we have in  
15 front of us. And I think there's a little more work to do before we make that move.

16 (Emphasis added).

17 71. Additionally, William Blair, reporting after Ultragenyx provided more data on the  
18 results in mid-January, noted that “the updated data from the Orbit study showed patients treated  
19 with setrusumab had numerically more breaks than patients treated with placebo ... the fracture  
20 rate in patients treated with setrusumab was 0.71, compared to 0.55 in the placebo group ...  
21 management indicated that the *study wasn't well powered to show a difference* in the negative  
22 binomial model selected for the primary endpoint.”

23 72. The fact that these analysts, and others, discussed the failure of Ultragenyx's Phase  
24 III OI Studies to demonstrate their primary endpoint of reduced AFR suggests the public placed  
25 significant weight on Ultragenyx's confidence in both the from of its Phase III OI Studies and their  
26 ability to demonstrate a reduction in fractures across all types of OI tested. The frequent in-depth  
27 discussions of the tests and their results confirm that Defendants' statements during the Class  
28 Period were material.

#### 29 **F. Additional Scienter Allegations**

30 73. During the Class Period, Defendants acted with scienter in that they knew, should  
31 have known, or otherwise were deliberately reckless in not knowing that the public statements

1 disseminated on behalf of Ultragenyx were materially false and misleading at the time they were  
2 made. Defendants had actual knowledge of, or access to, non-public information concerning both  
3 the existing results of setrusumab and the intended study design and scope of the Phase III Orbit  
4 and Cosmic studies.

5 74. Notwithstanding such, Defendants repeatedly and affirmatively represented to  
6 investors that Ultragenyx's study designs for its Phase III Orbit and Cosmic studies were well  
7 positioned to demonstrate the primary endpoint of a reduction in AFR.

8 75. Defendants further repeatedly claimed there would be no significant negative  
9 impact from the inclusion of a greater proportion of Type 3 and 4 OI patients in the studies than  
10 were present in the Phase II Orbit study.

11 76. Yet, Defendants made selective and misleading disclosures in articulating the  
12 breakdown and potential impact of the OI type variances being studied. Notably, during the  
13 February 13, 2025, earnings call, Defendants indicated there was a "fairly similar" make up in  
14 patient entry criteria between Phase II and III with some increase in Type 3 and 4s, "but not a  
15 dramatic difference." By the following earnings call on May 6, 2025, Defendants conceded that  
16 about half of Phase III patients were type 3 or 4, compared to less than a third in Phase II. In  
17 August the narrative shifted to "a lot more Type IIIs and Type IVs in the study," blaming the  
18 failure to reach an interim analysis partially on their "complex problems."

19 77. Defendants' scienter was further evidenced by their claims that the control group  
20 patients would generate enough fractures to properly compare them to the treatment populations.

21 78. Defendants repeatedly claimed that by forcing the control group to merely come  
22 into the clinic, "the incident of accident and fractures [would go] up."

23 79. Further, and despite acknowledging that patients in the Phase II Orbit study who  
24 felt improved on treatment tended to engage in more physical activity and thus trigger more  
25 fractures, Defendants argued there was no reason to implement any activity limitations on the  
26 patient population. Defendants were aware of the risk but dismissed them to investors, claiming  
27 they "we're not so worried about the ... noise of having more fracture risk at this point," and  
28

1 arguing that setrusumab would increase the strength of the bones sufficiently “to even compensate  
2 for any change [that] might occur because patients are more active.”

3 80. Defendants were aware of these risks yet continued to deliberately disregard or  
4 otherwise minimize them in their claims of confidence to investors. At one point Defendant  
5 Kakkis even claimed that he did not “see any uncontrolled factors” in the Phase III protocols.

6 81. Ultimately, these risks, which Defendants either knew or deliberately disregarded,  
7 came to fruition. The Phase III OI Studies failed to demonstrate a reduction in AFR as the control  
8 groups ultimately achieved similar reductions to the testing groups due (1) inflated pre-test bone  
9 breaks among the more severe OI type populations; (2) a failure to increase the fracture rate of  
10 control group patients by merely coming into the clinic; and (3) a smaller reduction in AFR among  
11 the treatment population because of their increased activity. Alternatively, the studies failed  
12 merely because setrusumab’s ability to increase material bone density does not truly cause or even  
13 correlate to a reduction in annualized fracture rate among OI patients, suggesting Defendants’  
14 repeated statements of confidence in the drug and its potential was, at best deliberately reckless.

