Pharming Group N.V. Joenja® FDA Approval Call

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Sijmen de Vries, MD – Chief Executive Officer:
Thank you, very much, and good morning, good afternoon, ladies and gentlemen, on the occasion of the approval of leniolisib. Now known under the brand name Joenja®. And we're very proud to have achieved this FDA approval, obviously. Before I go there, I would like to point out to the next slide about forward-looking statements.

As this presentation may contain, forward looking statements and forward-looking statements are statements of future expectations that are based upon management's current expectations and assumptions and involve known and unknown risks and uncertainties that could cause actual results, performance or events to differ materially from those expressed or implied in these statements. And of course, I leave it to you to further read that entire statement.

Then I would like to move on to the next slide because I'm here with a number of my colleagues, Dr. Anurag Relan, our Chief Medical Officer, Stephen Toor, our Chief Commercial Officer and Jeroen Wakkerman, our Chief Financial Officer. And we will be taking you through the following agenda that you can see on the next slide. I will do a very brief introduction, and then Dr. Relan will take you through the APDS overview and label and data, followed by Stephen Toor, who will take you to commercial launch plans.And then Jeroen Wakkerman will take you through some financial considerations. And I will finalize this call with a brief overview of the strategy and some closing remarks upon which we open the line for questions.

So let me start first then and show you this beautiful new branding on the next slide, where we are very proud of the brand name Joenja® for leniolisib going forward. And of course, if you look on the next slide, we are very proud that we now have the first and only FDA approvement for APDS. And APDS, of course, is a newly discovered disease that has a very serious impact on people's lives. It is one of those rare primary immune deficiencies that now, going forward in the USA, we'll have a treatment that treats the root cause of this disease. A very important step forward today for all those APDS patients aged 12 years and older that are now eligible for treatment with leniolisib -- with Joenja®. I should get used to that. And Joenja® is the PI3 kinase delta inhibitor with that demonstrated efficacy, safety and tolerability that were shown in a 12-week randomized placebo-controlled trial for the treatment of APDS. And Anurag will give you a lot more details on that.

And of course, last but not least, here we are already started the development for pediatric patients because we recently announced that our first pediatric study already enrolled the first patients. And we are absolutely fully prepared for the launch of Joenja® in early April. because it is not our

first rodeo. It's our second commercial rare disease product that we bring into the market. And we have a very experienced and dedicated commercial and medical teams that are in place. We also have the APDS assist program, to help those patients with medication, access, education and all sorts of support services. And Stephen will go into much more detail later on during this presentation on all this on the commercial preparedness that we have to launch Joenja® in the United States.

Last but not least, as you well know, the MAA is also still under review by the European authorities, and we expect a reply from the European authorities in the second half of this year. So, without further ado, I would like to now turn over to my colleague, Dr. Anurag Relan, to give you the APDS overview. Anurag, over to you.

Anurag Relan, MD – Chief Medical Officer:
Thank you, Sijmen. So, let's begin by talking about APDS, and then we can get into the data and the label on Joenja®. So as Sijmen mentioned, APDS is a condition that was first described in 2013. It's a rare primary immune deficiency that we believe affects more than 1,500 patients worldwide. And to date, we have already identified more than 500 of these patients. Up till now, the treatment for APDS has really been aimed at addressing the symptoms of the disease, which manifest in early childhood but not the root cause. And we'll be talking a little bit more what those symptoms are and what the root cause is.

The symptoms and signs vary among patients, but we know that these patients do experience significant delays to treatment and diagnosis because of the misdiagnosis and the difficulty in making the diagnosis in rare disease. But fortunately, there is a genetic test available that can make a definitive diagnosis. And we'll be talking a little bit about that as well. So, when we think about APDS, of course, we think about the physical manifestations which stem from the underlying immune defect that causes frequent infections, causes this problem of lymphoproliferation or swollen glands, manifests itself in the lungs and can cause shortness of breath and coughing and a whole variety of symptoms that you see there that greatly impact the patient's life. And of course, as those physical manifestations impact the patient's life, they impact the other aspects of their life too, their social well-being, their mental well-being, and then lead to these patients frequently being in the hospital, requiring multiple surgeries, sometimes unnecessary surgeries, requiring numerous doctor visits, numerous visits to specialists that all take up a significant part of their time and of course, have significant burden on these patients.

