Pharming Group N.V. 9M 2022 Analyst Call

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Sijmen de Vries, MD – Chief Executive Officer:

Good morning, ladies and gentlemen, or good afternoon. Very pleased to have you here at the nine months '22 results call. And with me here are my colleagues, Anurag Relan, our Chief Medical Officer and Jeroen Wakkerman, our Chief Financial Officer. And before we do that, of course, I would like you to look at that forward-looking statements slide, because this presentation may contain forward-looking statements that are based upon our current estimations and beliefs and expectations. And circumstances could change towards the future.

And having said that, I would immediately like to flip to slide number 5, where I would like to remind you of our strategic objectives, as we have first formulated them a while ago, and that are still standing here. And that is, we are here to build and continue to build a sustainable business by focusing on the RUCONEST® sales, that still is very much the case and will be the case for the foreseeable future.

Then the next step is to focus on the market approval and launch and commercialization of leniolisib in key markets of the U.S., U.K., and the European Union. We have our own sales force capabilities in all of these three markets, and that exactly will be the core of the leniolisib business that will be built on top of the RUCONEST® business.

And thirdly, the ongoing pipeline developments from our own internal projects, and projects that we have acquired over the course of time, and the management of these rare disease assets, because that is actually what we are doing. We are focusing ourselves on rare diseases, to bring solutions to patients that are unserved and suffer from rare diseases. And there are quite a few of these rare diseases that still have no cures, of which APDS is just one of them so far.

So, if you would like to please switch over to the slide number 6. And there you see the three main pillars of our business. And indeed, the importance for RUCONEST® is here, because the positive cash flow from RUCONEST® helps to fund all these wonderful things that we are aspiring to do, to fund leniolisib, to funds further pipeline development and management. So, in other words, those sales forces that are in the market, working on RUCONEST® will continue to do that for the foreseeable future, as our product has a place in the market and will continue to have a place in the market.

The next one on the right side is the anticipated approval and commercialization of leniolisib. It's a rare disease, it's a recently discovered rare disease. So, disease awareness is still relatively low. And there were some publications of course, that stated that it was estimated to be one and a half patients per million of population, which works out if you see that calculation that we, according to the literature, there should be 1350 patients. We have become very active now in starting to search systematically for these patients and are finding them on a regular basis in all sorts of places.

And then you see there below that, we believe that the leniolisib compounds could become a platform in itself, because we found some very interesting additional indications from research

alliances that Novartis has been doing with several very renowned institutions and are currently sort of prioritizing which one of these diseases to prioritize for subsequent developments. And bring them eventually to the market.

And on the right-hand side, as I was already alluding to, an ongoing pipeline development for rare disease assets through internal projects and the potential acquisition of new preferably late-stage assets to in-licensing and M&A opportunities so that we can actually build a portfolio going forward. And, internally, we already have in-licensed OTL-105, the ex vivo hematopoietic stem cell gene therapy candidate for hereditary angioedema and last but not least from our own platform, recombinant a-Glucosidase enzyme replacement therapy for Pompe disease. So, this is an overview of the way we see that we build a sustainable business.

And let's just reflect on that one more second here. This is an important stage for the company. I said this before, and I will continue to say that. We are about to basically turn the company with another big transformation, namely, from one product dependency on mainly one geography with RUCONEST® for the United States, towards a balanced portfolio of two products in the market. And a significant business that we expect outside of the United States in the European Union. But also, as you heard us say before, we're branching out. We're planning to branch out to Japan with leniolisib. So, we're really transforming the company going forward with the upcoming introduction of leniolisib into the market.

And having said that, let's just look at the leniolisib progress here on slide number 7. And you've seen back in time, that we have been very pleased that on September 28, we could actually announce the filing and acceptance for priority review of the New Drug Application to the U.S. FDA, and that we have a PDUFA goal date of March 29, 2023. And that is where we are gearing ourselves up to bring the product subsequently as soon as possible to the U.S. market.

Very important, we could announce that we have already received, well ahead of time of the approval of the product, an ICD-10 code, so that the patients can be classified, diagnosed and can be reimbursable as well, as the product comes to the market. And that's not an easy thing to get, an ICD-10 code, especially not for a rare disease. It means the rare disease is recognized and is recognized as severe and significant and badly in need for treatment.

And last but not least, we are on track for the commercial approval of leniolisib in the first quarter because of that PDUFA date of 29 March. And we are planning to bring the product, as soon as possible in the second quarter, to the U.S. market. And we'll keep you updated on progress regarding that.

