Pharming Group N.V. 2Q/1H 2024 Results Call

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Sijmen de Vries, MD – Chief Executive Officer:
Thank you very much. Good morning or good afternoon, ladies and gentlemen. Welcome to our results conference for the first half and second quarter of this year. And I'm here with my colleagues, Stephen Toor, our Chief Commercial Officer; Anurag Relan, our Chief Medical Officer; and Jeroen Wakkerman, our Chief Financial Officer and we will collectively guide you through the story.

But before I do that, I would like to point you to these forward-looking statements slide. We will be making forward-looking statements in this presentation. And as you well know, these are based upon future expectations that are based on our current expectations and assumptions, and may involve unknown risks and uncertainties, as you well know that the results eventually could differ materially from what we have expressed or implied in our statements.

Next slide, please. And then, you can immediately move on to slide number five, please.

So what we're doing is, this is the strategy that we've been embarked on for quite some time now. We're building this leading global rare disease biopharma company. And we do that on the basis of two strong pillars. The first one on the left is RUCONEST®, which has now been on the market for close to 10 years in the US, and delivers sales mainly from the US market.

We were very pleased to see that RUCONEST® continues to grow very significantly, both in context of the comparison to the previous quarters, in the second quarter 23% versus last year. And both when you compare the first half to last year's first half, 16%, which is, I would say, a very strong performance, which we're very pleased with. Stephen, a little bit later, will give you more details on the underlying positive indicators also going forward into the second half of the year.

And then, we have Joenja®, which was approved end of March last year, which we brought into the market beginning of the second quarter of last year. And we're very pleased to see that this continues to grow as well, second quarter compared to the first quarter was 16%, and 44% if you compare the first half of this year to the last half of last year.

So we are continuing to grow Joenja® in the market. And this, as we all know, is a very new disease and an ultra-rare indication. And our colleagues, Stephen and Anurag will address this and tell you why we are continuing to be very optimistic of the enormous commercial potential for Joenja®, not only in APDS but also in subsequent indications.

And that brings me to the pipeline on the right-hand side. We are very soon embarking on a Phase II study for the next indication for leniolisib and we are also exploring a third indication. Anurag Relan will talk to you about that in more detail.

And last but not least, we continue to focus on in-licensing or acquiring clinical stage opportunities in rare diseases to broaden our portfolio and which we can given our strong financial performance. And then I would like to have the next slide on the cascade of the disease overview.

And this slide is an important one, because RUCONEST® is in a very competitive market. RUCONEST® however is an unique product, as you can see here. Because these are the three pathways that represent an attack of hereditary angioedema, and C1 inhibitor is the missing protein, and RUCONEST® is protein replacement therapy, is the only actively promoted C1 inhibitor on the US market and addresses all the pathways, as you can see.

RUCONEST® has proven throughout the years to be a reliable product to actually treat those attacks of hereditary angioedema. And there is, of course, a lot of competition, but all of these competing products that are in development do not address all the three pathways.

A typical patient profile for RUCONEST®, therefore over the years, has evolved, and has become that type of patient that does not respond to products that are actually only serving that, for instance, kallikrein independent pathway in the middle or the HMWK, releasing the BK pathway on the bottom.

So RUCONEST® basically builds its own unique position there. And all those patients that are using the other products suffer from breakthrough attacks, and also in this case, RUCONEST® comes into view. So in other words, we strongly believe that despite current competition and previous competition which we have seen, and oncoming competition which all are serving that single pathway, RUCONEST® will be the go-to product for those severely affected patients, also known, for instance, as type III hereditary angioedema, of which more and more get diagnosed.

That explains to you why more and more patients come to RUCONEST®, and RUCONEST® becomes the mainstay for their therapy for hereditary angioedema because they cannot get by on any of these other products. Hence, we are very optimistic and very confident about the future delivery of RUCONEST® to basically underpin the growth of our company. And let's move then to the next slide, that's Joenja®, which we believe has a significant potential as well. This depicts here, and Stephen and Anurag will go into more detail, the fact where we are at the moment with Joenja®.

We have a significant portion of the US patients already on paid therapy, of the ones that have been identified so far. We however have a great potential going forward with regards to validating the Variants of Uncertain Significance. And Anurag will talk about that when and how that will happen, and what kind of potential big impact that will have on the number of patients that become available in the US market.

Outside of the US, we started to see sales, and will continue to see growing sales from patients on early access and named patient programs. We're working with more regulatory agencies and looking forward to bringing leniolisib for APDS in more territories in the world.