When we think about APDS, we can actually think about it as this genetic disease that evolves over time. And you see at the top here of the slide how this evolves. So, beginning early in life, these patients start to have infections, frequent infections, and this is very common with other primary immune deficiencies as well. One of the hallmarks, however, of the disease is what's called lymphoproliferation. So, this is swelling of the lymph nodes, enlargement of the spleen. And you can begin to see that also early in childhood. Eventually, this begins to manifest itself in the in the GI tract. And you can see a condition called enteropathy. Later in life you can – and by later in life I'm talking about still around the age of 10 – these patients can begin to have autoimmune manifestations and then again, early in childhood, early in their adolescence, they can have lung manifestations and a condition called bronchiectasis, where they have scarring from these recurrent infections and from this lymphoproliferation.

The most serious complication, of course, is malignancy. And that happens in a high proportion of

these patients due to this propensity to develop lymphoma. And as I mentioned, this condition also has numerous other manifestations, such as cytopenias, arthritis or other manifestations of immune dysregulation. As a result of this varying clinical presentation, all of these different symptoms, it's difficult for these patients to get a diagnosis, one, because the condition is rare; two, because up until now there hasn't been a specific treatment available; but three, because of all of these different manifestations.

And you see here some of those these initial diagnoses that these patients have had when they initially were presenting with these symptoms and you see a whole variety of things from hyper IgM syndrome, because many of these patients, or almost all of these patients have high elevated levels of IgM, a specific type of antibody. You see recurrent infections, you see other immune diseases that they're diagnosed with, including combined immune deficiency or a common variable immune deficiency. And in the worst case, you see that for some of these patients, their initial diagnosis was the lymphoma. And if you go back and look, you see that these patients unfortunately suffered for many years before they even had the diagnosis of lymphoma.

So clearly improved identification of symptoms, better genetic testing and earlier diagnosis are needed for these patients. And that's one of the things that we've been very much committed to in helping support the community with.

And then when we think about what actually leads to the problem in these patients, it's really quite straightforward in that there is a specific genetic abnormality in one of these two genes that leads to this hyperactive intracellular signaling pathway that you see in the cell there on the left. And that hyperactive PI3-k delta signaling pathway leads to a dysregulated development of the immune cells. So, B and T cells do not develop properly, and as a result, if they're not developing properly, they don't function properly. When the immune system doesn't function properly, the most obvious manifestation is recurrent infections, and you see that on the right. But as I mentioned earlier, lymphoproliferation and autoimmunity are also key manifestations of this condition, and that's from this dysregulated immune system.

And you see all of those other manifestations on the right, including lymphadenopathy, the enlarged spleen and liver. You see this proliferation of lymphoid tissue throughout the body, in the lung and in the in the gut, and then these autoimmune cytopenias and other autoimmune disorders that gravely affect these patients

And then lastly, it's important to remember that this is a progressive disease, so this gets worse over time. And that's one of the key manifestations of that is the bronchiectasis. And we also know that these patients do, like I said earlier, have this propensity to develop lymphoma. The management of APDS up until now has really been trying to address these different symptoms, these different manifestations of the condition. So, on the one hand, there's the immune deficiency, so that can be treated with, you know, giving antibiotics either preventively or to treat an infection. Most of these patients are also on what's called immunoglobulin replacement therapy. So that's basically collecting antibodies from plasma and giving it to these patients on a regular basis. But on top of that, remember that these patients have this dysregulation. So not only is their immune system not able to fight infections, it's actually overactive in a sense. So, it also needs to be controlled. And that's typically done with drugs such as corticosteroids, other immune suppressants or mTOR inhibitors, such as rapamycin. None of these therapies, however, are approved for the treatment of APDS by the FDA. And then, of course, in a small minority of patients,

STEM cell transplantation has also been used to try to address their underlying immune problem. However, this is not an easy procedure and also comes with a lot of its own complications and issues.

Now we have a new therapy available, Joenja®, which is an immune modulator, targeting the root cause of APDS. And the principle here is to try to modulate that overactive PI-3k delta pathway to allow for balanced immune function. So, allowing these immature cells to develop properly into functional cells and have a balance between these different aspects of the immune system so that they can develop properly and really trying to correct the underlying immune defect that's present in these patients. So, I'm going to walk you through now some of the data on Joenja®, as well as the label that was approved by FDA on Friday. And here's a graphical depiction of the bottle and the carton, as well as the overview of the prescribing information. So, you can see there the indication statement that it's Joenja® is approved or indicated for the treatment of APDS in adult and pediatric patients that are age 12 and older. There are no contraindications or boxed warnings. There is not a REMS or a risk evaluation and mitigation strategy in place. And you see some other details on the dosing there for patients who are over 45 kilos. There are some warnings and precautions that are mentioned there. And then the most common adverse reactions were headache, sinusitis, and atopic dermatitis.