#### 15 **G. Loss Causation and Economic Loss**

16 82. During the Class Period, as detailed herein, Defendants made materially false and  
17 misleading statements and engaged in a scheme to deceive the market and a course of conduct that  
18 artificially inflated the price of Ultragenyx’s common stock and operated as a fraud or deceit on  
19 Class Period purchasers of Ultragenyx’s common stock by materially misleading the investing  
20 public. Later, Defendants’ prior misrepresentations and fraudulent conduct became apparent to the  
21 market, the price of Ultragenyx’s common stock materially declined, as the prior artificial inflation  
22 came out of the price over time. As a result of their purchases of Ultragenyx’s common stock  
23 during the Class Period, Plaintiff and other members of the Class suffered economic loss, *i.e.*,  
24 damages under federal securities laws.

25 83. Ultragenyx’s stock price fell in response to the corrective events on July 9, 2025  
26 and December 26, 2025, as alleged *supra*. On July 9, 2025, Ultragenyx revealed that it would be  
27 progressing with the study instead of ending it early. From a closing market price of \$41.44 per  
28

1 share on July 9, 2025, Ultragenyx's stock price fell to \$31.03 per share on July 10, 2025, a decline  
2 of about 25.12% in the span of just a single day.

3 84. On December 26, 2025, Ultragenyx announced both its Phase III Orbit and Cosmic  
4 studies failed demonstrate that setrusumab triggered a statistically significant reduction in  
5 annualized fracture rates for patients with osteogenesis imperfecta. The price of Ultragenyx's  
6 common stock declined dramatically. From a closing market price of \$34.19 per share on  
7 December 26, 2025, Ultragenyx's stock price fell to \$19.72 per share on December 29, 2025, a  
8 decline of about 42.32% in the span of just a single day.

9 **H. Presumption of Reliance; Fraud-On-The-Market**

10 85. At all relevant times, the market for Ultragenyx's common stock was an efficient  
11 market for the following reasons, among others:

12 (a) Ultragenyx's common stock met the requirements for listing and was listed and  
13 actively traded on the NASDAQ during the Class Period, a highly efficient and automated market;

14 (b) Ultragenyx communicated with public investors via established market  
15 communication mechanisms, including disseminations of press releases on the national circuits of  
16 major newswire services and other wide-ranging public disclosures, such as communications with  
17 the financial press and other similar reporting services;

18 (c) Ultragenyx was followed by several securities analysts employed by major  
19 brokerage firms who wrote reports that were distributed to the sales force and certain customers  
20 of their respective brokerage firms during the Class Period. Each of these reports was publicly  
21 available and entered the public marketplace; and

22 (d) Unexpected material news about Ultragenyx was reflected in and incorporated into  
23 the Company's stock price during the Class Period.

24 86. As a result of the foregoing, the market for Ultragenyx's common stock promptly  
25 digested current information regarding the Company from all publicly available sources and  
26 reflected such information in Ultragenyx's stock price. Under these circumstances, all purchasers  
27 of Ultragenyx's common stock during the Class Period suffered similar injury through their  
28

1 purchase of Ultragenyx's common stock at artificially inflated prices, and a presumption of  
2 reliance applies.

3 87. Alternatively, reliance need not be proven in this action because the action involves  
4 omissions and deficient disclosures. Positive proof of reliance is not a prerequisite to recovery  
5 pursuant to ruling of the United States Supreme Court in *Affiliated Ute Citizens of Utah v. United*  
6 *States*, 406 U.S. 128 (1972). All that is necessary is that the facts withheld be material in the sense  
7 that a reasonable investor might have considered the omitted information important in deciding  
8 whether to buy or sell the subject security.

9 **I. No Safe Harbor; Inapplicability of Bespeaks Caution Doctrine**

10 88. The statutory safe harbor provided for forward-looking statements under certain  
11 circumstances does not apply to any of the material misrepresentations and omissions alleged in  
12 this Complaint. As alleged above, Defendants' liability stems from the fact that they provided  
13 investors with revenue projections while at the same time failing to maintain adequate forecasting  
14 processes. Defendants provided the public with forecasts that failed to account for this decline in  
15 sales and/or adequately disclose the fact that the Company at the current time did not have adequate  
16 forecasting processes.