And last but not least, an estimated 25% of patients are below 12 and can be served as and when the pediatric studies will report and as and when we get the pediatric label expansion as well. So in other words, leniolisib or Joenja® in APDS has a very significant potential, we believe even way beyond RUCONEST® at this point in time. And that's only for APDS.

So the other thing on the right-hand side there is that we now have identified the second indication, and we'll start a Phase II trial in that second indication, which is, as you can see on this slide, about more than three times the estimated incidence of APDS, the PIDs or primary immune deficiency.

In addition to that, we are now seeking regulatory feedback on a third primary immune deficiency indication. So in other words, we believe that not only does Joenja® have an enormous potential over the coming years to develop itself into a very significant commercial asset for our company in APDS, but on top of that, it has even bigger potential to actually become a pipeline in a product, given that we have now identified at least two indications from which we could start development programs very soon.

So with this said, I happily hand over to our Chief Commercial Officer, Stephen Toor, to take you through a little bit more details on the revenues of RUCONEST® and Joenja®.

Stephen Toor – Chief Commercial Officer:
Thank you, Sijmen. Good morning and good afternoon, everybody. We can go to the next slide. So I will, as Sijmen said, take you through the RUCONEST® and the Joenja® performance so far, and then on the last slide for me, before handing over to Anurag, just give you a little update on our kind of medium-term expectations of why we're so confident in the business.

So looking at this slide and specifically RUCONEST®, you can see, I think in those first four boxes at the top that the consistent strength in performance really relates to the unique attributes of RUCONEST® in the patient population we serve that Sijmen alluded to that more severely affected group.

RUCONEST® is, as you know, the only recombinant C1 esterase inhibitor, and those key core benefits of 97% of patients whose attack is resolved in a single dose and that sustained effect over a period of days, is really why those patients, between icatibant and other products that don't work as well, find a home with RUCONEST®, but it's what drives our continued strong performance. And that performance over a decade now has made RUCONEST® the second most prescribed acute therapy in the US, and of course still posting solid results.

In the first half '24, new patient enrolments have continued to strengthen over and above last year. And in that first half, we actually enrolled 170 new patients, and that represents an increase of 18% over the first half of '23. That, as you would expect, is driven by an increase in new prescribers as well as maintaining our existing ones, and our sales teams added another 36 new prescribers in the first half of '24, taking the totals to over 760, which is an all-time high.

So as you would expect, this translates into that quarterly growth of 23% and that plus 16% versus the first half of last year that Sijmen alluded to. And I think for the attributes I mentioned, the patient population we serve and also the clinical overview Sijmen gave of where RUCONEST®

operates in all three pathways, is why we're very confident that we're well positioned even as the market evolves in the second half of next year. Next slide, please.

So switching gears now to Joenja®, that is, as Sijmen said, a product that we launched on 31st March last year to treat the ultra-rare disease, APDS. And just as a reminder, that's a serious and progressive disease with high mortality. And until Joenja® was launched, there was no indicated disease modifying treatment.

As you also know, we were strong out of the gate with the US launch, and patients who were on Joenja® were fully reimbursed within days, within less than a week, in fact. So we continue to make good progress in 2024. At the end of Q2, 91 patients were on Joenja®, another two were in process at the end of the quarter and who should come on to therapy early in Q3. We added 10 newly diagnosed patients in the quarter, taking us past 230, which is close to half the total number of the literature suggests are out there already, just 15 months post-launch.

And we believe it's highly likely, as with any ultra-rare disease, now that we're out there, more actively patient finding that actually there will be more patients than literature suggests.

We also have, in our pipeline, 40 more diagnosed patients whose doctors we're working with to enroll in our program, plus 60 and counting pediatric patients who've been diagnosed within our pipeline who'll be ready to go on Joenja® when we get the label expansion in the fullness of time. So just to summarize Joenja® performance. We exited Q2 with $11.1 million in sales, which, as Sijmen said, is an increase of 16% over Q1. Next slide, please.

Our teams remain, as you would expect, firmly focused on finding new patients, and then when found, mapping and testing the whole family, given this is an autosomal dominant disease.

In this approach, as you're aware, netted an additional 28 patient leads in Q2 that we're now working through to confirm whether they're actually APDS patients. And it's through these efforts we remain excited and confident in the value we can bring to the APDS community, both in the US and ultimately globally. And as a result, our financial results keep us on track and are in line with the guidance that we've given for the year.

Now, if we look a little bit further forward, I think we've expressed confidence in both RUCONEST®, and of course, the future of Joenja®. And that's based on a few key factors. So the first is the continued strength of RUCONEST® and the reasons that we've already mentioned for why that holds the position it does in the market, which is, of course, underpinned by growth of prescribers, new enrolments and sales year-on-year.