Let's go through some of the data on the clinical trial itself. The trial really was in three parts. Part one was the dose finding part, and this was done in six patients looking at three different doses to make sure that the correct dose was selected. And that was done on the basis of the immune findings, as well as the clinical findings and safety and tolerability. And on that basis, the 70 milligrams twice daily dose was selected for part two. As Sijmen mentioned, this was a 12-week randomized, blinded, controlled study, a placebo-controlled study. And what we saw there, what we were looking for was changes in the immune phenotype. So, looking at how immune cells function and then also looking at this underlying fundamental issue in APDS, which is lymphoproliferation. And so, we looked at the size of lymph nodes in these patients, numerous secondary and exploratory endpoints, and of course, safety was a critical concern. And then these patients then had the ability to roll over into the open label extension study on the far right there -- you see there. And you see that there were in total 37 patients. This is a study that's ongoing. We reported some of these data at the ASH conference at the end of 2022, and we expect to continue to report these data throughout the course of this year, as well as wrap up this study as the regulatory approvals come in.

Let's look at the data and what we can see here when we look at the primary endpoints is that Joenja® restores this immune balance again, correcting that underlying immune defect. You see that on the left. When we look at the immune dysregulation aspect, which is looking at the size of lymph nodes and you see a dramatic change even in 12 weeks, you can see that on the scan there, on the image there as well as in when we look at all patients and you see a statistically significant difference when we look at the patients who received Joenja® versus placebo in terms of the reduction of these index lymph node lesions. And then on the right panel, you can see the immune deficiency aspect. And so this is a measure of what's called naive B cells. So naive B cells are B cells that can respond to infections and antigens. And you see a dramatic increase again in a matter of 12 weeks in Joenja® treated patients versus the placebo treated patients. And this really was the heart and the basis of the FDA decision to approve Joenja® on the basis of these primary endpoints.

On top of that, you can see the safety profile in this slide. So, in the phase three profile, in the phase

three study, you can see the most common adverse events reported by patients treated with Joenja® in at least two patients. And you see the list there. And then in the open label extension study, where we had patients treated going up to several years. We can see the tolerability profile there. And across all of these studies, you see that, you know, we had a median exposure of two years as well as some patients who were greater than five years of exposure since this study began. And then when we begin to look at some of the secondary endpoints, we can also see how correcting that immune defect, addressing that overactive pathway begins to manifest itself in these patients. And one of the clear manifestations is that when we look at something such as the size of the spleen, these patients again have enlarged spleens as a manifestation of that lymph or proliferation. And you can see that in the images on the on the right there, we have an example patient of a 17-year-old male who had an enlarged spleen. And then even by 12 weeks, we can see a significant reduction in the size of his spleen. And this was seen also when we did a comparison across all patients in the study in terms of Joenja® treated patients and placebo treated patients. And do you see a statistically significant difference in the size of their spleens over the treatment of this 12-week period. And we presented data at ASH, as I said earlier, where we showed that this this type of reduction continues in the open label extension study. So, when these patients are treated for a longer period of time as well.

Likewise, I mentioned earlier that IGM elevation is a clear hallmark of the disease. Again, a manifestation that these patients' immune system is not developing properly. In this case, their immune cells are not doing what's called class switching. So, they're not switching from IgM production to IGT production. And what you see here is that they have high IgM at baseline. But when patients were treated with Joenja® and you can see that beginning to happen as early as four weeks, you see that their IgM levels begin to drop and they're within the normal range, certainly by four weeks and then continuing to 12 weeks. Again, we've seen this data even in the open label extension study where patients are treated for much longer periods of time. In contrast, you see the placebo treated patients at the top and you see those patients who do not change their IgM level significantly. On top of that -- and we'll be sharing more of this data as we move forward -- when we treat those placebo-treated patients with Joenja®, we can see those levels come down to, which is nice for these patients. And then probably one of the most important aspects is, okay, now you've shown that you can correct the underlying immune defect. You can allow these patients' immune cells to develop properly, and you can address the lymphoproliferation. You can reduce the size of the spleen. We can show demonstrations and lower IgM levels, but what about other clinically relevant manifestations? And you can see here the number of infections that these patients experience, the number of days of inspection and infections over time. How that comes down nicely as the patients are treated with Joenja®.

And likewise, when we were observing these patients, we noticed that there were fewer patients now using immune globulin replacement therapy, this was actually not driven by the protocol. This was a sort of a spontaneous decision that investigators and patients made where they said, look, the patient is doing better. We can take them off this IRT therapy. And we see that a little bit more than a third of patients, again, spontaneously did this. And what was interesting was this was happening not only during the study, which occurred during COVID, where patients that were coming off of IG replacement therapy at that time. But we also see while they were coming off, they had less infections, which is again, I think, demonstration that the underlying immune defect was being corrected.