Then let's move to the next one, the strategic highlights of leniolisib progress outside of the U.S. on slide number 8. We were very pleased at the beginning of the year to receive the PIP, the Pediatric Investigation Plan, approval for the European authorities. Because the pediatric trials use the same endpoints as our adults, as our 12-plus trial, on the basis of which leniolisib is hopefully going to be approved. So, that was a pretty good news. There was buy in from the European regulator for that as well.

And then we were very pleasantly surprised by the EMA granting us an accelerated assessment for our file for leniolisib. Because that is a very rare event that EMA grants accelerated assessment, and therefore recognizes that both innovative character of the treatment is

significant, and the disease is very significant and needs urgent treatment. And recently in October, you will have seen the announcement that we submitted the Marketing Authorization Application to the EMA. And we are expecting, now anytime soon, a validation of the file by the Europeans and that the review continues.

And then on the right-hand side, the U.K. authorities have granted us in April, the Promising Innovation Medicine designation. Again, recognition that there is a serious disease at hand here and as an innovative treatment that is making its way through the regulatory pathway. And we were very pleased that the U.K. government announced that they have extended the ECDRP as a recognition route for the European files until the end of '23.

And as soon as we have the positive opinion from the CHMP, which is expected somewhere in the second quarter, we will be able to hand over the file to the United Kingdom authority, the MHRA, and in that respect, we will expect to gather approval from them in second half of 2023 because it takes about two months for them to review. That is very helpful because it means that we will have a generalized label, generalized packaging throughout the European Union and the United Kingdom rather than a separate product and with separate labeling potentially in the United Kingdom, which gives a lot of additional complication and a lot of additional regulatory work. So, we're very pleased with the decision by the U.K. government.

And let's move on to the next slide, number 9 on our preclinical compounds, OTL-105. We have made some good progress. I should say our colleagues at Orchard have made some good progress because they are the expert of course on developing that lentiviral vector to enhance the C1 inhibitor expression, and we're now starting to test this in preclinical HAE disease models. And as it says here on the slide, we anticipate to provide further updates as we get peer reviews on when we can actually expect to go forward to the IND filing, and of course, the subsequent clinical trials following an IND filing.

And then on the right-hand side, last but not least in our pipeline, our alpha-glucosidase for Pompe, where we are looking for differentiating features. Pompe is still a significant unmet medical need, and we believe that our platform may have the potential to have differentiating features versus the existing alpha-glucosidase enzyme replacement therapies. And that is why we are continuing to search for that. And if we find these, we will start developing these compounds going forward.

And that brings me to slide number 10. An overview of the pipeline that is now consisting of a product in the market, a product in regulatory review on both sides of the Atlantic, leniolisib with the accelerated procedures ongoing, OTL-105 gene therapy, and alpha-glucosidase for Pompe. And you see there that it would be good for the balance, for the portfolio and the pipeline, if there were some additional in-licensed or acquired products that are in between. That are in a clinical phase, preferably in the latest phase of development, to actually get our launch calendar even a little bit fuller towards the coming years.

And this brings me then on my last slide with the operational highlights. On slide number 11, something we're very proud of, that RUCONEST® has again realized significant sales and will continue to generate significant sales. RUCONEST® has broad sales of $151 million these nine months. And we are very pleased with the product that is already for such a period of time in the market, that it has found its place in the market and is serving an increasing number of patients

and is prescribed by an increasing number of physicians, because of the fact that prophylactic therapy patients need a good medication for that breakthrough attacks.

And RUCONEST® has a different mode of action than the prophylactic therapy. So, it is a very rational choice. If you use bradykinin/kallikrein submission prophylaxis, either oral or injectable that RUCONEST® is a very rational choice as your breakthrough medication. And we're very pleased that more physicians continue to see that, and more patients continue to see that. As RUCONEST® will continue to play a significant role in that market as a safe and effective acute treatment for hereditary angioedema. And therefore, we guided at the beginning of the year, that RUCONEST® will continue to have single digit growth of revenues in 2022. As you can see that we are delivering on that. We think that is a very great compliment to our colleagues who work very hard every day to bring RUCONEST® to additional patients in mainly the U.S. market.

And with that said, I'm happy to hand over to my colleague, Dr. Anurag Relan, our Chief Medical Officer to take you through APDS and leniolisib highlights. Anurag, over to you, please.

