UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): September 22, 2017

ULTRAGENYX PHARMACEUTICAL INC.
(Exact name of registrant as specified in charter)

Delaware	**001-36276**	**27-2546083**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

60 Leveroni Court, Novato, California	**94949**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (415) 483-8800

Not Applicable
(Former name or former address, if changed since last report)

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

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☒ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

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

Emerging growth company ☐

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

Item 8.01. Other Events.

On September 22, 2017, Ultragenyx Pharmaceutical Inc. (the "***Company***") presented as part of JPM's 2017 Fall Biotech Conference Call series.

A transcript of the conference call is filed herewith as Exhibit 99.1.

Item 9.01 Financial Statements and Exhibits

(d) Exhibits

Exhibit No.	**Description**
99.1	Transcript of Conference Call on September 22, 2017

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SIGNATURE

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

Date: September 25, 2017

Ultragenyx Pharmaceutical Inc.

By: /s/ Shalini Sharp
Name: Shalini Sharp
Title: Executive Vice President, Chief Financial Officer

RARE JPM 2017 Fall Biotech Conference Call Series
September 22, 2017 – 7:30 AM PST – Conference Call Transcript

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Operator:

Please disconnect now. At this time, all participants will be on a listen only mode for the entire duration of today's conference. I would now like to turn the call over to Cory Kasimov, you may begin.

Cory Kasimov, Senior Biotechnology Analyst at JPMorgan:

KASIMOV: Great. Thank you, Mari, and good morning everyone. My name is Cory Kasimov. I'm a Senior Biotechnology Analyst at JPMorgan, and I'm here with Shawn Fu and Brittany Turner from our team, and we appreciate you joining us for the latest installment of our 2017 Fall Biotech Conference Call Series on what is in fact the first official day of fall. Today it's our pleasure to be joined by Ultragenyx, and we're lucky to have both the CEO, Emil Kakkis, and CFO, Shalini Sharp, in addition to Ryan Martins and Danielle Keatley from IR, so thank you very much for participating today. We really do appreciate you taking the time. Now, we'll have our standard format for this call. Following some brief opening comments by Emil, we'll move into Q&A, and first discuss the recent news around Dimension, and then walk through the company's pipeline and overall strategy. We have a lot to get through but as usual, feel free to email us questions throughout the call, and we'll ask as many as we can time permitting. Now before I hand it over to Emil, Danielle will read some forward looking statements, so Danielle, why don't I turn it to you first?

DANIELLE KEATLEY: Thanks, Cory. So except for historical information, the matters discussed on the call, including statements relating to Ultragenyx's intentions, expectations, or predictions of its future and business environment, or statements relating to Ultragenyx's offer and the potential benefits of the transaction with Dimension are forward-looking statements. Such forward-looking statements involve substantial risk and uncertainties that could cause our future results, performance, or achievements to differ significantly from those expressed or implied by the forward-looking statements. There is no assurance that the potential transaction with Dimension will be consummated. For further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, see Ultragenyx's periodic reports filed with the SEC. If and when Ultragenyx's proposed tender offer for Dimension's shares commences, Ultragenyx will file with the SEC a tender offer statement on Schedule TO, including an offer to purchase, a letter of transmittal, and related materials. Investors and security holders are urged to read both the tender offer statement and any solicitation recommendation statement filed by Dimension regarding the offer when they become available because they will contain important information about the offer. When available, investors and security holders may obtain free copies of these materials at the website maintained by the SEC at sec.gov, or by directing requests for such materials to the information agent for the offer, which will be named in the tender offer statement. Cory, I'll turn it back to you.

KASIMOV: All right, thanks, that's a mouthful. All right, so now with that out of the way, Emil, do you want to start us off with some brief introductory comments on the state of Ultragenyx?

Dr. Emil D. Kakkis, Chief Executive Officer and President of Ultragenyx Pharmaceutical:

EMIL: Sure, and first of all I want to thank Cory and JPMorgan for having us on the call today. Ultragenyx, since our founding in 2010 with just two employees, we have made tremendous progress on the clinical development and regulatory front, with two products now filed in the U.S. and Europe. This is an important accomplishment for any biotech company, particularly for a company of our age. Our preparation for global commercialization is also well underway, and the Ultragenyx team is highly focused on the potential of Burosumab particularly, pending the FDA review of our BLA. It is one of the major drivers of the company in 2018 and beyond. We can get into details about Burosumab and other programs in the Q&A section, but before we do, I'd like to review a few key points regarding our offer to acquire Dimension Therapeutics earlier this week. As you can imagine, I'm not going to provide further updates on the specifics of our proposal today but I can talk about the strategic and scientific benefits that have led us to make our offer for Dimension. We offered to buy Dimension because we have a compelling opportunity to create a more valuable next-generation Rare Disease company by bringing together Ultragenyx's advanced clinical and regulatory expertise as well as our Rare metabolic and commercial infrastructure with Dimension's Rare Disease focused gene therapies and talented team of scientists. More specifically with this combination, there are a number of key points that we should make. First, we gain a technology platform to expand into gene therapy, which makes sense as part of our broader goal to become a comprehensive rare disease company. Second, the products acquired are an excellent therapeutic fit in the metabolic genetic disease area, and third, the acquired technology is complementary with our small molecule protein MRNA modes of treatment, allowing us to choose the best approach to treatment for any disease. Finally, the acquired programs are at an early stage of clinical development that are complementary to stage 2, Ultragenyx's later stage and filed programs. As you know, I have served on Dimension's scientific advisory board since the inception of Dimension so I am familiar with the work they have been doing over the last several years. I have great respect for the team's expertise that they have assembled for gene therapy and their requisite AAV process development and manufacturing technology, which is a key factor in executing AAV clinical trials and bringing these gene therapies to market. As experts in the metabolic rare disease space, we are confident that our scientific, clinical, regulatory, and commercial skills are highly complementary to Dimension's technology programs and people. There is an excellent therapeutic fit. We see an opportunity to seamlessly integrate Dimension's technology and manufacturing expertise to advance the treatment of certain genetic diseases. We believe that we are

well positioned to support clinical development and the potential global filing and commercialization for any products successfully developed from Dimension's portfolio, also providing us additional catalysts in 2018 and 2019. Thank you for allowing me to make these introductory remarks, and I'm happy to take some of your questions now.