So in the end, what we have with Joenja® is a medication that's indicated for the treatment of APDS

is an adult and pediatric patients over the age of 12. We've seen randomized placebo-controlled data showing both primary end points from that with significance. And we've seen other improvements in the secondary endpoints in exploratory parameters. Overall, we've seen that the drug was generally safe and well tolerated, including from long term use in the open label extension study. We've seen improvements there in some infections and the use of IRT, and we've also seen that these results are consistent with the RCT study. So, with that, we are positioned to hit the ground running with Joenja® and I'm going to turn it over now to my colleague Stephen Toor to talk to you a little bit more about how we're going to bring to Joenja® to patients.

Stephen Toor – Chief Commerical Officer

Thank you, Anurag, and thank you all for joining the call this morning to discuss this significant event for the APDS and broader PRD community and, of course, Pharming. Over the next few minutes, I'll walk you through the strategic imperatives that have driven our planning over the past three years, and that will underpin the execution of the launch, our core business drivers and how we structure them for successful launch. And I'll confirm the price of Joenja®. The strategic imperatives you see on this slide are most easily summarized by the phrase "find, treatment, keep." Or find patients, treat patients, keep patients. And that's exactly what these four strategic imperatives are designed to do.

So firstly, identify it. That's achieved through a combination of our deep understanding of the patient journey analytics, partnerships with relevant stakeholders and working directly with treating HTPs or physicians. As previously stated, we believe there are at least 1,500 patients or more across the U.S., E.U., Canada and Japan, and we've already identified 500 patients globally with just under 200 of those in the US, and that includes approximately 25 in the EAP and OLE, and they'll start transition to pay products in the coming months. We've also identified the majority of the physicians that patients, current patients and future patients, are likely to see to get diagnosed and treated.

Finally, if APDS is suspected, we've partnered with Invitae, the country's biggest genetic testing provider. But of course, allied to identifying patients is education. This disease, as Anurag said, was defined only ten years ago. It's incredibly rare and most ACPs are unaware. So therefore, patients are easily misdiagnosed and they're often hiding in plain sight. In addition to the work of our own team, we've effectively partnered with patient organizations, health care provider societies, such as the JMF, IDF and the American Society of Hematology and others you see on this slide, primarily to expand their knowledge of APDS because it's critical to ensure that ACPs recognize the constellation of different symptoms Anurag mentioned that could be APDS and it would therefore trigger their need to test and then subsequently treat and treat early. That effort has been ongoing for the last two years and it's going to continue for some years to come as we uncover more and more patients globally.

The third strategic imperative: differentiate Joenja®. It seems really obvious, but we can't afford to be complacent. It is key for us to emphasize that this is the first indicator treatment is disease modifying, which is the root cause of the disease because all other treatments focus purely on the symptoms and the consequences. So, we won't launch assuming being the first indicated product is enough, will continue to drive this messages home to ACPs and really drive their need to recognize this and test and treat early. And then finally establish access. Once all that heavy lifting is done, we need to get Joenja® into patients homes as quickly as possible and to ensure that we've created APDS Assist, and industry leading program like RUCONEST® Solutions. And we'll go into that

in more detail in subsequent slides.

On this slide, you can see how with we're setting up for success as we go to market. So in the first column there you see our commercial field teams. That's 54 sales representatives and leaders. Half of them is the current RUCONEST® team, and we believe 30% of patients are treated by customers already well served by the HAE Team. Additionally, we've set out the new Joenja® institutional team and they'll focus on the central locations where specialties such as pulmonology, hematological oncology and GI are based and where we believe the other 70% of patients will be treated. So, between these two excellent teams, the vast majority of the APDS market, if not all, will be covered. And importantly, I want to flag, like RUCONEST®, the new teams comprise of sales representatives with rare disease experience, especially in hospital experience and experience of finding patients and launching products.

So as with RUCONEST®®, we've built a team of award winning salespeople to drive a successful launch. The other feet on the street are identifying patients. We also, though, have other key colleagues, including clinical educators to drive family mapping and testing. And I just want to remind us all that APDS is genetic. So there's a 50/50 chance of each child in a family having APDS. So family mapping and family testing is an important source of new patients for Pharming, and it's a key step in ensuring all patients get access to this much needed therapy, which, as we've seen from Anurag's presentation, treats a progressive disease with significant, significant sort of clinical consequences. Now let's look at the support services and APDS Assist, which has been built trained and staffed to get patients on therapy and keep them on therapy despite the challenges sometimes presented by a health care system. APDS Assist is a dedicated full service concierge program that ensures once a patient is diagnosed, there are zero distractions to addressing the challenges of getting Joenja® in a patient's hands. The program covers financial aid, filling prescriptions and ongoing support to ensure adherence and ongoing access. And the staff includes APDS Assist care coordinators. And they provide a single point of contact for patients, and it often be the same person; that delivers a consistency of service and care and we believe provides reassurance to patients versus the more commoditized call center approach.