Anurag Relan, MD – Chief Medical Officer:
Thank you, Sijmen. So, we can jump to slide 13. Here you see that APDS is a primary immune deficiency -- and you see on this slide -- with many serious clinical manifestations. At the heart of it, it's an abnormal development of the immune system, and because of that abnormal development you have what's called nonmalignant lymphoproliferation. So, this manifests itself as swollen lymph nodes, and enlarged spleen and liver. You can also see this in the GI tract. Another key feature of APDS, because of this abnormal development of the immune system, are the recurrent infections and a whole variety of infections are seen in these patients. Because of these recurrent infections, and because of this abnormal development, these patients also develop a progressive lung disease and worsening of their airways with recurrent infections, but also a condition called bronchiectasis, which is irreversible loss of function.

On top of that, these patients have, because of this lymphoproliferation, the ability to transform into something malignant process such as lymphoma. So, this is a serious consequence of the condition and it's observed unfortunately, quite frequently in these patients. Lastly, these patients, although they have an immune deficiency, they also have an immune dysregulation disorder. So, they also exhibit some autoimmune phenomenon, and we can see this manifests itself in anemia and other types of cytopenias. But it can also be seen in the in the GI tract, as well as in liver disease.
On the next slide, we have the results from the randomized double-blind placebo-controlled study with leniolisib. This was a 12-week study, looking at two co-primary endpoints. The first co-primary endpoint is presented on this slide, number 14, where you can see that leniolisib had reduced lymphadenopathy. And it did it in a rapid manner in this 12-week study, again, compared to placebo. You can see that both on the left panel and the primary outcome analysis showing a statistically significant reduction versus placebo in the size of these so-called index lesions. And then you can see that on an individual basis also, you can see the placebo patients, for example, either remaining stable largely or sometimes in some cases, worsening, but you can see the leniolisib treated patients, you can see the size of their lymph nodes decreasing.

On the next slide, we have the other co-primary endpoint. I mentioned earlier that you see an abnormal development of these cells in APDS patients and because of that abnormal development, they'd have all of those other clinical consequences we've talked about. One type

of B cells that doesn't develop properly over one manifestation of this abnormal development are what we call naive B cells. And so, what we see in APDS patients is, they have a low proportion of naive B cells. When we treat them with leniolisib, you can see on the left with the primary analysis, again, a statistically significant increase in the proportion of naive B cells. But you can see on the right panel where we included the full set of patients. You can see, first of all, it's quite rapid. You see, even by the first month, there's a significant jump in this proportion of naive B cells and you see that this sustained over time for these patients versus the placebo patients who do not respond. This I think, again, gets to the heart of the immune phenotype that is seen in these patients, specifically that their B cells now are able to function and produce antibodies and recognize antigens.

On the next slide, we see the safety profile. This is again from the double-blind placebo-controlled study, where we see that leniolisib was generally well tolerated, with the severity and grade of AEs across placebo and leniolisib patients were similar, there were no deaths reported in this study, and there were no AEs led that led to a study discontinuation during this randomized study. Then lastly, there were no serious adverse events that were related to study treatment.

And then now moving on. So, these patients I mentioned were treated for 12 weeks in the double-blind placebo-controlled study, but then they went on into an open-label extension study. And here are some data that were recently presented at a conference in Europe, just a couple of weeks ago. This is showing patients who were in this randomized study and then went on to receive leniolisib. You can see data out of almost a year and these patients, you see on the left panel, you can see that their lymph nodes actually continued to decrease in size. So, you see that initial decrease that they've had and then over time, that continued further out.

And on the right side, you can see some images, showing some representative samples of what this looks like. Again, on the top you have patients who were treated with leniolisib in the double-blind study, and then you can see their lymph nodes decrease in time at the 12-week mark, and then further out at the day-252 mark.

And then on the bottom panel, you see a placebo patient, you see actually very nicely that there's almost no change in the size of this patient's lymph nodes between the screening time period and the day-85 time period. Then the patient receives leniolisib and you can start to see that the lymph nodes decrease in size.

Similarly, we can see this on slide 18, with the size of the spleen. I mentioned earlier because of this abnormal development, these patients' immune system, they also get lymphoproliferation and that can also be manifested in these massively enlarged spleens that these patients have. So, on the left panel, you can see again, these patients have an enlarged spleen that comes from a decrease in size during the first 12 weeks of study, but then that continued to decrease over the course of the extension study, the long-term study.

Then if we look on the right with the images, you can see in the top panel a patient who was treated with leniolisib to see that improvement, again, rapid improvement in the first 12 weeks, and then continued and sustained decrease in the size of the spleen. Then on the bottom panel, you see a placebo patient whose spleen actually increased in size over the first 12 weeks, but then over the course of the following, nearly a year, you see that spleen significantly decrease in size. So, I think these are all consistent aspects that we're seeing with the treatment of leniolisib.