KASIMOV: All right, thanks Emil. Obviously, the timing of this call clearly worked out quite well with the announcement earlier this week of that proposed acquisition of Dimension. And I guess some of my questions will be somewhat repetitive of some of the things you have discussed, and I assume there would be some others that you might not be able to answer but I'll ask them anyway and you can just tell me if you can't. But I guess maybe we can start the discussion by walking through the strategic rationale of this move a little bit more, in what maybe specifically attracted you to this company in particular and maybe gene therapy more broadly.

EMIL: Well, let's start with sort our strategic development of Ultragenyx to begin with. We focused originally on straightforward small molecules and well-characterized biologics as a way to build the company without creating any technology platform risk, and our view was we would do that to start, generate products that are let's say fileable and on the way to commercial revenue, and then think about expanding our technology base, and that's what we've been doing. After the first two products got to that point, we did add some programs from mRNA therapeutics, we're now adding these for gene therapy, and so our view is when you look at any particular genetic disease, there may be several ways to approach their treatment, and rather than only approaching a treatment with the one method you have in house, I'd rather be able to have the option to figure out what's the best approach you could take. And so having gene therapy now in the list does provide us another opportunity to approach therapy, and if you think in the long run with the progress being made in gene therapy, it seems like an important piece for any company that's going to focus on rare disease therapeutics.

KASIMOV: Okay, so then can you describe Dimension's overall gene therapy capabilities and platform?

EMIL: Well, I've been on their SAB from the very beginning of the company, and the Dimension group, basically a number of them including their Chief Science Officer, come from Genzyme, and Genzyme has been involved in AAV for many years, in fact one of the leaders in AAV strategies. In addition, because they were at a company that had strong knowledge about GMP manufacturing, they also were working on scalable AAV manufacturing, and I think those are really key pieces of the ability to do gene therapy these days is being able to develop scalable AAV GMP manufacturing strategies. In addition to that, they have brought in some people with rare disease experience to help on developing the therapeutic strategies, and as an SAB member, they worked through picking their targets which they announced. A number of the targets are metabolic targets which are I think good targets in the sense that they have readily assessable biomarkers that you can tell within weeks to months that something is actually

happening and you can quantify to what degree you're having an impact on a patient, and those diseases also are a really good fit for us. We have a lot of history in them. So I think the people there were able to work in a space which I think has a great potential for being able to use gene therapy and understand how to develop it, during the process of figuring out what the right dose is and whether you're achieving what needs to be achieved from a biochemistry standpoint.

KASIMOV: Okay. So what are the key programs that are currently under evaluation at Dimension, and what's your understanding of the potential market opportunities associated with them?

EMIL: Well, the three programs closest to the clinic or in the clinic, first is DTX301 which is the urea cycle disorder Ornithine Transcarbamylase Deficiency, so that one they are now dosing their first patients. DTX401 is for von Gierke disease or Glycogen Storage Disease Type 1, which is a disease which patients can't release glucose from their liver, and their livers get enlarged and hard, and they have hypoglycemia problems. That one is expected to be in the clinic sometime next year. The third program is they have a Factor VIII program in partnership with Bayer. That's DTX201. That's basically a hemophilia A, factor VIII basically, mini-gene, and they are working on that scalable manufacturing. That is expected, based on their public statements, to be in the clinic next year.

KASIMOV: Okay. All right, and then with regard to the hemophilia program, and they had hemophilia D, what happened with hemophilia B and what's the potential read-through in your opinion to other Dimension programs, if any?

EMIL: Well, the hemophilia B program, speaking from public statements, they successfully achieved expression but they had some inflammatory reactions which in fact all the gene therapy companies have had, requiring steroids, and the question with that type of those reactions are to what degree do they hurt expression over the long haul, and they had some effects on expression, and I think they made the determination and announced that compared to the other programs and where they're at, that they didn't feel it was competitive and met the target profile they preferred, so I think that made practical sense. But I think the issue of inflammation in the liver using AAV is something that's pervasive among all the companies to some degree, and so I don't think there's anything particularly dramatic there. Now, they used a particular strain of Clade E called AAVrh10. Clade E is where AAV8 is, that type, and there's some variations in that and this is called the AAVrh10. Whether that particular vector is an issue or not, is unknown. Each of these Clades, these particular variations have certain features, but the thing that's important is that that particular strain of Clade E AAV with viruses was only being used for the Factor B program. So the two programs I talked about, 301 and 401 on the inborn errors are using AAV8, so the one that's probably more common among more companies. So I would look at what happened in B as being, one, a common problem, and two, if there is anything related to the vector, it really only affects the Factor B program and not the other part of the portfolio.