We also, as I mentioned, have APDS clinical educators that provide overall support, education to patients. And importantly, there will be clinical pharmacists on hand 24/7 to process the prescriptions and answer any and all questions patients might have. I also want to note that we've partnered with PANTHERx through to provide these services. PANTHERx specializes in rare and ultra rare therapeutic conditions, and that really gives them unique insights to both what ultra rare disease patients need and the highly personalized service standards pharming needs to be delivered. Our dedicated program and staff will speed access by minimizing bureaucracy of mistakes and catering to the very specific needs of individual patients and their families. Delivering such a high quality access program as we have in hereditary angioedema is one of the reasons we expect this launch to be very successful. I'd like now to provide a little more color about what happens when a patient's enrolled and the support they can expect at that point. So once the benefits are verified, patients are entered into our starter program, that means they'll get a 30 day supply within one week of enrollment. Most patients should then be on paid therapy the end of that time. However, as we all know, the insurance process and approval can sometimes take a little longer. In that instance, a bridge program is available that will take the patient through until insurance is confirmed. For commercially insured patients we'll also provide copay assurance, which can help with some out of pocket costs, but importantly can bring the cost of the monthly prescription down to as little as $0 per month.

Finally, we have a patient assistance program in place so that any patients who are uninsured or who their plan doesn't covered will still receive Joenja®. So with these options, we believe we have all bases and all scenarios covered for our patients. As Anurag and I shared, Joenja® is the only indicated treatment for APDS; it's disease modifying, it works on the root cause of APDS for both immune deficiency and dysregulation. It's a precision medication. So if a patient tests positive ASPs and payers know that providing and paying for the right option. And as you've seen, Pharming's about innovation to education to ensure all stakeholders understand the value Joenja® delivers to patients and their ACPs and payers. And we're providing those concierge level support services to ensure patients get quick access and continued access to Joenja®, the very least this patient population deserves.

Finally, I'd like to cover the price of Joenja®, which represents value -- the value that Joenja® delivers to all of Pharming's stakeholders. Joenja® will launch a $750 per tablet with an annual cost of $547,500 per year. As you know, we have a track record of success in rare disease and rare disease development, and we prepared meticulously for this launch. We've used the commercial knowledge gained in the execution of the HAE program, and we put in place programs that we believe will get Joenja® into the hands of the patients and their families as quickly as possible. I'd like now to hand over to Jeroen Wakkerman, our CFO to go through the financial considerations.

Jeroen Wakkerman – Chief Financial Officer:
Yes, thank you very much, Steve. And indeed, I will take you through some of the financial considerations of this FDA approval of Joenja®. So Pharming licenses the global rights to leniolisib from Novartis in 2019. And at the time contractual terms were agreed if we got the approval and started commercializing. And the contractual financial terms are as follows. Number one is we will pay shortly a near-term milestone payment to Novartis and another party for an amount of 10.5 million for the approval and the first commercial sale of Joenja® in the U.S. The second is the future potential milestone payments. And those sales milestones can be up to, in total, $190 million and they are related to the net sales level and are structured in a layered way. And basically, the story is here, the more we sell, the more we pay and the higher the sales level, the higher the particular milestone payments. The third financial contractual term is the royalties. So, we've got royalties on net sales ranging from the low to the high teens percentages. And the fourth term is concerning the priority review voucher received by Pharming from the FDA. And Novartis has agreed the right to purchase the voucher for a small minority share of the value of the voucher. And the value of the voucher is based on the reasons, VRV, transactions. So overall, we have market-based conditions for a contract of this nature. And the more we sell, the more we pay. And obviously, we will be happy to do so. With that, I would like to hand over to Sijmen de Vries for closing remarks.

Sijmen de Vries, MD – Chief Executive Officer:
Thank you, Jeroen. Yes, and on the next slide, you see that this today marks a very important day for our company because we have just transformed from this one product, one market company to a two-product company because leniolisib and RUCONEST® will now help to fund the future investments in our pipeline and the management of our assets. And of course, we are now about to embark on the commercialization of Joenja® in the United States, but obviously Joenja® will also support our business going forward and will enable us to establish a very strong business basis in Europe and beyond. And last but not least, as we all know, as stated before, we have plans to actually branch out to Japan as well on the basis of Joenja®. And furthermore, we will also update

you later on during the year on our plans to develop the subsequent indications for Joenja®, because Novartis has done already a lot of research in various new additional indications where we have built upon, and we are exploring additional further indications as well and that will be updated later on during the year.