And then I think the slide 19 also highlights another important aspect is that because of this abnormal development of the immune system, and specifically B cells, they have what's called a class switch defect. So, these patients do not transition to produce IgG type antibodies, but their immune system gets stuck producing IgM antibodies. What you see here are three lines showing that patients who were treated or not treated with leniolisib in the placebo study. So those in the red line, that's no previous leniolisib. And you say they have high levels, and those come down over time, and continue to decrease. Then patients who were treated with leniolisib, you see that they started at a lower level, but they also continue to decrease over time. And then when we take all patients together, you can see that same trend, that for these patients, now their immune system is functioning properly, because they're not stuck making just this one type of antibodies, and they're able to class switch and produce specifically IgG antibodies.

On the next slide, on slide 20, you can see some of the milestones for leniolisib. Sijmen highlighted that we have now seen acceptance of the FDA file with priority review. We have completed the submission to the EMA also earlier this month and later this year, we hope to start recruitment for the pediatric studies and then followed by some significant events also in 2023, with regulatory approvals that are anticipated, as well as commercial launches.

And with that, I will turn it over to our CFO Jeroen Wakkerman.

Jeroen Wakkerman – Chief Financial Officer:
Thank you very much, Anurag. First, the financial highlights of the first nine months, we had an increase in revenues of 3 percent from US$146 million to US$151 million. In Q3 specifically, we had a turnover of US$64.2 million, which means a growth of 2.6 percent in the quarter versus previous year. Our gross profit increased by 7 percent to US$139.7 million and that was driven by in first place growth in revenues, but also by production efficiencies and a favorable tailwind from currency translation effects. You probably all know that our sales are mainly in U.S. dollars and our cost of goods are in Europe. So, that is being reflected here.

Our net profit increased by more than 100 percent compared to the same period last year and that was driven by an increase in other income. You may remember that that is largely due to the reduction in the stake of BioConnection, our fill and finish partner. A transaction that we did in Q2 and the profit on that transaction was US$13.8 million.

The cash and cash equivalents together with the restricted cash decreased from US$193 million at the end of last year to US$189.9 million at the end of the third quarter 2022 driven by, on the positive side, a strong operational cash flow, offset by foreign exchange effect because we've got a lot of cash in euros. Still a strong treasure chest, also to be able to fund future growth and potential acquisitions.

Moving to slide 23. The key numbers, a growth of 3.4 percent to US$151 million in revenue, a growth of 7 percent in gross profit to US$139.7 million. Operating profits going up by 85 percent to US$28.4 million. Here again you see reflected the gain on the BioConnection sale of shares in Q2 and a net profit of US$28.3 million, which is an increase of more than 100 percent.

The quarterly development over the last two years. In H1, we have a sales of US$96.8 million. So, far this year, Q3, US$151 million. That means sales of US$54.2 million in Q3 compared to US$52.9 million in Q3 last year. So, I would say a steady growth in revenue, which is seen here.

And moving to slide 25 explaining the profits before tax growth from US$21.3 million in Q3 last year, to US$33.1 million year-to-date-Q3 this year. Starting off with the growth in the business, so it just explains the gross profit increase, then an increase in costs. You see the different categories. First one is R&D expenditure that was largely related to leniolisib. The preparation for the launch, this includes also manufacturing costs, and also additional costs in OTL-105 as Sijmen just described as well.

Increased G&A expenditure, that's the collection of many costs, think about IT costs, think about recruitment costs, because we have recruited a lot of people also to identify patients in the U.S. for leniolisib. The latter category is marketing and sales expenditure that grew by almost US$13 million. Again, that is largely due to our out-of-pocket costs for leniolisib, almost US$8 million. And a big chunk of it is because of payroll, so for increased marketing and sales staff.

The next two bars are pretty high, first one that they almost wash out, but the one is the negative impact on profit last year from the OTL-105 investment, the collaboration with Orchard Therapeutics and this year, the BioConnection sale of the shares and that overall brings us to a profit before tax of US$33.1 million.

Moving to slide 26 You see the development of cash from beginning of the year till the end of Q3, starting off with US$192 million at the beginning of the year. As I said, strong operational cash flow before working capital was plus US$26.7 million cash, because of an increase in working capital, especially in inventory was US$4.6 million, and we pay taxes of US$ 5 million and then you get to the net cash flow generated from operating activities of US$17.2 million. Cash flow from investing activities was largely a cash inflow because of the BioConnection transaction, the cash part of that was US$7.4 million, and that was offset by capital expenditure and that was mainly in IT. The cash flow from financing activities minus US$5.3 million is regular lease costs and interest and the exchange rate effects of minus US$20.9 million is mainly because we have Euro cash in a Euro reporting entity, but we are reporting our results here in U.S. dollars. So, overall, that brings us to a cash and cash equivalents of at the end of Q3 of US$188.7 million. So, we're very pleased with this development, especially on the operational cash flow, and a strong balance of cash to support future growth.