KASIMOV: Okay. All right, and you have mentioned manufacturing previously on this call and earlier in the week, can you talk a little bit more about Dimension's manufacturing capabilities, and maybe now as Ultragenyx is transitioning into a commercial organization, how you could potentially ramp up the capacity there?

EMIL: Yeah, so they're using suspension-based cell culture, mammalian cell culture system to produce the AAV virus, which I think are the sensible choice. And they're scalable because they're a suspension culture, and they have been running it at 250 liters scale, and they also have a 1,000 liter scale that's out there that they're developing. So the strategies they're using are credible, scalable GMP approaches, and that contrasts with the earlier AAV years when people were using adherent cells or things in roller balls and that type of thing, which are very difficult to scale and were a critical problem because if you can't make enough of the AAV virus, and these doses require substantial amounts of virus, then you can't really do gene therapy. So the group there clearly has a curve on developing strategies for manufacturing the AAV virus and we think that's a critical piece, and as I said when we wanted to get into the technology platform of gene therapy, the manufacturing component of it is a critical component, and that was why this made more sense to us than other things that might be done.

KASIMOV: Okay. So then with regards to the transaction and the proposal itself, and just the overall competitiveness of this process, can you talk about timing a little bit and why the offer was made two weeks after the process began with news of the REGENX-Dimension deal?

EMIL: Well, I can talk about the timing. Look, we were aware of Dimension for obviously since its founding, and we watched them all year thinking about it, but we got interested in doing it when they announced the transaction with REGENX, which did catch us off-guard. I had thought they were going to continue for a while. But in any case, that kind of opened the door to the fact that they were considering or would consider being acquired, and put us into action. I'll let Shalini fill us in a little bit about the process going forward.

Shalini Sharp, Chief Financial Officer:

SHALINI: Sure, so as we said on the prior call earlier this week, we expect the conditions for the transaction to be satisfied so that the tender offer could complete as soon as 25 business days after a merger agreement would be signed, and that would follow any due diligence period as well, and we are pleased, of course, that Dimension's board made a determination that allows Dimension to provide information to and to conduct discussions with us regarding our proposal.

KASIMOV: Okay, and then in terms of expecting, not expecting next steps between now and getting a merger agreement signed, I assume that's a little bit up in the air, or just maybe TBD is a better way to look at it?

SHALINI: We're really not able to comment on a lot of the day-to-day activities related to the process that's going on right now. I think as we said originally, we were looking basically at publicly available information on Dimension, and we were asking for an abbreviated period to conduct due diligence to confirm some of the public information that we've seen, and then it's the tender offer process which I have already described, and we do think that that's at least a meaningfully faster process than the all-share transition that was proposed by REGENX because the all-cash offer would then be completed hopefully as a tender offer which would be complete again as soon as 25 business days after an agreement was signed.

KASIMOV: Okay, makes sense. So looking to some of the other side just for a second, in the event the deal does not go through, what does this say about your commitment to expanding your development strategy over to gene therapy? And Emil, you made an interesting comment early on that if you're in the orphan disease business, you really need to be looking at gene therapy, so what does this overall move signal for Ultragenyx?

EMIL: Well, I think it signals that we recognize that gene therapy has come of age, and that there is potential to successfully treat diseases now with the advance that's been made. The Dimension offer doesn't necessarily mean we will buy anything but we are looking at ways to utilize gene therapy technology. That could be through partnerships or other types of activities if we didn't do this. So it doesn't necessarily say we would acquire anything just to get in, I think this is a particularly reasonable opportunity for us, but the need to be in gene therapy I think for certain disease states is pretty clear that this is going to change things. I think there have been some very exciting successes by other companies out in the space that really open the door to treating some diseases that you couldn't treat any other way, and that's where we get excited about being able to approach a disease that might be difficult to do enzyme therapy or a small molecule or any other strategy, but where gene therapy might have the particular edge at solving a problem, and if we can find those indications that will do that, we will to try work on them. There are so many thousands of diseases untreated that it's a wide open field, and so having this option would be important. We would find one way or another to do it, but obviously in this case we looked at an acquisition, but other possible strategies would not necessarily involve an acquisition.

KASIMOV: Okay. And then lastly on Dimension, can you I guess briefly review the scope of their IP and overall patent portfolio in this emerging space?

EMIL: Well, I can't go deep into their IP at this point but what I can say is that they have licensed their vectors, in fact from REGENX, and REGENX and Jim Wilson's group at UPenn have been the core AAV technology that's being used in a lot of places, at a lot of companies that is, and they have licensed this particular indication from REGENX for those purposes. They have one more option, free option available to execute, but it's very similar to what everyone else is using in terms of its source from the great work that Jim Wilson has done at UPenn.

KASIMOV: Okay. All right, terrific, so we'll stop there for now on Dimension. Again, happy to ask some more email questions if we get them on that subject, but for now let's move on to KRN23 or Burosumab, and maybe start with a regulatory update, and maybe more specifically do you view the acceptance of the filing at this point as more or less a – "given" may not be the right word – but based on your interactions with the agency, or do you think there is lingering risk on that front?

EMIL: Well, in the process of making the filing for Burosumab, we did hold a detailed preliminary meeting with the FDA where we discussed the list of specific items they wanted, and we actually took some extra time to fulfil those requests from the agency, so we believe we have fulfilled all the requests that they had asked of us in the dataset, and any other additional information, for example on more biopsy data, we could provide during review, which they understand. So I don't see any, at this point, any significant risk to that, but we haven't yet announced of course acceptance because now since the change in how it works, it takes two months before you get the validation or acceptance of the filing and then – or excuse me. We submit, the FDA files, so they will give us the announcement when they are finished doing that review, and then – the initial review part, and then we'll find out more about PDUFA dates, etcetera.