And then last but not least, because we have a very scalable commercial operation and we have a strong track record in the development and commercialization of rare disease assets, we continue our hunt to get advanced projects, products in advanced clinical stage to add to our pipeline. And you can still see that, of course, on the next slide, our pipeline is now significantly strengthened with Joenja®, of course, being approved for commercialization in the U.S. There's still a very significant gap between Joenja® and leniolisib, of course, in the European Union and U.K. And the early stage, the internal projects that we have. So, we are still very active in the business development front, do either in license or acquire additional rare disease assets where we can again make a big difference for patients that are suffering from these rare diseases. And on the next slide, you see the milestones for Joenja® are going forward. We now, of course, have achieved the FDA regulatory approval. You heard from Stephen that we are more than ready to launch in the U.S., the commercial launch. We will start the Japanese clinical trial shortly. And of course, in the second half of the year, we look forward to the response from EMA respectively, followed by the filing in the United Kingdom.

And that brings me to the outlook, which we shared with you recently when we actually presented our full year results for 2022. So, the outlook continues as it was. We continue to expect low single digit growth in RUCONEST® revenues during 2023. Of course, we are starting to now launch Joenja® very soon in the United States, and we'll have the product available in April, as you heard before. We still expect the positive CHMP decision in the second half of 2023 and followed by the marketing authorization in Europe two months later. We then filed leniolisib with the U.K. MHRA following the ECDRP route. We continue to invest significantly to accelerate further growth. We'll update you on our plans to develop leniolisib for additional indications, as I said before, in the second half of 2023 and we continue to focus on the potential acquisitions or in-licensing of other late-stage opportunities to treat rare diseases. And this brings me to the last slide of this. A big thank you. A big thank you to the patients and their families who participated in the clinical trials, first and foremost. A big thank you to all the investigators, caregivers and physicians that worked diligently on the development of leniolisib. A big thank you to the patient advocacy organizations who are so important for patients suffering from rare diseases.

And last but not least, a big thank you to our Pharming and, of course, the Novartis teams that supported the development of Joenja® and can be very proud of this FDA approval for Joenja® today. That brings me then to the next stage of this meeting, opening the floor for questions. Operator, you can head over for questions.

Operator:
Thank you. If you would like to ask a question today, please press star followed by one on your telephone keypad. If you choose to withdraw question please press star, followed by two. When preparing to ask your question, please ensure your phone is unmuted locally. And our first question today, goes to Christian Glennie of Stifel. Christian, please go ahead. Your line is open.

Christian Glennie - Stifel
Good afternoon, guys. And my congratulations on the FDA approval for Joenja®. Quite a significant

achievement for you guys. Then I guess the first question is then around pricing, just to follow up on sort of pricing and reimbursement and uptake. So is your understanding, obviously, on the reimbursement side, there's obviously nothing predetermined in terms of the confirmed genetic tests as required by the FDA label, but is it your understanding that insurance companies that may well be a prerequisite for it?

Sijmen de Vries, MD – Chief Executive Officer
Stephen?

Stephen Toor – Chief Commerical Officer
Yeah. So, Christian, it's possible and we expect that we'll be put through the normal insurance process of prioritizations, et cetera, and they may well require that, but there are no policies as yet. Those policies will be developed as the first patients come in. At this point, we expect almost all patients to go through the medical exception process and be approved that way, and that will take the normal 30 to 60 days.

Christian Glennie - Stifel
Okay, then that's helpful. And then thinking about the price, obviously you said, effectively an annual basis $547,000. Just so we're clear, you know wouldn't expect much of a sort of gross to net or discounting here. But just to clarify that you expected the net price and then linked to that, any, clearly the data shows that the duration of treatment is, continues to be ongoing. The open label, you know, the patient's continued treatment, assuming they continue to tolerate and get disease control. But any reason why, you know, duration of treatment on an ongoing basis would be less than 12 months.

Stephen Toor – Chief Commerical Officer
So, I'll take the first part of that question and I'll ask Anurag to take a second. I think your assumptions around net pricing are reasonable. That said, until we see the patient mix in the coming quarters, it would be tough to determine. But in terms of, the ongoing treatment and whether a patient will be treated for less than 12 months, Anurag, could you --.

Anurag Relan, MD – Chief Medical Officer
No, we do expect that these patients would be treated chronically and continuously with, Joenja®.