17 89. To the extent certain of the statements alleged to be misleading or inaccurate may  
18 be characterized as forward looking, they were not identified as "forward-looking statements"  
19 when made and there were no meaningful cautionary statements identifying important factors that  
20 could cause actual results to differ materially from those in the purportedly forward-looking  
21 statements.

22 90. Defendants are also liable for any false or misleading "forward-looking statements"  
23 pleaded because, at the time each "forward-looking statement" was made, the speaker knew the  
24 "forward-looking statement" was false or misleading and the "forward-looking statement" was  
25 authorized and/or approved by an executive officer of Ultragenyx who knew that the "forward-  
26 looking statement" was false. Alternatively, none of the historic or present-tense statements made  
27 by Defendants were assumptions underlying or relating to any plan, projection, or statement of  
28 future economic performance, as they were not stated to be such assumptions underlying or

1 relating to any projection or statement of future economic performance when made, nor were any  
2 of the projections or forecasts made by the defendants expressly related to or stated to be dependent  
3 on those historic or present-tense statements when made.

4 **CLASS ACTION ALLEGATIONS**

5 91. Plaintiff brings this action as a class action pursuant to Federal Rule of Civil  
6 Procedure 23(a) and (b)(3) on behalf of a Class, consisting of all those who purchased or otherwise  
7 acquired Ultragenyx’s common stock during the Class Period (the “Class”); and were damaged  
8 upon the revelation of the alleged corrective disclosure. Excluded from the Class are defendants  
9 herein, the officers and directors of the Company, at all relevant times, members of their immediate  
10 families and their legal representatives, heirs, successors or assigns and any entity in which  
11 defendants have or had a controlling interest.

12 92. The members of the Class are so numerous that joinder of all members is  
13 impracticable. Throughout the Class Period, Ultragenyx’s common stock were actively traded on  
14 the NASDAQ. While the exact number of Class members is unknown to Plaintiff at this time and  
15 can be ascertained only through appropriate discovery, Plaintiff believes that there are hundreds  
16 or thousands of members in the proposed Class. Record owners and other members of the Class  
17 may be identified from records maintained by Ultragenyx or its transfer agent and may be notified  
18 of the pendency of this action by mail, using the form of notice similar to that customarily used in  
19 securities class actions. As of October 30, 2025, there were 96.47 million shares of the Company’s  
20 common stock outstanding. Upon information and belief, these shares are held by thousands, if  
21 not millions, of individuals located throughout the country and possibly the world. Joinder would  
22 be highly impracticable.

23 93. Plaintiff’s claims are typical of the claims of the members of the Class as all  
24 members of the Class are similarly affected by Defendants’ wrongful conduct in violation of  
25 federal law that is complained of herein.

26 94. Plaintiff will fairly and adequately protect the interests of the members of the Class  
27 and has retained counsel competent and experienced in class and securities litigation. Plaintiff has  
28 no interests antagonistic to or in conflict with those of the Class.

1 95. Common questions of law and fact exist as to all members of the Class and  
2 predominate over any questions solely affecting individual members of the Class. Among the  
3 questions of law and fact common to the Class are:

4 (a) whether the federal securities laws were violated by Defendants' acts as alleged  
5 herein;

6 (b) whether statements made by Defendants to the investing public during the Class  
7 Period misrepresented material facts about the business, operations and management of  
8 Ultragenyx;

9 (c) whether the Individual Defendants caused Ultragenyx to issue false and misleading  
10 financial statements during the Class Period;

11 (d) whether Defendants acted knowingly or recklessly in issuing false and misleading  
12 financial statements;

13 (e) whether the prices of Ultragenyx's common stock during the Class Period were  
14 artificially inflated because of the Defendants' conduct complained of herein; and

15 (f) whether the members of the Class have sustained damages and, if so, what is the  
16 proper measure of damages.

17 96. A class action is superior to all other available methods for the fair and efficient  
18 adjudication of this controversy since joinder of all members is impracticable. Furthermore, as the  
19 damages suffered by individual Class members may be relatively small, the expense and burden  
20 of individual litigation make it impossible for members of the Class to individually redress the  
21 wrongs done to them. There will be no difficulty in the management of this action as a class action.