KASIMOV: Okay, and at this point, and based on the conversations in your pre-BLA meeting, would you expect the FDA to convene an advisory committee?

EMIL: Our expectation is that they would convene an advisory committee because it's a new mechanism of action in a new chemical entity, new molecular entity. So as an NME, new mechanism of action, it's in a reasonably-sized population of patients, I think it's likely, but we haven't received and we didn't disclose any specific definitive statement about that. We will probably hear about that when we find out about the submission.

KASIMOV: Right, okay. So then maybe for our listeners who might not be aware, can you remind us of what's included in the filing and how the U.S. package might differ from that in Europe?

EMIL: Yeah, so the U.S. package has a pediatric filing that includes the Study 201, which is in 52 patients, ages 5 to 12, and that includes 64 weeks of data from those patients. It also includes from the peds package 24-week data from the under-5-year-old study as well, so those are 13 patients. So those two studies are kind of the support for the

pediatric indication. On the adult side, it includes the randomized control study data through 24 weeks for the adult study, called study 303. That program had 134 patients and we included just 24 weeks of data through that program. In addition to that, we have study 203 which is an extension study of 20 patients that had been on earlier studies with KRN that were treated now for another year, so we have an additional year-long of treatment for those 20 patients. And then there are some earlier studies from the phase 1, phase 1/2 studies that I don't need to go through. So the main thing is the Phase 3 adults with the second study for extension, and the peds is the big 5-to-12 and the smaller under-5 study. Those are the main components. Now for the adults, we did provide two biopsies out of the expected program in study 304, that's the bone quality study, two biopsies, and that data we put out showing a profound change from severe osteomalacia to mild over a 48-week period on Burosumab. So those two biopsies are also included, and we would expect to supply some additional biopsy data as the filing progresses.

KASIMOV: Okay. All right, so then as we start to think about potential commercialization here, can you comment on the strategy that you and your partner have in the U.S., Europe, and maybe LatAm, and how it differs between the territories?

EMIL: Well, I think in any territory, the key thing that starts all commercialization with rare disease is finding patients, not just – to find each individual patient at particular doctors so you know where they are. I think that's the key and it's true whatever country or region you're in. In the U.S., we have taken the decision to actually hire, we have hired and are operating now a 30-person Patient Diagnosis Liaison team. Now, the PDL team is a special team that we have at Ultragenyx whose job is really to launch the disease. They go out and talk about disease only, no talk about product, only about disease, and they basically help doctors make diagnoses and help us determine where are all the XLH patients. So that group will be going out and finding all the patients that are out there with XLH, adult and peds, throughout the U.S., and using a number of techniques including IMS data and others to basically find as many individual patients as we can ahead of launch, and they will continue to operate after launch to bolster our diagnosis rates. Now, in Europe, Kirin has MSLs in the field that are doing the patient diagnosis work and in South America we have MSLs that are doing this as well. The efforts in Europe are run by our partner, not by us. In South America, we are getting going, a little further behind from where we are in the U.S. but our plan would be for South America, assuming an approval in the U.S., that we would look to do named patient sales in Latin America for patients with this disease, and so we're starting the process. The one thing that's a little different between the U.S., let's say, and Europe or Latin America, is in the U.S. there tends to be more fragmentation. Patients are scattered among a lot of different doctors. There are a few big centers but there are a lot more distribution. Whereas in Latin America and in Europe, they tend to have major centers that touch most of the patients, a much higher fraction of the patients, and so that allows you...it doesn't take quite as much work there to get into and find a larger set of patients in those areas.

KASIMOV: Okay. I guess on this process of patient identification, I'm curious about the relative difficulty for this disease relative to maybe other rare diseases or rare conditions.

EMIL: Well, in absolute numbers, XLH is a lot easier because you can find patients in groups of you know a few to a couple dozen in different centers, so there's quite a few of them but that doesn't reduce the need to touch as many as possible. The pediatric patients tend to be on treatment, so they are usually seeing a specialist right now. The adults are a little different. They may be off treatment and they may not necessarily be coming to the specialists at centers, so they tend to be more lost and out in the public somewhere in the health system, so they have a lot of healthcare issues. They need bone, orthopedic, surgery issues. They have other types of physical problems that require symptomatic treatment. They are seeing doctors, it's just they may not be seeing doctors that are treating them, and so for the adults, we need to look at some of those secondary specialties as well as the key centers to find patients. There is one other feature for this disease that's unique, not unique but let's say particularly advantageous, and that is that it's X-linked dominant, and that means when you find one patient, you can find 4 or 5 or 6 who are relatives – that means sisters, brothers, nieces, nephews – and that can help you if you find one essentially to extend to other patients who may be local or may be somewhere else across the country, so we think that's particularly important. It was for Fabry disease and Hunter syndrome in identifying cohorts of patients that are related to each other, and we will be using that as well to help us once we get a lead to be able to follow through. Of course, this has to be done in a compliant manner but there are ways to manage that with the investigator assisting.

KASIMOV: Okay. Is the initial diagnosis of XLH pretty straightforward or just the opposite and quite complicated?