The second is the execution around the Joenja® launch, and the progress being made in patient finding, family testing and building a pipeline for future months and years. But also for Joenja®, I just want to expand briefly on some of the other items on this slide. There are another few factors, there are another four factors that give us good confidence in the future. So one is the VUS resolution efforts that Sijmen alluded to and that Anurag will discuss, that'll be a significant inflection point for us and should deliver a bolus of patients in 2025.

Another important factor is geographic expansion. Right now, we're launching in the US, but we will launch in other key markets, which include, Japan, the world's second biggest market in the broader APAC region, the United Kingdom, the European Union, Canada, the Middle East. And across these countries and regions, we so far found almost 900 patients which represents almost half of the 2,000 of prevalence data would suggest that in these markets.

And additionally, where we're currently assessing while we work through those other key markets, the key countries in LATAM and our options there. We have, as I alluded to the pediatric patients, and we're building that pipeline up globally. And over time, when we get that indication that will be another bolus of patients that comes through in the future.

And then finally, and Sijmen talked about this, the life cycle management of leniolisib to create a pipeline of new indications for the molecule. And as these launches and events occur, we see multiple years of growth ahead from Joenja® for APDS and potentially those other indications.

So to expand on these and other related themes, I'd like now to hand over to our Chief Medical Officer, Anurag Relan.

Anurag Relan, MD – Chief Medical Officer:

Thanks, Steve. Now, we can jump to the next slide. And we can first review some detail about Joenja®. So Joenja® is FDA-approved to treat activated PI3K-delta syndrome, or APDS, in adult and pediatric patients who are 12 years of age and older. APDS, as Steve mentioned, is a rare, serious, genetic disease caused by hyperactivity in this PI3K pathway, and it's associated with early mortality, often due to lymphoma. And it's also important to note that APDS is progressive. So experts state that early treatment is important.

Joenja® is a PI3K-delta inhibitor which regulates this hyperactive signaling pathway that's found in APDS patients. The FDA approval last year was based on a randomized pivotal study as well as an open label long-term extension study. And Joenja® treats the root cause of APDS by correcting the underlying immune defect, thereby addressing both the immune deficiency and immune dysregulation that's found in APDS patients.

The safety of Joenja® was evaluated in this placebo-controlled study as well as the long-term study that is just wrapping up, in fact. And no drug-related serious adverse events or study withdrawals were seen in these trials.

And on the next slide, we can see some of our patient finding efforts. Specifically, we are supporting numerous activities to raise the awareness of APDS and share data about leniolisib and Joenja®. So on the left, you can see the medical education types of things that we engage with, and the organizations that we're working with to raise this type of awareness. But also importantly, we have several efforts to help patients get an accurate diagnosis, the first of which is genetic testing.

We have a sponsored no-cost genetic testing program. We have support from genetic counsellors. And as Steve mentioned, we're also working to help perform family testing among patients who've already been diagnosed with APDS. Because APDS is an inherited disease, we expect to find patients within families, but most APDS that patients that have been diagnosed and that are in our databases actually don't have family members diagnosed. So we're supporting clinicians to be able

to educate and encourage family testing and also offering patient-initiated testing so that patients with family members can get those family members tested easily.

And on the right side, one large area where we're focused on is when a patient actually goes through all of this process and receives their genetic test results, but unfortunately, it's what's called a Variant of Uncertain Significance, or a VUS. And in essence, this is an inconclusive result that indicates that a patient has a novel gene abnormality, but it is not known whether this abnormality causes APDS or not.

To help doctors and patients, we have several projects which will enable these VUS results to be definitively classified. So some ways that we do this is, first is what's called variant curation, which is collecting known data about the variant. In addition, we also make available and support programs to allow functional testing to occur in patients. So actually measuring the activity of the pathway in a patient who has a VUS diagnosis or a VUS result.

And then lastly, we're supporting a large-scale experiment, what's called a multiplexed assay of a variant effect, which is a high throughput method, whereby we can do in vitro testing of every or almost every possible variant that could exist. And this is a study that's going to read out later this year, which we think will be very important in helping these VUS resolution efforts.

And on the next slide, we can talk a little bit more about the scale of the problem, because this VUS problem is something that frustrates patients and doctors and limits the diagnosis of genetic diseases such as APDS. We are aware of more than 1,200 or approximately 1,200 patients in the US that have received a VUS result in either of the PIK3CD gene or PIK3R1 gene.