With that, I would like to hand over back to Sijmen.

Sijmen de Vries, MD – Chief Executive Officer:
Thank you, Jeroen. Then that takes me to the slide number 27. The outlook, the final slide of this presentation.

And as we said before, we continue to guide for the single digit growth of the remainder of this year for RUCONEST® sales. We already alluded about the commercial approval, subject to the positive outcome of the FDA review, that we anticipate launch in the U.S. soon thereafter. So, in the first half of '23. Then, subject to the positive review of the EMA, the positive opinion from the CHMP, followed by the issuance of the EMA by the European Commission. There's some time in between that, so you can anticipate both of them in the first half of '23. That means that as soon

as possible after, we will start rolling out the individual European markets in the second half of next year.

Then the very pleasant surprise I was alluding to earlier, the extension of the ECDRP filing for leniolisib by the MHRA, which means that we can work by submitting the European file to the U.K. authority, and expect a much quicker decision, namely about two months after the CHMP positive opinion and can go to market in the U.K. faster than anticipated as well. Then we continue and as you saw from the numbers that Jeroen was outlining, we continue to allocate significant resources towards the anticipated launch and commercialization of leniolisib. With the view that we are accelerating future growth as we start to build next year, expect to build the leniolisib business on top of the RUCONEST® business.

And last but not least, we are continuing to hunt for new opportunities to fill the pipeline, potential acquisition or in-licensing of new late-stage, preferably late-stage development opportunities in rare diseases. Last but not least, all of the current activities can be funded. This is very clear from our current balance sheet and only in the case of acquisitions, we think we may actually have to do additional financing, of course, depending on the size of the acquisitions.

I think that concludes the outlook and that concludes the presentation. So, operators, we could now turn the floor over to the Q&A section of this presentation. Thank you very much.

Operator:
Thank you. If you would like to ask a question, then please press star followed by one on your telephone keypad. If you change your mind, please press star followed by two. Our first question comes from Hartaj Singh from Oppenheimer. Hartaj, please go ahead.

Hartaj Singh – Oppenheimer & Co:
Great, thank you for the updates and the question. A couple of questions. One is different, one is on RUCONEST® and one is on leniolisib. One, just what we're hearing, Sijmen, the increased use of prophylaxis therapies, especially the orals out there is leading to an increased use or at least patients having acute treatments on hand, you know, like a RUCONEST®. How do you expect that going forward? Do you expect that to be sort of a tailwind to revenues for RUCONEST® going forward? And how long could that last? Then when you listed, we get a lot of calls from investors who are interested in which other conditions, primary immunodeficiency disorders, could you go after and when could we start seeing some some thoughts or some insights there? Thank you for the questions.

Sijmen de Vries, MD – Chief Executive Officer:
Okay. Let me try to answer that first one first, Hartaj. Good morning, by the way. RUCONEST® prophylaxis. Yes, I was alluding already to this that we could see continuing positive trends in a number of physicians and patients using RUCONEST®. In the past, RUCONEST® was never used for breakthrough attacks, also, because the prophylactic therapy was mainly C1 inhibitor, and it did not make much sense in this case to use it and RUCONEST® was typically used for the very severely affected patients. Now those severely affected patients are still a lot of the core business of RUCONEST® because they can't get anything else. Although there's also patients who then switch over to prophylaxis and are reducing their use of RUCONEST®, but they continue to have breakthrough attacks.

And that's exactly why we are pleased to see with the paradigm shift, that has taken place over the past few years, towards bradykinin kallikrein submission, although prophylactic therapies are significantly improved. Sometimes people tell me more than half the patients should expect either on a regular basis or incidental basis to have breakthrough attacks. Even worse, I was recently at an International Patient conference and key opinion leaders were warning these patients, please, even if you don't have any breakthrough attacks for a considerable period of time, please always have rescue therapy at hands, because this is a nasty disease, it's stress driven, and you can never know when a breakthrough attack can come by. The biggest danger is that people are sort of getting comfortable with their prophylaxis and that they get an attack still, because of this unpredictable disease, and have nowhere to go without any rescue therapy.

So, that emphasis is being brought out more and more also, from the key opinion leaders to the patients and to make them aware of that. That is the trend that we see and that is supporting and will continue to support the RUCONEST® business towards the future. When a very high using patient switch over to prophylaxis, we have to replace that patient with several patients that are on breakthrough medications, but that is exactly what our people are doing. What our people are continuing to do and where we continue to make progress and see a lot of opportunity there, because we still have a relatively modest market share in this market.