EMIL: It's relative straightforward to get to the point of thinking it's XLH. Mainly patients show up, either adult or even small, but they have significant bone issues. In children, they have rickets. When you take the x-rays, it's distinctive. Every radiologist will know what rickets is. And when you work up rickets, you're going to deal with vitamin D deficiency and you're going to look at mineral and metabolites, calcium, phosphate, etcetera. Those assays and tests are like routine, any hospital will have those things, and so it's not hard for someone looking at bone issues to pull out and find out the patient has low phosphate and rickets, but maybe not vitamin D deficient rickets. The next step, though, does require recognizing it's XLH. Among all the diseases that it might be, XLH is actually the most common one, or vitamin D resistant rickets. So there they need to then look at the effects of mutations, or more commonly people are looking at FGF23 levels. If FGF23 is high, phosphate is low, then you have narrowed it down to just a few diseases – XLH, which is the most common, autosomal recessive and autosomal dominant, hypophosphatemic rickets which are caused by different defects within the

phosphate control system. But XLH is now the most common one, and then you can further dive deeper with PHEX mutation. So it's not that hard to do. I think many people will have done the first part of it. Finishing it with FGF23 and sequencing PHEX are a little more difficult, particularly PHEX mutations and sequencing. In the U.S., most health plans will not pay for sequencing but we as a company generally support sequencing programs for all of our diseases and so we can help people make that final step. But I would say the majority of patients are properly diagnosed, I would not think that there is a large fraction undiagnosed, however you don't really know for sure until you get out there and really operate with a product where you can actually start discovering how many patients are being newly diagnosed versus having lived with the disease all their life.

KASIMOV: Okay, and can you just quickly remind us of the prevalence for the adult and the pediatric patient population?

EMIL: Overall, we believe in the U.S. it's around 12,000 patients. That is based on an incidence of about 1 in 20,000 births. However we assume that the patients don't live a normal life and so instead of being, let's say, 16,000 expected based on U.S. population, we are estimating 12,000. And based on the age cuts, we are assuming that that's three-fourths adults which is 9,000, and around 3,000 for the children.

KASIMOV: Okay, and then how should we be thinking about pricing for Burosumab, and how might this differ between the different doses used for adults and pediatrics?

EMIL: I'll let Shalini talk about pricing.

SHALINI: Sure, so to answer the second question first, there is actually a little bit of complexity around dosing in that the adults receive treatment once a month and the children are treated twice a month, and so there is some equalization of the amount of drug that's given across the two populations, which actually provides some equalization in terms of the pricing because it's weight-based dosing. Now, we haven't made any final decisions on pricing for the product but there are some data points out there among your colleagues on the sell side, and there's quite a cluster of sell-side analysts who are modeling somewhere between $100,000 to $150,000 per patient per year on average for the average patient. So again, we haven't made a final decision but that's a data point that is available.

KASIMOV: Okay. All right, so I guess trying to piece all this together, given where you are with your patient identification progress at this point and what you believe the ultimate prevalence is, what's your current thinking as to what the launch curve could look like and building up to that ultimate market potential? How do you want or how do you think people should be thinking about this?

EMIL: Are you trying to get me in trouble?

KASIMOV: Trying to ask.

EMIL: Well, we think we'll have a good launch curve but we haven't projected how that's going to play out. I think the key for us is really keeping our head down around getting patients diagnosed, and that will help drive whatever happens on launch. I think when you look at the product, Cory, you look at its profile so far, we're seeing a product that normalizes phosphate in the vast majority of both teens and adults. It improves bone mineral metabolites, the other bone mineral metabolites as well. It results in improved bone turnover and bone healing, whether it's by rickets reduction or fracture healing, and it's shown improvement in symptoms as well, both walking, pain, stiffness, physical functioning in children, and to some extent it's reported in adults as well. And then from a safety perspective, injection site reactions at least in adults were relatively low at 11%, the same as with placebo, which is the most complete data we have. And we haven't seen recurrent hypersensitivity, an allergic type reaction that you might see with biologics that are subcutaneously injected, and so, from a safety perspective, we feel very comfortable about the profile. So when you think about it in terms of product features, it's a subcutaneous administered drug, it's every 2 to 4 weeks, with very consistent efficacy and we think a good safety profile. So we think it's a product that we think will do well in the sense that there is, we think, a strong benefit-to-risk for taking it. So far at the conferences, we feel there has been a pretty positive buzz from the audiences, and I think there were some discussions from the most recent ASBMR data that was presented, both showing improvements in bowing in pediatrics, which adds to the story with pediatrics under age 5, as well as some additional data on TIO. I think it's just showing that anti-FGF23 antibody, Burosumab, is going to have an important impact on XLH disease, and we think it will be something which transforms the field in managing these patients. Having been a doctor using oral phosphate, I can imagine the excitement of having something that really works, that's not going to have the same risks and difficulties of administering. We're feeling good about how it should go, but of course feeling good doesn't necessarily translate into actual launch. We're going to have to make sure we're highly focused on finding patients and getting our systems up, and our commercial team has been doing that. We're creating our own Ultra-Care Center. We'll have the field team set up with sort of a high-touch, scientifically sound field team and a strong MSL group. So all that's coming together now. I feel pretty good about being set up to do what you have to do in these kind of rare diseases. We've learned from the experiences in the past, particularly learning during the Naglazyme launch when I was at BioMarin on what you need to really focus on to make sure this happens, and that's going all the way from finding patients to getting through the health reimbursement system, and getting products shipped and delivered to them and ready to go. I feel pretty good about where we are in terms of getting it going, but as you know in rare disease products, it takes times to get through and to get all this to happen, but we're going to be pressing for as good a launch as we can get.

KASIMOV: Okay, and then the last question I have on this program, and you have referred to it a couple times, but the recently-presented data on patients less than 5 years old at ASBMR, and maybe how this relates to how we should be thinking about the potential expansion of this product over time.