This figure will continue to grow over time, because any time that a patient gets a genetic test done, this remains a possibility. And in fact, VUS results or VUS patients are identified at approximately four times the rate of an APDS or what's called a likely pathogenic or pathogenic variant. Of course, this is a worldwide problem since these patients who get genetic testing can get this type of results anywhere.

And when we look in the literature, across all genes what we see is that when there are reclassification efforts put in place that approximately 20% of all of the VUSs that are out there get upgraded to a likely pathogenic or pathogenic or what's called disease-causing, and this again is across many genes.

In the case of APDS, we've done a pilot study with 25 patients who have a VUS result, and we found consistent findings of APDS in five of these 25 patients or 20%. And one of these patients is already preparing for enrolment now. So the key takeaway for us is that there is a significant opportunity to identify incremental patients with APDS through these VUS resolution efforts. And we'll look for more news for this as the year goes on, especially towards the end of the year.

On the next slide, we'd like to talk to you a little bit about some of the other efforts beyond the current FDA approval. As we've previously discussed, the CHMP review has been extended to January 2026. There is a single outstanding CMC request. And the CHMP have determined positive clinical benefit as well as safety, which has now concluded.

In addition, we are expecting a decision from the UK MHRA later this year. And importantly, no major objections were noted in our Day 70 questions from the MHRA. We've also completed our Japanese clinical study, and we're engaged with PMDA to discuss the filing strategy there following the completion of the necessary studies.

And you've seen in our press release too, there are significant clinician interest in our Expanded Access and Named Patient Programs, again reflecting the number of patients that are diagnosed out there, but also the unmet need in this patient population.

And as previously mentioned, we received marketing authorization in Israel earlier this year. We have submissions under review in Canada as well as Australia. And we have two pediatric studies, which are also very important, because as we mentioned, this is a progressive disease. We've already identified a significant number of patients who are below the age of 12, and we have now completed enrolment in our first study that goes down to age four, and then there is a second study where enrolment is continuing. And then I'll spend the next couple of slides talking to you a little bit about our plans beyond APDS with leniolisib.

So when we think about that, we see several development opportunities for leniolisib. Just as a review, primary immune deficiencies are a broad group of disorders with several key features. Often, they have a genetic basis. Of course, as an immune deficiency, they have an increased risk of infection, but there's also a subset of these immune deficiencies that also have a feature of immune dysregulation. Specifically, that immune dysregulation causes lymphoproliferation, autoimmunity and other auto-inflammatory conditions.

And because of that, these PIDs are associated with high morbidity and mortality. APDS, of course, is an example of one of these immune deficiencies with this regulation and now we are looking at leniolisib for other PIDs with these same features.

The first of which we're looking at PIDs with immune dysregulation linked to this specific signaling pathway. And we'll talk a little bit about this in the next slide, but these are, again, the patients who have clinical manifestations, disease onset and severity very similar to APDS. There are no specifically approved therapies for this, and we're beginning with a Phase II study imminently.

In addition, as Sijmen mentioned, we are working on another disease in the same area. And we're in the midst of obtaining regulatory feedback on the proposed clinical development plan. But in essence, this is another primary immune deficiency with the same clinical phenotype of immune dysregulation. So something obviously very common across these three indications that we're pursuing.

And then on the next slide, you can see some details about the Phase II study that is about to start. And this is a Phase II proof-of-concept study that's going to be starting soon at the NIH with 12 patients. These are going to be patients that are known to have hyperactive signaling based on a genetic diagnosis of one of the these – and you see there are several of the genes that are involved, including what's called the ALPS-FAS gene, CTLA4, PTEN, as well as a couple of others.

Overall, this represents a treatable population estimated at approximately five per million or which is about three times as large as APDS. This Phase II study will look at dosing, but also safety and tolerability, and we'll also have some exploratory efficacy measures here. And the goal is to pick the best dose regimen for the Phase III study.

And as I mentioned, we're expecting the final IRB approvals imminently which will enable us to start the study this month. So with that, I will turn over to my colleague, Jeroen, to review our financials.

Jeroen Wakkerman – Chief Financial Officer:
Thank you very much, Anurag, and good morning, good afternoon, everybody. Starting off with the financial highlights of the second quarter 2024 versus last year, you see that we grew our revenues by 35%, and that was driven by volume of both RUCONEST® and Joenja®. RUCONEST® went up by 23%.

Gross profit was fairly stable at 89%. So the margin was at 89%. So the gross profit basically grew in line with our revenues. For the OPEX development, the OPEX went from $65.8 million last year in the period to $70.1 million, and that is reflecting a continued investment in Joenja®, both in the US and EU/Rest of the World and also investment in compliance, IT, HR related areas, and that is to support the growth of the company.