22 **COUNT I**

23 ***Against All Defendants for Violations of***

24 **Section 10(b) and Rule 10b-5 Promulgated Thereunder**

25 97. Plaintiff repeats and realleges each and every allegation contained above as if fully  
26 set forth herein.

27 98. This Count is asserted against defendants and is based upon Section 10(b) of the  
28 Exchange Act, 15 U.S.C. § 78j(b), and Rule 10b-5 promulgated thereunder by the SEC.

1           99. During the Class Period, Defendants engaged in a plan, scheme, conspiracy and  
2 course of conduct, pursuant to which they knowingly or recklessly engaged in acts, transactions,  
3 practices and courses of business which operated as a fraud and deceit upon Plaintiff and the other  
4 members of the Class; made various untrue statements of material facts and omitted to state  
5 material facts necessary in order to make the statements made, in light of the circumstances under  
6 which they were made, not misleading; and employed devices, schemes and artifices to defraud in  
7 connection with the purchase and sale of securities. Such scheme was intended to, and, throughout  
8 the Class Period, did: (i) deceive the investing public, including Plaintiff and other Class members,  
9 as alleged herein; (ii) artificially inflate and maintain the market price of Ultragenyx common  
10 stock; and (iii) cause Plaintiff and other members of the Class to purchase or otherwise acquire  
11 Ultragenyx's securities at artificially inflated prices. In furtherance of this unlawful scheme, plan  
12 and course of conduct, Defendants, and each of them, took the actions set forth herein.

13           100. Pursuant to the above plan, scheme, conspiracy and course of conduct, each of the  
14 defendants participated directly or indirectly in the preparation and/or issuance of the quarterly  
15 and annual reports, SEC filings, press releases and other statements and documents described  
16 above, including statements made to securities analysts and the media that were designed to  
17 influence the market for Ultragenyx's securities. Such reports, filings, releases and statements were  
18 materially false and misleading in that they failed to disclose material adverse information and  
19 misrepresented the truth about the Company.

20           101. By virtue of their positions at the Company, Defendants had actual knowledge of  
21 the materially false and misleading statements and material omissions alleged herein and intended  
22 thereby to deceive Plaintiff and the other members of the Class, or, in the alternative, Defendants  
23 acted with reckless disregard for the truth in that they failed or refused to ascertain and disclose  
24 such facts as would reveal the materially false and misleading nature of the statements made,  
25 although such facts were readily available to Defendants. Said acts and omissions of defendants  
26 were committed willfully or with reckless disregard for the truth. In addition, each defendant knew  
27 or recklessly disregarded that material facts were being misrepresented or omitted as described  
28 above.

1           102. Information showing that Defendants acted knowingly or with reckless disregard  
2 for the truth is peculiarly within defendants' knowledge and control. As the senior managers and/or  
3 directors of the Company, the Individual Defendants had knowledge of the details of Ultragenyx's  
4 internal affairs.

5           103. The Individual Defendants are liable both directly and indirectly for the wrongs  
6 complained of herein. Because of their positions of control and authority, the Individual  
7 Defendants were able to and did, directly or indirectly, control the content of the statements of the  
8 Company. As officers and/or directors of a publicly-held company, the Individual Defendants had  
9 a duty to disseminate timely, accurate, and truthful information with respect to Ultragenyx's  
10 businesses, operations, future financial condition and future prospects. As a result of the  
11 dissemination of the aforementioned false and misleading reports, releases and public statements,  
12 the market price of Ultragenyx's common stock was artificially inflated throughout the Class  
13 Period. In ignorance of the adverse facts concerning the Company which were concealed by  
14 Defendants, Plaintiff and the other members of the Class purchased or otherwise acquired  
15 Ultragenyx's common stock at artificially inflated prices and relied upon the price of the common  
16 stock, the integrity of the market for the common stock and/or upon statements disseminated by  
17 Defendants, and were damaged thereby.