EMIL: Well, we think if you look at oral phosphate therapy, which is what is being used in those very young patients, you end up with maybe a fourth of them or a third of them having renal injury with nephrocalcinosis, by current therapy. We haven't seen any of that with Burosumab. So when you talk about treating a little kid and creating injury for life, I think that's something that's quite important. Now, at the same time if you could take a little kid who – I don't know if any of you on the call have a little kid – trying to give your little kid a liquid treatment five times a day, if you had... just giving them one Tylenol once during a fever is hard enough, so this is going to eliminate the need to do all that. So with a really young kid, it's an injection, yes, but it's subcutaneous, it's quick, and we think that that's going to be just such a much greater regimen to treat really young patients. If the bowing, as we have seen from that data, shows a significant improvement in bowing, and combined with the rickets reduction as we have seen before, we think the potential is if you treat these kids really early, that an improvement in bowing could translate in the long run towards a more normal bone structure, which we think would have lifelong implications. The earlier you treat there, the potential, the better the bone effect may be. So we think if you look at the market over time, it's really important to get first-line patients who get diagnosed to get put on a drug that won't hurt their kidneys, that will optimize their bone effect which I think will change their life, and so we'd expect that group to grow and accumulate over time. So I think that's going to be one important dynamic that will change over time as we start treating kids from first diagnosis rather than after 40 years of disease.

KASIMOV: Okay. All right, I want to just very quickly touch on rhGUS for MPS 7, which is one where you have a PDUFA date coming up in just a couple of months. So recognizing that MPS is a small indication in terms of patient population, but also that this would be potentially your first approved product, can you talk about the benefits of establishing some commercial infrastructure with this particular program, and does this kind of help in your mind with the launch of other products down the road?

EMIL: Well, I think it definitely does, and though I didn't mention it as a major driver, everyone knows that it's a relatively smaller product, but for those patients I think it will be a big product because if you have a disease that you thought no one would ever, ever develop a treatment for, it's a big deal. What it does allow us to do as a company, though, is set up both our field presence as well as our Ultra-Care system patient call center, to get all those systems up and running, also the specialty pharmacy as well as distribution network. It gets us to get that with not quite a dry run but let's say a soft launch with Burosumab and the patients in the U.S., and get that system all up and running presumably some months before the Burosumab launch. So I do think it's an excellent starting place for us to get going, and the people that are going to be doing Burosumab launch will be participating in the rhGUS launch so it will be great preparation for the much bigger Burosumab launch.

KASIMOV: Okay, so it is going to be the same reps. You're able to lever the reps from Burosumab for rhGus?

EMIL: Yes, we're going to have one Ultra-Care field team.

KASIMOV: Okay. All right, I like the name. So let's talk about trihep a little bit, and I guess start off with FAOD. Maybe just to start, can you remind us what you learned from the Phase 2 trial that's informing your discussions with regulators?

EMIL: Yeah, so the Phase 2 201 study for UX007 in FAOD showed two things. At 24 weeks, we showed a significant improvement in exercise tolerance, both walking and cycling, which we were able to demonstrate continued for walking at week 78, but at week 78 we also saw a 50% reduction, approximately 50% reduction in major clinical events, which means ER visits or hospitalization, as well as days in the hospital. We were quite impressed with the effect that we're seeing. It was consistent with our retrospective study on compassionate use patients we had done before, but an effect on major clinical events we think is just such a more compelling story regarding reimbursement that we decided to shift our direction toward looking at major clinical events rather than just an exercise tolerance study. That major event could allow us to study young patients who don't necessarily walk or can't do the cycle odometer test in a compliant way, so it would allow us to expand the population, and we think the indication for reducing events would be a far better commercial proposition and value proposition than talking about exercise tolerance in a more limited set of patients. So what we have been doing is working through the design of that study, and no doubt it would take a longer study and more patients than an exercise tolerance study, but we do think it's going to be much more valuable for us to do. We've been talking through this with regulators, getting the design right, and we haven't quite finished that, and that's where we are right now. The expectation is to get that finished this year and to be heading into a study.

KASIMOV: You said you do expect it to finish this year?

EMIL: Expect to finish the discussion this year to have a plan.

KASIMOV: Okay, so I guess it sounds like then the reason that setting up this Phase 3 design is taking relatively longer than what we've seen from you guys in the past is the switchover to the event-based outcomes.

EMIL: Yes, and the complexities of doing that and other aspects of discussing this with regulators, so it has taken a little bit longer. The product though, remember, is already in a Phase 3 for movement disorder, which is progressing, so that phase 3 is already initiated and ongoing so there is already one indication that's in play for Phase 3.

KASIMOV: Okay, right, and we'll get to those in just a sec. So when you say this study would take longer, obviously that makes sense given what you're going to be measuring. Do you have a sense, based on how the design is evolving, not what it will ultimately be, but how long the study might ultimately take?

EMIL: Well, we're basing it on what we did in Phase 2, that is a 78-week study, so that's an 18-month design is what we're thinking about but we don't have regulator agreement on that. The balance point, obviously you go longer, it gives you more power, but then it takes longer. So we're trying to find that right balance point between long enough to collect enough events to show the difference but not taking so long for the in-live portion, so there is that. We also have to look at feasibility, where are the patients, how many to enroll, and depict criteria for who is going to enroll that would assure we can execute a study. What we're thinking is a 78-week in-live is what we're thinking about at the moment but it's not finalized.