We see an operating profit that we adjusted, so this is not the reported operating profit, but adjusted for a few one-offs that we had last year, and we had a milestone payment of $10.5 million. So that was a cost, but we also had a gain on the Priority Review Voucher, that you may remember. But basically, on a like-for-like basis, we see that the operating profit (loss) gap narrowed from $5.3 million last year to $3.1 million this year.

And the net profit was around $1.3 million last year, minus $1.2 million, so a loss this year. And please be aware for the analysts that in the finance result, we had a gain of $3.4 million this year versus a loss of $1.8 million. And that gain is related to the convertible bonds and a reclassification of the derivative to equity issuance, technical adjustment that you need to be aware of.

And the overall cash and marketable securities, they went down by almost $42 million. The biggest driver of that was the issue and the repurchase of the bonds. The old bonds had a nominal value of €125 million. The new one that we issued this year had a value of €100 million. And overall, the cash out because of the payback was €30 million. And the remainder is mainly driven by an increase in receivables from higher sales quarter before.

So moving on to the same KPIs, but for the first half of the year. Revenues increased by 33%, again, mainly volume from both our products. RUCONEST® went up 16% as was mentioned before. Gross profit for the first half was 87%. Gross margin was 87%. And yeah, the gross profit increased to $113.3 million.

OPEX reflects basically the same development as I've just mentioned, so it went up by $15.5 million to $134 million. The adjusted operating loss was roughly the same as it was last year. And the net profit was a loss of $13.7 million, a slight increase versus last year. And in the first half year, for the reasons that I've just mentioned, overall cash went down by $53 million to $161.8 million.

A bit of a focus on the Joenja® revenues on the next slide. So that's the breakdown of the geographies in the different periods. So quarterly, the revenue almost tripled to $11.1 million and the Q2 2024 revenue mainly came obviously from the US, but also already from the Early Access and Named Patient Programs outside of the US.

And for the first half year, we increased the Joenja® sales by 44% against second half last year, and you see the different numbers per region. And by the end of Q2, we have 91 patients on therapy in the US, which meant an increase of eight patients in Q2, and in Q1, we had an increase of two patients. And also important to note is that we've had a very stable gross to net discount percentage of 15% versus previous year, i.e., the discounts doesn't play a role in increased sales.

Now looking at the financial guidance on the next slide for 2024. So we reconfirm our revenue guidance of 14-20% sales growth being between $280 million and $295 million for the full year. And obviously, Joenja® will be a significant driver, but we also expect to continue RUCONEST® growth.

And for Joenja®, the revenue assumptions are continued growth in patients on paid therapy, as we have shown so far this year; continued high adherence or compliance rate of 85%; and the US pricing with an annual cost of US$566,000 and continuing GTN discount of around 15%. For the second half of 2024, in terms of OPEX, we are making some adjustments and savings therefore because of the EMA delay. And with that, I would like to hand over back to Sijmen de Vries for the 2024 outlook.

Sijmen de Vries, MD – Chief Executive Officer:
Thank you, Jeroen, and thank you very much. So yes, you have just heard from Jeroen that we are sticking to our total revenue guidance for this year between $280 million and $295 million. Obviously, there were these quarterly fluctuations which are typical.

Then you heard about our patient finding efforts on all fronts for Joenja® and a number of increasing patients that we have identified and especially the expectations that we currently have, on the basis of current initial results from that small trial with regards to the VUS validation efforts, which amount to about 20% of those 1,200 patients that we expect to become available over the coming year, and of course, will drive significantly the growth of Joenja® in the US in '25 and onwards.

The ex-US leniolisib sales, you have heard that there is a great interest. And obviously these Named Patient Programs have a lot of administrative procedures and are of course not always very fast, but we know that there's quite a few patients in the pipeline waiting for clearance to enter into the program all over the world.

The clinical trials, you heard Anurag talk about for the regulatory filings for Japan, the second biggest market in the world. And of course, the pediatric label expansion which will make, again, a bolus of at least 25% of additional patients available for therapy for Joenja®.

You heard about the regulatory approval progress, especially in the United Kingdom, where we expect in the fourth quarter of this year to hear back from the regulators. And of course, that we

are confident that we will be able to speak to EMA again following the submission in January '26 of the last remaining question by EMA.

And the confirmation, of course, that EMA confirmed the clinical benefits and safety of leniolisib makes us very confident as we're looking forward to also getting into the European markets in 2026. Then you heard about the initiation of that Phase II clinical trial for that second indication which Anurag described for PIDs with immune dysregulation and our plans for the third that have been submitted to the regulators and where we're expecting feedback, and hopefully, starting a trial in the not-too-distant future as well. So in other words, we will then start developing two subsequent indications for Joenja®.