Christian Glennie - Stifel
Okay, Thank you. Then one final one for me, if I can, then jump in the queue. Just to clarify, I think you mentioned there were 25 U.S. patients that are currently on the extension trial. And if that's the right number and then the expectation that presumably they all -- assuming they want to continue on drug, they all, you know, will then convert to the commercial drug and obviously the pricing, you know, according to their insurance plans or whatever. But what should that transition time period be for those 25 patients be?

Stephen Toor – Chief Commerical Officer
I think, Christian, there -- I mean, there are patients -- there are approximately 25. It's around the number and they're in the EAP or the early access program and the open label extension. That overall transition will be several months, but it will be this year depending on therapies the patients have on hand at the speed at which we can pull them through the insurance process. But it will happen this year.

Christian Glennie – Stifel
Right. Okay. Thank you, guys.

Stephen Toor – Chief Commerical Officer
Thank you.

Operator:
Thank you. And that question goes to Hartaj Singh of Oppenheimer. Hartaj, please go ahead. Your line is open.

Hartaj Singh – Oppenheimer & Co.
Great. Thank you. And thanks for the question. Congratulations again on a really important approval. You know, I think you touched on this little bit, can you just -- maybe you can just, you know, divide the -- in the U.S., what is the process you're going to go through, or patients are going to go through for private versus public reimbursement? And is there a PMS procedure that's going to be in play here? And how to just think about that? And I just got a quick follow up question.

Stephen Toor – Chief Commerical Officer
So, I think that the process is broadly similar regardless of the type of insurance you have, Hartaj, on who covers you. There will be that prior authorization process. Some patients may require a confirmed genetic test. It's entirely possible that the insurance companies will want to have a peer to peer and better understand and be educated on the disease state. We expect that to probably be enough in most cases, regardless of the payer type. And most patients should be approved at that mid-point in the process, and that would take anywhere between 30 to 60 days typically. And as you saw, until that process finishes, we'll make sure that patients have therapy on how to treat their APDS.

Hartaj Singh – Oppenheimer & Co.
Great. Thank you, Stephen. And then the other question is just a more broader question, which is that, you know, as we're thinking about European and U.K. Approval, potentially Japan, how do you think about. I know this might be early days. This is a very high value therapy and an ultra-rare disease condition. Some therapies analogous to this, you know, for Solaris, for example, had a very tiny, you know, difference between ex-U.S. and U.S. pricing. So Stephen, any thoughts there and thanks for all the questions.

Stephen Toor – Chief Commerical Officer
Certainly. I mean, obviously that's some time out, so we can't give specifics. And the Alexion launch was, as you know, some time ago. I think in the current environment, especially in Europe, it's our expectation that the price will be somewhere in the 60 to 70% range of the U.S. price. But that's work ongoing and still to be determined. But I think that's a reasonable expectation at this point.

Hartaj Singh – Oppenheimer & Co.
Great. Thank you. And congratulations.

Stephen Toor – Chief Commerical Officer
Thank you.

Operator:
Thank you. And the next question goes to Joe Pantginis of H.C. Wainwright. Joe, please go ahead. Your line is open.

Joe Pantginis – H.C. Wainwright
Hey, everybody. Congratulations as well. Couple of questions. Thank you. So, first on the PRV. Is there a timeline for Novartis' right to pursue the small minority share and, you know, what freedom do you have right now ahead of that or after that to be able to sell it externally?

Sijmen de Vries, MD – Chief Executive Officer
So, there is -- in the contract, it's clearly defined how this works. We can't go into too much specifics, but one of the options is that Novartis obviously uses the PRV for its own purposes. The alternatives, as you rightly point out, we jointly agree to sell it off to a third party and we will, of course, be updating the market as and when there's further news on what Novartis decides on what to do with the PRV.

Joe Pantginis – H.C. Wainwright
Got it. Yep, and one quick logistical question before my other question is making sure that we have the checkbox of supply being all set. And the other checkbox is among the 54 sales reps and leaders, are they all in place currently or is there still any ramp?

Sijmen de Vries, MD – Chief Executive Officer
And in both cases, I can confirm we are ready to roll. Supplies are being sorted as we speak there. The product has already landed in the U.S. for a while, and the final labeling, of course, was known as well. So basically speaking, we expect to product to be ready by mid-April. Is that correct, Stephen?

Stephen Toor – Chief Commerical Officer
That's correct. Sijmen.

Sijmen de Vries, MD – Chief Executive Officer
And then with regards to the sales reps, we can confirm that as well, I think, Stephen, right?