KASIMOV: Okay, okay, and when you say you just don't have final agreement yet, is there push-back on the switch from regulators or is it just the process of collecting all the feedback that's necessary.

EMIL: It's more of the process of getting feedback, plus also not just regulators, it's our work we have to do in the field to understand the population of patients with this particular endpoint, which we weren't as prepared for. So we have to figure out how many people are out there who could do it and how it would be done because you don't really want to go to regulators right off without having that part of the story worked out, how are you going to characterize these major clinical events. Things get a lot tighter in Phase 3 so you really want to go in there with a really tight view of what you're going to do, and so we've been talking with the regulators as well as with our investigators in the field to come up with the best plan.

KASIMOV: Okay. All right, so let's talk a little bit about trihep or UX007 and Glut 1 deficiency, which you mentioned, where Phase 3 is currently ongoing. Can you just remind us of the design and endpoints there, and what the possible timing is on that trial?

EMIL: Well, the trial is basically a randomized control crossover design in which patients will get either a drug or a placebo for a 2-month period and the crossover to get the opposite treatment for 2 months, then we'll compare their disabling movement disorder events during the two phases of treatment, and this will be done. We're expecting to enroll 40 patients. These patients have these disabling movement events or problems where they can't control their body effectively which causes them to discontinue whatever they are doing and be disabled for a period of time. In the pilot

study that was done, these events lasted around 45 minutes and happened maybe every other day, so they're sort of almost like a seizure but they're not a true seizure. They're a motor dysfunction event in the brain. So we're going to count those events by diary and compare both the placebo period and the drug-treated period in the study. The study is enrolling. Site startup has been going along. It's an international study, that means a lot of countries and a lot of languages and a lot of jurisdictions, and so that definitely takes time in getting those kind of multinational studies up and running but it is enrolling. Our expectation is the data from the study would be available sometime next year, assume the second half.

KASIMOV: Okay. All right, great, and then what's the latest on absence seizures kind of specifically and the plan for those patients at this point?

EMIL: Well, we're expecting to do a smaller absence seizure randomized control study. We're coming up with the design right now. We want to verify the seizure types and what's happening in those patients that we have treated that had a reduction, because remember there were 4 out of 7 that had 100% reduction, and the mean reduction in those patients was 92%. So we think it had a very profound effect, and we're just doing a little more evaluation of that, but our expectation is to come up with a randomized control study, which we would expect to start next year. That study would probably be relatively small because we think we would have enough power with a relatively smaller study. So that's our plan. We haven't discussed it with regulators but we think that a randomized control study demonstrating reduction of absence seizures when combined with our Phase 3 Glut 1 study would give us potential for a broader label that would then maybe include younger patients who might not yet have a substantial movement disorder, but might have absence seizures. So from a standpoint of commercialization, it would make sense to be able to offer treatment to younger patients that might benefit. So we think it's more of a label expanding strategy rather than a single pivotal study by itself.

KASIMOV: Okay. All right, and then just a couple more on UX007. The tolerability of the product, how do you view that at this point, and how big of an issue might this be if this drug were to be commercialized?

EMIL: Well, we've been looking at that and actually put some information in our deck about patients on drug for many years, in fact. We have more experience in the FAOD area but we have patients who have been on drug for many years and what we find is that in the beginning, it takes some adaptation, and so we had some early dropouts in the program and the tolerability issues, when you're adding the oil, you have to manage it in the right way so that you don't create GI disturbance which will cause the patients to stop. So it needs to be titrated and managed well, and needs a little bit more dietitian effort. When we've done that, I think that's helped reduce that, the dropout, but the people who get used to is, as I've said, we have people who are almost like 17 years on the treatment, from the beginning of the very beginning of the program, so quite a few

people are on drug for 5 years or more. So we think, once you get used to it and get it worked into your system, it's fine and you can stay on it long-term. It's really in the beginning, the first few months that you need some help in getting it worked into your system, and it just takes a little more proactive effect. When you're in a clinical study, sometimes things are hectic, busy, you're moving around to your new center, and you don't get the kind of support needed, whereas if you're in your home clinic with the doctor you know and with a dietician you know, you can get the kind of care to help you get through that beginning part. So one of the things we'll do, assuming we are able to get it through, get it approved, and commercialized, we're going to have to do a good job with dietician and support so that they understand how to apply it and help reduce the dropout rate early on. We think it's a manageable thing and we've gotten better at it from seeing some of the challenges we've seen earlier on. I would point out for Glut 1 that ketogenic diet is also equally hard to start, and a lot of places put people in the hospital for a week to get started because it's so difficult to get oriented and get set. We think it's a manageable problem and we're working to take care of it, and when we go commercial, assuming we do, we will certainly want to have the right dietician support for the program.

KASIMOV: Okay, then the last one on trihep is can you just remind us of the IP surrounding this product?

EMIL: Yeah, the IP on triheptanoin involves some composition like claims for the compound which just got issued and that go into the mid-20s without patent extension, and up to I think 2030 for one of them as well, which we assume would get some additional patent extension. We also have use patents for FAOD treatment, and working on the Glut 1 as well. So it's a combination of composition like claims as well as indication claims that we're working on, so we have some issued patents and some still pending but we think it's reasonably protected, and of course it would get Orphan Drug exclusivity in those territories as well.