And last but not least, the continued focus on potential acquisitions and in-licensing of clinical stage opportunities in rare diseases to further build our portfolio and diversify the company further. And let me tell you, we have a lot of activity going on there, but we are, of course, very precise in terms of what kind of opportunities we actually will bolt-on to our company. So that concludes the presentation and I would like to now go back to the operator and ask and open the floor for questions. Thank you.

Operator: Thank you. As a reminder, to ask a question, you will need to press star one-one on your telephone and wait for your name to be announced. To withdraw your question, please press star one-one again. Please stand by while we compile the Q&A roster. We will now take our first question. Please stand by. And the first question comes from the line of Sushila Hernandez from Van Lanschot Kempen. Please go ahead. Your line is now open.

Sushila Hernandez (Van Lanschot Kempen): Yes, thank you for taking my questions. I have a few, if I may. On leniolisib, so it's a first in APDS that you're about to start the Phase II studies in PIDs with immune dysregulation and now looking into a third indication. Could you share a bit more on what prompts you going after this third indication? And are you expecting that this would expand addressable patient population significantly?

And also on the VUS validation studies, could you elaborate on the 12,000 patients identified in the US? How did you find these patients? And how many of these patients would you expect to be diagnosed with APDS and confer to enter treatment?

And then lastly, with the MHRA decision near, how many patients have you already identified in the UK? And similar to the US, can we expect a large portion of these patients to get on paid therapy in the first half year of the launch? Thank you.

Sijmen de Vries: Thank you, Sushila. I'm happily handing over to Anurag to start answering your questions. Anurag?

Anurag Relan: Hi, Sushila. So with respect to your first question about the Phase II study that we're starting, so that one is in patients who have one of these several genes. So the examples I gave were PTEN, CTLA4 or ALPS-FAS. These are genes that are known to be linked through hyperactive signaling and these patients have an immune deficiency as well as an immune dysregulation or the dysregulation is often times a predominant feature in these patients.

So that's the first indication that we're pursuing outside of APDS. In addition to that, we are looking at another indication, which is, in fact, even larger. So yes, to your question that this will expand the potential population. But we're looking at this third indication, which also has immune dysregulation and is a subset of primary immune deficiency, and it has features again similar to APDS. So I think that's something you can see across these three potential indications is that they all have these features of immune dysregulation or autoimmunity and auto inflammation.

So the second question was about the VUS resolution efforts and how we expect that to evolve? So what we've identified already is 1,200 patients. So what does that mean? That means that these are patients who have had a genetic test usually as a part of a primary immune deficiency panel. And again, these are patients that had genetic testing most of which that we were not involved with.

So they had this genetic testing performed. The result came back with a result that showed either in one of those two genes, this VUS result. And we are aware of this through these databases that we have access to at large genetic testing companies in the US. And we expect that over time, we'll be able to eventually resolve these VUSs.

Now we know, again, historically, looking at other genes, that's about 20% of the VUSs get resolved and converted into disease causing or what's called likely pathogenic or pathogenic. The other data point that we have is that we recently tested 25 of these US patients, and we had what's called functional testing performed in these patients, and we found a similar number, so about 20%, five out of the 25 were then upgraded or reclassified into APDS. So when you start doing some simple math, you see that this could significantly increase the population of APDS patients in the US.

Sijmen de Vries: Thanks, Anurag. And with regards to your question about the UK, Sushila, we have currently 11 patients on early access therapy in the UK. There are 61 patients identified, of which 37 are over 12 years of age. So these are already a quite an interesting population in the UK available. And of course, we expect that once we have the reimbursement, which will take some time and will be somewhere, I suppose, normally in the first half next year, those first patients will go on paid therapy pretty quickly. By that time, we will have also clarified the VUSs and of course in the UK there will also be patients with VUSs. So they will be additionally, potentially coming on to therapy as well.

So that's the sort of numbers for the UK that we currently see. And of course, we continue to seek for patients in the UK, but there's already one per million identified, as you can see from 61 out of a population of roughly 60 million in the UK. I hope that answers your question, Sushila.

Sushila Hernandez: Yes, thank you. And if I may ask one other question. Could you provide an update on your BD efforts? Have you broadened your search? Thank you.

Sijmen de Vries: Yes, we have basically a lot more incoming and also we reached out a lot more because we have now a Chief Business Officer on board since the last quarter of last year. That has led to quite a few interactions, which actually even resulted in some non-binding offers that we issued. But of course, when you then look into due diligence following your non-binding offer, you sometimes find stuff that you were not expecting.