18           104. During the Class Period, Ultragenyx's common stock was traded on an active and  
19 efficient market. Plaintiff and the other members of the Class, relying on the materially false and  
20 misleading statements described herein, which the defendants made, issued or caused to be  
21 disseminated, or relying upon the integrity of the market, purchased or otherwise acquired shares  
22 of Ultragenyx's common stock at prices artificially inflated by defendants' wrongful conduct. Had  
23 Plaintiff and the other members of the Class known the truth, they would not have purchased or  
24 otherwise acquired said common stock, or would not have purchased or otherwise acquired them  
25 at the inflated prices that were paid. At the time of the purchases and/or acquisitions by Plaintiff  
26 and the Class, the true value of Ultragenyx's common stock was substantially lower than the prices  
27 paid by Plaintiff and the other members of the Class. The market price of Ultragenyx's common  
28

1 stock declined sharply upon public disclosure of the facts alleged herein to the injury of Plaintiff  
2 and Class members.

3 105. By reason of the conduct alleged herein, Defendants knowingly or recklessly,  
4 directly or indirectly, have violated Section 10(b) of the Exchange Act and Rule 10b-5  
5 promulgated thereunder.

6 106. As a direct and proximate result of defendants' wrongful conduct, Plaintiff and the  
7 other members of the Class suffered damages in connection with their respective purchases,  
8 acquisitions and sales of the Company's common stock during the Class Period, upon the  
9 disclosure that the Company had been disseminating misrepresented financial statements to the  
10 investing public.

11 **COUNT II**

12 ***Against the Individual Defendants***

13 ***for Violations of Section 20(a) of the Exchange Act***

14 107. Plaintiff repeats and realleges each and every allegation contained in the foregoing  
15 paragraphs as if fully set forth herein.

16 108. During the Class Period, the Individual Defendants participated in the operation  
17 and management of the Company, and conducted and participated, directly and indirectly, in the  
18 conduct of the Company's business affairs. Because of their senior positions, they knew the  
19 adverse non-public information about Ultragenyx's misstatements.

20 109. As officers and/or directors of a publicly owned company, the Individual  
21 Defendants had a duty to disseminate accurate and truthful information, and to correct promptly  
22 any public statements issued by Ultragenyx which had become materially false or misleading.

23 110. Because of their positions of control and authority as senior officers, the Individual  
24 Defendants were able to, and did, control the contents of the various reports, press releases and  
25 public filings which Ultragenyx disseminated in the marketplace during the Class Period  
26 concerning the misrepresentations. Throughout the Class Period, the Individual Defendants  
27 exercised their power and authority to cause Ultragenyx to engage in the wrongful acts complained  
28 of herein. The Individual Defendants therefore, were "controlling persons" of the Company within

1 the meaning of Section 20(a) of the Exchange Act. In this capacity, they participated in the  
2 unlawful conduct alleged which artificially inflated the market price of Ultragenyx's common  
3 stock.

4 111. Each of the Individual Defendants, therefore, acted as a controlling person of the  
5 Company. By reason of their senior management positions and/or being directors of the Company,  
6 each of the Individual Defendants had the power to direct the actions of, and exercised the same  
7 to cause Ultragenyx to engage in the unlawful acts and conduct complained of herein. Each of the  
8 Individual Defendants exercised control over the general operations of the Company and possessed  
9 the power to control the specific activities which comprise the primary violations about which  
10 Plaintiff and the other members of the Class complain.

11 112. By reason of the above conduct, the Individual Defendants and/or Ultragenyx are  
12 liable pursuant to Section 20(a) of the Exchange Act for the violations committed by the Company.

13 **PRAYER FOR RELIEF**

14 **WHEREFORE**, Plaintiff demand judgment against defendants as follows:

15 A. Determining that the instant action may be maintained as a class action under Rule  
16 23 of the Federal Rules of Civil Procedure, and certifying Plaintiff as the Class representatives;

17 B. Requiring Defendants to pay damages sustained by Plaintiff and the Class by reason  
18 of the acts and transactions alleged herein;

19 C. Awarding Plaintiff and the other members of the Class pre-judgment and post-  
20 judgment interest, as well as their reasonable attorneys' fees, expert fees and other costs; and

21 D. Awarding such other and further relief as this Court may deem just and proper.

22 **DEMAND FOR TRIAL BY JURY**

23 Plaintiff hereby demands a trial by jury.  
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25  
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