But for the foreseeable future, RUCONEST® we'll continue to play that role in the market. And for the foreseeable future, this will be a necessity, also, when other additional bradykinin/kallikrein inhibitors may come to the market, there's always the danger for breakthrough attacks and RUCONEST® is there, with the unique mode of action that RUCONEST® has compared to all its competitors, and future competitors, because we see no C1 inhibitor being in development anywhere in the pipelines of any of the other companies. Simply because C1 inhibitor is a notoriously difficult compound to make and to develop, other than that, you get from blood donors. And those products are indeed not actively promoted anymore for acute treatment. I hope that answers your first question. Maybe Anurag, could you shine light on that question about new indications for leniolisib because you're more at the heart of it than I was recently.

Anurag Relan, MD – Chief Medical Officer:
Sure, thanks, Sijmen and good morning, Hartaj. So, we are looking at additional indications for leniolisib. These are not actually in the area of other primary immune deficiencies, but we are looking at a number of indications. As Sijmen mentioned, these include areas where Novartis had actually started some work and has already some research collaborations ongoing. So, we're trying to leverage that, but we're also looking at some new areas. I don't think we're ready yet to disclose what those areas are today, but as soon as we make some more progress with this, and I think we'll be able to talk about that in the near future, which specific areas these include.

Hartaj Singh – Oppenheimer & Co:
Great, thank you, everyone.

Sijmen de Vries, MD – Chief Executive Officer:
Thank you, Hartaj.

Operator:
Thank you. Our next question comes from Joe Pantginis from HC Wainwright. Joe, please go ahead.

Joe Pantginis – H.C. Wainwright:
Hey, everybody. Good morning and thanks for taking the questions. Hartaj was asking some really good questions about the market dynamic, and I guess, as you guys continue to block and tackle getting more patients on RUCONEST® because of the ongoing need for rescue therapies. Can you remind us first about current patients and how often they need to get a new prescription either through expiration or other?

Sijmen de Vries, MD – Chief Executive Officer:
Yeah, that's an interesting question, Joe. Typically, this is 12 months, the prior authorizations in the U.S. So, every 12 months need to be renewed. We see some trends, disturbances of that due to COVID where plans couldn't handle every 12 months and extended that to a number of years. And then they took that back and did it for three or six months, but generally speaking, I think it's still the 12 months prior authorization that is actually very valid in the U.S. market. A lot of that is concentrated in the beginning of the year. So, patients that have been on drug for a long time, mostly are getting their prior authorization renewed during the first quarter, which is then of course a lot of admin work for those doctors' offices. We have our teams to help with doctors' offices and process that paperwork and facilitate, whichever way we can. That is what all rare disease companies do to actually make sure that patients are not without any medication at any time during that process, because it can be a bit of a tedious process from time to time.

Joe Pantginis – H.C. Wainwright:
Got it. Makes sense. Then so, my main set of questions really focuses on logistics and maybe some information that might be a little out of your hands, so I appreciate that ahead of time. So, first, with regard to B.D., obviously you've been saying for quite some time now you're looking to be opportunistic with regard to expanding the pipeline in rare diseases and what have you. So, I just wanted to do a bit of a status check with regard to where some of these discussions stand and level of maturities.

Sijmen de Vries, MD – Chief Executive Officer:
Yeah, yeah. We get a lot of inbound, Joe, from various banks that we work with and consultancies and of course our own folks. We've got a lot of inbound stuff and a lot of it is, unfortunately, it's repurposed molecules and then for some rare indication where sometimes, the one rare disease is not the other one. Leniolisib serves APDS disease which is very severe and has a very high unmet need. Some of these rare diseases may not be so severe and these repurposed molecules may not be the business model that you're looking for, because there's already generics available inside or outside the U.S. and we do not believe that this is a sustainable business model, but we're looking for more true innovative treatments and leniolisib is a good example in a case in point here.

So, in other words, we're being very, very precise, also because it's our first M&A deal, of course. So, we'd better get that right. That's why it takes maybe a little bit more critical approach from our side. On the other hand, we've been very close with one or two companies over this year. We came very, very close and at the end still decide to step away, because we couldn’t, in a specific rare disease, really validate the numbers that this company was quoting for these patients. Of course, that's always the case in rare diseases, right? In rare diseases, the numbers of patients that you find is a critical issue and we have built up a significant database in the meanwhile with our genetic testing of genetic diseases.