And of course, this is also sometimes possible that the other party does not necessarily, in the end, want to conclude the deal because it takes two to tango, as you know. But yes, there's been a lot of activity and we're virtually all the time assessing an asset under due diligence as we speak. So there's quite a lot of intensity here going on.

Sushila Hernandez: Thank you. That's clear.

Operator: Thank you. We will now take our next question. Please stand by. And the next question comes from the line of Jeff Jones from Oppenheimer. Please go ahead. Your line is now open.

Jeff Jones (Oppenheimer): Great. Congratulations on the quarter, gentlemen. Good morning and thanks for taking the call. Just two from us. You spoke to it to a degree early on, but for RUCONEST® with the anticipated launch of a competing product or competing products in '25 and beyond, what do you see the impact to be, and how are you planning your response?

And then for leniolisib in Europe or in the EU specifically, can you provide any additional detail on the work that needs to be done in completing your definition of regulatory starting materials? And when would you anticipate being able to respond to the CHMP? Sijmen, I think you almost said January of '26. And in that case, how does that impact your potential approval timeline?

Sijmen de Vries: All right, Jeff. Thanks. So let me just first answer your second question about Europe. Yes, we have already initiated that work, and we have a precise timeline, that's why we agreed with the European authorities to actually grant us the extension until January '26. That is when we plan to hand in the response. We precisely do what they want, so that is also very clear. And then in that case, we expect that probably towards the end of the first quarter, there could be an opinion, which we are quite confident because we have received the confirmation of clinical benefit and safety of the product.

And when we have resolved that, we are quite confident about the opinion being positive. So all that said, then it takes two months for the European Commission to confirm that. So in other words, you could expect that we enter the first European market, that's probably Germany in, let's say, the end of the second quarter, beginning of the third quarter of '26. That's basically the timeline at this point in time for entering the European markets.

And then your first question was about the competition for RUCONEST®. Well, the slide I showed about the hereditary angioedema market is there showing that basically RUCONEST® is protein replacement therapy. And Stephen alluded to the consistent response rates on RUCONEST®.

Sebetralstat is a product that works on that bradykinin/kallikrein pathway and has, of course, good results. So it's good news for patients that there is new therapeutic options available. However, we're also aware that sebetralstat was tested in a patient population that is generally responsive to icatibant or FIRAZYR. And it's exactly the difference between the patient population that they tested and the patient population that we are serving, i.e., we serve patients that have failed on icatibant, and therefore, they must use RUCONEST® because they can't get by on a product that only serves the bradykinin/kallikrein pathway.

So in other words, we're pretty confident that this, in the end, will not have a significant impact on RUCONEST® going forward because we serve that unique patient population. Having said that, we are, of course, very aware that in the very beginning of the product being launched, a number of our patients, as we have seen with previous competitive entries will try, of course, whether they can be successful in treating their hereditary angioedema attacks with the oral alternative.

Having said that, you also have to realize that if you take a pill, which is, of course, a much more convenient way, and you actually then see that you have to take a second dose, which is not rarely the case with products like sebetralstat. If I read the clinical trials correctly, then that patient will continue to suffer enormously from that very, very painful hereditary angioedema attack. You just have to realize that, right.

And then if you take, after six hours of suffering, another pill because the symptoms don't necessarily go away or come back, and that is a very different experience than when you are used to RUCONEST®, where you actually place the shot, which is admittedly less convenient because you have to basically place the shot, but you are well-trained and confident. And almost all of our patients do that in the privacy of their own home.

Then you basically have a normal experience where almost immediately the symptoms starts fading away and the attack doesn't come through, and that is basically, if you look at the RUCONEST® response rate, you see nothing about breakthrough attacks or hardly anything about or nothing about second shots being necessary.

So I think you should really carefully consider those elements when you look at an oncoming new competitor. That is, of course, good news for patients who now have to give stinging and painful subcutaneous shots, for instance, icatibant and then the pill, of course, is a very nice alternative. But unfortunately, for our patients, they probably will not have the best of experiences in most of the cases. And we are therefore confident that RUCONEST® will continue to bring them the benefits and the good experience that they have with RUCONEST® over a longer time.

Again, having said that, we are aware, of course that people will start trying this drug. But in the long-term, we believe that RUCONEST® is there to stay. Hence why we showed this slide, where it is absolutely clear that the missing protein C1 esterase inhibitor is the protein that we replace in very good doses, in a very high doses and in the bolus injection RUCONEST® has the protein is immediately there to actually make the attack go away.

Sorry for the long-winded answer, Jeff, but I thought it was necessary to actually explain these ailments here.