Stephen Toor – Chief Commerical Officer
Yep. We have our people in place. They'll go through their final training this week now that we have the label, Joe, and they will launch at the end of this week.

Joe Pantginis – H.C. Wainwright
Perfect. Perfect. And then I guess, you know, maybe just something regarding the kinetics of the disease and especially when you had that, you know, longer term AE profile around the two rear mark where you have some infections, where, you know, based on, you know, seeing the switch to IGM to ITG over time that you would potentially expect to see those infection rates continue to come down.

Anurag Relan, MD – Chief Medical Officer
That's right, Joe. And that's exactly right, Joe. We've seen that in the open label extension study data is how those infection rates come down over time. And then into the concomitant, we see that the use of IG decreases over time. So, both of those things that we've seen over time and,

again, the IG use decrease was really spontaneous. That was something that the protocol did not direct the investigators to do or even guide them how to do this. This is something that they started to do on their own as they saw these patients improve.

Joe Pantginis – H.C. Wainwright
Fantastic. Thanks a lot and best of luck with the launch.

Sijmen de Vries, MD – Chief Executive Officer
Thanks you, Joe.

Operator:
Thank you. And as a reminder, if you would like to ask question today, please press star followed by one telephone keypad. And our next question goes to Max Herrmann of Stifel. Max, please go ahead. Your line is open.

Max Herrmann - Stifel
All right. Thanks very much for taking my questions and congratulations on the approval. Great milestone. Just a couple. One, is you talk about 500 patients identified in the U.S., over 1,500 globally, I wonder how many are actually suitable for treatment versus those that have had already bone marrow transplants and may not be, therefore, needing of therapy. And then a second follow up question.

Anurag Relan, MD – Chief Medical Officer
Those really are a very small percentage, probably it's less than 10% that have had a transplant already. Interestingly enough, we do also know of patients who've had transplants but are still not doing well and actually we have had physicians reach out to us and request compassionate use access even for post-transplant patients, which we haven't studied yet, of course. But to answer your question, it's less than 10% of patients that have had transplant.

Max Herrmann - Stifel
Great. Thank you. And then just on, in terms of drug compliance in this area of orphan disease, when it comes a bit to the net to- or gross to net calculation, do you expect pretty much 100% compliance or do you normally expect a bit of mixing of doses, so we should do some sort of adjustment between you expecting the BID treatment?

Anurag Relan, MD – Chief Medical Officer
I mean, this is a serious disease and the condition we know worsens over time. And we also know that patients improve rapidly on therapy, which likewise means they would rapidly not improve if they withdrew from therapy. And we've seen that actually in some patients early on who were switching from one study to another when Novartis was moving them. So, I would expect a very high compliance rate.

Max Herrmann - Stifel
Okay. Thank you very much.

Anurag Relan, MD – Chief Medical Officer
We're going to educate patients on them, too.

Max Herrmann - Stifel
Great.

Operator:
Thank you. And our final question goes to Christian Glennie of Stifel. Christian, please go ahead. Your line is open.

Christian Glennie - Stifel
Thanks. Just one follow up then. Just curious on the testing side, on the VT side. Obviously, at the moment or until now, you have been paying for those tests to be conducted, obviously, and a clear rationale for that. Now, that it's commercial is there a scenario in which the test itself also gets reimbursed and therefore you don't have to provide that or do you think that will continue on.

Stephen Toor – Chief Commerical Officer
So, Christian, it's certainly possible, but it's obviously early days. So at this point, we're simply focused on getting patients on therapy and getting payers to put their policies in place. As part of that discussion, we would certainly follow up and talk to them about the coverage of testing. But the situation regarding that's not immediately clear and it's obviously not a launch priority. We're going to continue to provide testing in order to get patients on therapy.

Christian Glennie - Stifel
That makes sense. Thank you.

Stephen Toor – Chief Commerical Officer
Thank you.

Operator:
Thank you. We have no further questions. I'll hand back to Dr. Sijmen for any closing remarks.

Sijmen de Vries, MD – Chief Executive Officer
Thank you very much. Thank you, ladies and gentlemen, for being here today on this very important day for both APDS patients and for our company. As you just heard, we have today transformed from a one product to a two-product commercial company. We have experienced and dedicated commercial and medical teams in place in the U.S. undergoing their final training this week to launch leniolisib and bring it to those APDS patients that are in need of a treatment that treats the root cause of their disease. And we have all the assist programs in place to help them with access to medication, education and support services. So, we look forward to bringing this to the patients from next week onwards and to update you in the future about how we progress into the market, into the U.S. market with Joenja®. Thank you very much for being here and forward to speaking you the next time. Goodbye.

[end of transcript]