We also have bought a significant amount of other data that, we think, we have very good insights in a number of mutation patterns that leads to certain diseases and therefore, you know, that helps our business development folks to actually make a choice and Anurag, who is an integral part of that group, sits here nodding his head opposite me -- that this is really always a challenge here. But we're very active in this market and with business development, you can never say -- it could be, you know, very soon. It could be that another one bounces off and we have to continue on and we continue on as such, but we have increased our capacity significantly over the last year, also having learned from some of these experiences where you spend a lot of time and then eventually decide not to do it.

Anurag Relan, MD – Chief Medical Officer:
I was just going to add that, you know, we look at a whole range of different opportunities and we do it in a systematic way and I think, as Sijmen said, we want to be cautious and careful and make sure that we bring in the right opportunity, where we could add value and we can leverage the work that's already been done.

Joe Pantginis – H.C. Wainwright:
Got it. And then just lastly, this is really the part I alluded to where your hands might be tied with regard to how you answer it. So, with OTL-105, obviously there's a bit of growing excitement for potential gene therapy around HAE and this certainly came out at the recent HAE conference that we hosted. So, I'm just wondering, right now, if you'll give us information as it comes out. Is there anything that we could look to even without timing that says, the plan would be to release X type of preclinical data, to be able to tease the profile of the asset?

Anurag Relan, MD – Chief Medical Officer:
So, Joe, that's really the goal here, right? So, I think first of all, what got us into this position or why did we enter this partnership with Orchard was that we believe, we know C1 inhibitor is the root cause in these patients, and we wanted to be able to provide these patients with C1 inhibitor in the same way that we do with RUCONEST®, to be able to do that with a gene therapy. The other modalities that we looked at really didn't, you know, present themselves with a reliable way to do that.

So, the goal now in terms of these preclinical models is to be able to use a vector that now has been refined by the team at Orchard and to be able to show that we can actually increase C1 inhibitor levels in these disease models. So, these are disease models, being knocked-out mice, that have -- that don't have the C1 inhibitor gene in place, and now can you increase those levels to levels that we think would be meaningful in a clinical situation? And we're doing that testing now, so I'm hopeful to be able to provide, you know, an update on that soon, but those are the -- that's the type of information that we can look for -- is to -- can we show meaningful increases in C1 inhibitor expression levels in these pre-clinical disease models that could translate into, you know, the type of benefit that we would need to see in patients.

Joe Pantginis – H.C. Wainwright:
Got it. Thank you, guys.

Operator:
Thank you. Our next question comes from Simon Scholes from First Berlin. Simon, please go ahead.

Simon Scholes – First Berlin:
Yes, hello. Thanks for taking my questions. I've got four. So, you've mentioned that you identified 400 potential leniolisib patients and I was just wondering if you could tell us how many of those are, if any, are pediatric patients. Then on the ICD-10 designation, in the last call, well in this call as well, you mentioned that this gives you the open sesame to start reimbursement discussions. I was just wondering how those reimbursement discussions are progressing. I mean, presumably you would expect to complete them by the time of approval in the U.S. in March.

And then on pricing of leniolisib, I don't know to what extent you can comment, but I was just wondering if you expect -- I mean, presumably, the difference in pricing with this product between Europe and the U.S. is not likely to be any way as large as it is with RUCONEST®, and I was just wondering if you expect any pricing differential at all or what the size of the pricing differential might be like compared with RUCONEST®.

And then, lastly -- you mentioned that there aren't any C1 inhibitor products currently under development. Does that also extend to C1 gene therapies besides your own pipeline product? And that's it.

Anurag Relan, MD – Chief Medical Officer:
I'll take the first question, Sijmen, and then the last one.

Sijmen de Vries, MD – Chief Executive Officer:
Yeah.

Anurag Relan, MD – Chief Medical Officer:
With respect to the patients that we're finding and the patients that were in the study, it's important to note that, first of all, it's a genetic disease. So, these patients are born with this genetic abnormality. They have these variants in one of these two genes at birth and the disease can begin to manifest itself very early in life. So, it is a serious disease in that it can manifest very early and then it's progressive. So, it gets worse over time.

In the clinical trial, we identified and treated patients that were at least 12 years of age and about half of the patients were actually in this age range between 12 and 18. I think the median age was actually 19. So, it was a significant portion of patients between 12 and 18 years old, which, you know, they're adolescents but, using a formal definition, they're still pediatric patients. Beyond that, so in this younger age group, we are finding patients in that age group as well and it's probably in the range of around 20 to 30 percent of patients that we're finding that are even below the age of 12.

So, hopefully that gives you some idea of the types of patients that have been treated so far in the clinical program and the types of patients that we're finding, but also that we're planning clinical trials in this younger population too, because there certainly is an unmet need there.