KASIMOV: Okay. All right, just a few broader strategic questions, and maybe if there's any lingering email questions but I think I worked most of them in, that I want to get to before we wrap up. This kind of comes back full circle with where we are, and if all goes as planned, you're going to be transitioning to this commercial stage organization and you will be left with one late-stage asset in the clinic. Now, you do have some very early-stage internal programs, and of course you're hoping to bring in Dimension, but how should we think just kind of broadly about the replenishment of your pipeline beyond what might or might not happen with Dimension?

EMIL: Well, we do have two early-stage programs. 104 will probably get to an IND within a few years but the other programs we're unclear exactly when they would get there. They're moving along in their progression so we're pleased with that, but we had intentionally in the last couple years focused on getting the larger number of programs we had moved forward so it's a little bit of by design of getting the two filings. The

dropout of 001, of course, leaves us with more of a gap there in the middle but what we want to do is be sensible and smart. I think Dimension is one way to look at the early pipeline but we've been looking for other well-characterized biologics that make sense for us that are rare or ultra-rare, and I think it would make sense for us to look for one more asset in the earlier stages that come from a well-characterized biologic type strategy, so that's something we're doing and looking for. And we had hoped that Dimension, if that happens, would give us some early-stage pipeline, but I would want to be clear, we wouldn't become a pure gene therapy company, only doing that. We would also be looking for other things that are treatable with other strategies because gene therapy cannot solve all the genetic diseases for sure, so we wouldn't rest on that alone. We would still be looking for other assets and using other strategies.

KASIMOV: Okay. All right, three questions left here. I think two of them will be for Shalini and then one final one for Emil. So Shalini, one email question for you is if you do in fact succeed in purchasing Dimension, would you need to finance the company to be able to do it?

SHALINI: We are actually pretty well capitalized, Cory. So as of June 30th of 2017, we had $457.5 million in cash and investments on the balance sheet, so we're quite well capitalized from that perspective. Also with the discontinuation of Ace-ER, we are able to reduce expenditures from some of our existing programs in order to provide some offset to the spending on the Dimension portfolio. And then as we discussed on our conference call on Dimension earlier this week, Dimension also has its own cash resources as well as anticipated potential partnering revenues, so there are several potential offsets to the additional expenditures related to the gene therapy portfolio.

KASIMOV: Okay, great, and then as a kind of a follow-up to that, something I wanted to ask from a financial standpoint is how we should broadly be thinking about expense tends over the next couple of years as you become a commercial organization and running some other pivotal programs and do this work, whether it's via Dimension or elsewhere, in terms of replenishing the pipeline, not asking for specific guidance but just kind of broad strokes how we should be thinking about this.

SHALINI: Sure. From a big picture perspective heading into 2018/19, we are obviously working on building up our sales and marketing commercial capabilities because we're supporting two product launches in multiple territories right now, so that's an area where we're investing at the moment. On the R&D side, we are expecting the growth rate in R&D expenditures to start to plateau heading into next year, particularly with the discontinuation of the Ace-ER. This is all, obviously, in the absence of the Dimension portfolio. If that were added to our pipeline, we would be able to look at that and provide additional guidance on what would happen with R&D, but again, there a lot of potential offsets there from our current portfolio and we do expect things to start to plateau on the R&D side and invest more in the commercial side.

KASIMOV: Okay, terrific, and then the final question, Emil, I wanted to ask you is as Ultragenyx is potentially on the verge of becoming one of the gene therapy companies that's out there, I'm curious, as we have discussed orphan drug pricing in the past, I'm curious as to your thoughts on pricing of gene therapies, the potential pricing of gene therapies. I know it's a difficult topic, and we may get some clarity coming up here relatively soon but we don't have one yet, so how do you think about responsibly pricing these types of products and a one-time potential treatment in the future when they are commercially available?

EMIL: Thanks, Cory, it's obviously a difficult topic and I would hardly be the most expert person to solve the problem of how to finance it. I do think, though, that a single shot therapy that's getting a single payment is probably going to be a hard thing to do because the revenue impact or benefit to the company compared to the price you might provide is going to always going to be at odds with each other, combined with the fact that there may be some uncertainty as to what benefit each individual patient might actually get, and so a sense that if someone gave you a very large check and then it faded, would you have not gotten value for treatment? My expectation is that some level of payment involving some years of annuity-like design would probably be better. How long and how that worked would probably align value delivered better with revenue deserved for companies, and help reduce the sense of risk that paying for something that somehow fades after a year or two, that might not be properly paid for. Now, I know there's a lot of complexities to that but my sense is that that was going to be a middle ground between an annuity for life or a single payment, which I think are two extremes that may not be the best answer. I would also say whatever the number is, it's going to have to make some sense in terms of the value provided to the patient in terms of efficacy and safety. We're always going to have that whether it's gene therapy or anything else, and more scrutiny on that globally. I think the challenges lately with gene therapy programs, the ones that people have talked about like Glybera, those things are extremely rare and I think we oughtn't make broad conclusions from how those are doing compared to how everything else would do. I think it would be a lot more instructive to see how some diseases are a little bit more calm that actually get a gene therapy indication, how they do, and I think that will be a better test for how reimbursement is going to work than the extremely rare indication that have been approved so far.

KASIMOV: Okay. All right, terrific. Well, we are now back up at the top of the hour so we will stop there. Emil, Shalini, Danielle, Ryan, thank you all very much for taking the time today to speak to us. It was very helpful and insightful, so really do appreciate it, and we're around today if anybody has any follow-up questions. So appreciate it, and have a great weekend.

EMIL: Thanks so much, Cory. Thank you for having us on.

KASIMOV: All right, we'll talk soon.

OPERATOR: That concludes today’s conference. Thank you for your participation. You may now disconnect.