Sijmen de Vries, MD – Chief Executive Officer:
Looking to the future, wouldn't it be that as the disease becomes more known and more recognized that these patients are caught earlier, because we know we see that it takes many, many years for them to come to diagnosis. So, the earlier you catch them, the better.

Anurag Relan, MD – Chief Medical Officer:
I think certainly as we increase disease awareness, but also hopefully a specific treatment becomes available, that also oftentimes can drives further diagnosis. So, I think those were all sorts of trends in a favorable direction.

On the question of other C1 inhibitor therapies in development, so I think really Sijmen was alluding to -- there's no acute C1 inhibitor therapies in development and there's really no actively promoted acute C1 inhibitor therapy other than there is a plasma drive therapy also. But there are gene therapies aside from our program that are in development and in different modalities, different mechanisms to deliver the vector and to be able to express C1 inhibitor. But I do think that we have still a unique method and partnership here with Orchard that could be differentiating with respect to this ability to express C1 inhibitor.

Simon Scholes – First Berlin:
Okay.

Sijmen de Vries, MD – Chief Executive Officer:
And then, Simon, you had a couple of questions about pricing. We do not give any guidance on that because, you know, we always think that analysts are the experts on this, to make up their minds what they think is typical pricing.

And with regards to your question about the difference between pricing in Europe and the U.S., I think there's also quite a number of rare disease compounds on the market and you can actually see what the difference is between Europe and the U.S. We think European prices are typically in the 60 to 70 percent range of what the U.S. price is. So, the price gap has significantly narrowed or is significantly narrower in these rare diseases than in maybe most markets or diseases where all sorts of reference pricing systems kick in and that's not the case necessarily with the rare diseases. So, I hope that answers your question there as well.

And lastly, ICD-10 code is important because you can work ahead, and indeed you've got it right there. You can work ahead to actually discuss coverage, not necessarily reimbursement because the U.S. of course has decentralized healthcare systems where you serve a number of the government-funded like Medicare and Medicaid systems, for instance to mention two. But the majority of the market is of course a private market, commercial market as we call it, and there you get coverage by the big insurance companies and the big healthcare plans. And that's where having an ICD-10 code is incredibly helpful in this respect. Otherwise, it may take quite a long time before these patients could be reimbursed.

So, yes, our folks are really preparing there to actually get coverage for the patients immediately after the product comes on the market, and that is of course, the nice thing of the United States market, that these things are progressing way faster than sometimes in the European markets because that's also the issue in the European markets. It's often, despite the fact that you have a rare disease, it takes quite a considerable amount of time before you get a reimbursement, and of course your own country is an exception, Germany. But many more European countries take a lot longer to unfortunately give patients that therapy that they so badly need.

But we will do our utmost best obviously also to accelerate the rollout of this unique and very severe rare disease as quickly as possible in the European markets. And the good news is, again,

there are positive exceptions possible if you have a good dossier and if you have a good healthcare economic underpinning, and that is what our teams are working around the clock on to actually make sure that all happens so that we can hopefully swiftly get reimbursed in all of the European Union markets as well.

Hope that answers your question.

Simon Scholes – First Berlin:
No, that's very helpful. Thanks very much.

Sijmen de Vries, MD – Chief Executive Officer:
Okay.

Operator:
Thank you. As a reminder to ask any further questions, please press star followed by one on your telephone keypads. Okay. We currently have no further questions registered, so I'll now hand you back to the management team for closing remarks.

Sijmen de Vries, MD – Chief Executive Officer:
Thank you very much, operator, and yes, ladies and gentlemen. Thank you for attending our Nine Months '22 conference call on the results. And as we come to the end of this exciting year, 2022, where we were very successful not only with of course continuing the growth of RUCONEST® sales, but also securing the FDA and EMA accelerated review which, again, is very rare that you get it on both sides of the oceans. We look forward towards moving into the next year where we anticipate that we could have the approval date of March 29 and could go into the U.S. market soon thereafter, and of course the accelerated review by the Europeans where we could actually also go into the markets and get the marketing authorization before the end of the first half and go as soon as possible into the European markets and lastly the U.K. market where we can work on the direct recognition.

So, we look back to a very busy '22 and we also look forward to a very intense '23 where we will be starting soon to execute on the significant transformation of our company from a one-product company and one geography towards a multiple product company and multiple geographies driven by our own commercialization infrastructure on both sides of the oceans.
And that concludes this conference. Thank you very much for your attendance again and we look forward to updating you probably somewhere in March on our full year results, 2022. Thank you and have a nice day. Goodbye.

[end of transcript]