Jeff Jones: Greatly appreciate it, Sijmen. And thank you very much for taking the questions.

Sijmen de Vries: Pleasure.

Operator: Thank you. We will now take our next question. Please stand by. And the next question comes from the line of Alistair Campbell from Royal Bank of Canada. Please go ahead. Your line is now open.

Alistair Campbell (Royal Bank of Canada): Thanks, everyone. Thanks for taking the question. I just really wanted to talk a little bit about Joenja®. You've obviously got quite a significant pool of diagnosed patients in the US. Can you talk about the pathway from getting a diagnosed patient to be basically enrolled? What are the key hurdles you have to overcome and then how onerous is that process? Thank you.

Sijmen de Vries: Yeah. So I'll hand over to Stephen here in this case. Steve?

Stephen Toor: Hi, Alistair. Thanks for the question. It is, as you would expect, can be quite convoluted but we try to make that as smooth as possible through our own patient services. So essentially, the first part of the process is obviously the patient coming in. That can take some years sometimes, although we're calling on all those key centers of excellence.

Then once the symptoms are reviewed and the patient is worked up, it's the genetic test. And if they get that positive test, then they immediately can go into our enrolment program, where we'll start to work with their payer on getting them approved. We've seen a mixed picture there with the payers, but what I will say is that our approval rate is at 98%. And that 2% is they're NDC blocks. So they will eventually come on stream. They just take a little longer to actually pull through the entire market access or managed care system.

So that's the kind of simplified version, which is patient comes in, patient gets diagnosed. They work with outpatient services and then land on therapy. What can sometimes slow things down, and that's why you see a bolus in the first part of the launch and then slower. But nevertheless, still growth as we move forward before those bigger inflection points that Anurag referred to with the VUS population and the pediatrics is we're now into those groups where there may be other complications. So perhaps they're on chemotherapy or for whatever reason there are other co-morbidities that are being managed. So they remain within our diagnosed pool. We monitor and we worked already with the doctor, and when we can, the patient, tell them the right time they can move on to therapy. So I think that's the high level overview of what happens with managed care. That's where we are today with the existing pool of patients before we get those next big boluses in '25, '26 and beyond. Is that okay, Alistair? Was there any other questions on that?

Alistair Campbell: Yeah, maybe can I just follow-up on that? So you've got, let's say, pool of 50 diagnosed patients over 12. So you have some of these hurdles to maybe sort of get them on therapy. Do you have any kind of sense of the pace at which you see them sort of come on to therapy ahead of the boluses to come? I'm just trying to get a sense of the tempo we should be thinking about in terms of patient adds before some of those big boluses you've pointed come through.

Stephen Toor: I would love to give you a specific answer on that, but unlike the mass markets I've worked on in the past, these are very low absolute numbers. So for example, we added eight this quarter. I think it was two last quarter, and we have these ones that we're working through today. The good news is we would expect that to keep going. But it just won't be linear. Whereas if we say, cholesterol lowering, you can very easily predict that.

With this, I'll give you an example. There was literally one patient who's going to come in, in July because they needed to finish their school year first. But what I can say is that those over 40 patients are close to 50 right now that we're working through, we know every detail, there is some pretty much know about where they're at and what the tipping point will be, even down to patients whose 12th birthday will be this year. We're ready in front to go and speak to those physicians and say, okay, the 12th birthday is coming up, are they in the right place now, are they the right weight, etc.

But the simpler answer is I couldn't give you a good prediction on the pace of which that all those patients will come in and over what time period. Only that we're working very hard on every single one of them on a very regular basis and in a very detailed way.

Alistair Campbell: That's great. I appreciate the color. Thank you.

Stephen Toor: Thank you.

Operator: Thank you. As a reminder, to ask a question, please press star one-one on your telephone and wait for your name to be announced. To withdraw your question, please press star one-one again. We will now take our next question. Please stand by. And the next question comes from the line of Simon Scholes from First Berlin. Please go ahead. Your line is now open.

Simon Scholes (First Berlin): Yes, hello. Thanks very much for taking my questions. I've got two. The first is on the second indication for leniolisib. I mean I gather that you're expecting the Phase II data early next year. Once you get the Phase II data, I was just wondering what the further timetable might look like as regards to Phase III.

And then the second question is on approval in Canada and Australia. I mean you're now talking about 2025 for both markets. Can you give us a slightly more precise timing for those markets? I mean is it likely to be H1 or H2?

Sijmen de Vries: Yeah. Maybe, first of all, Simon, I think you're a tad optimistic here with regards to when this Phase II study reports. Obviously, it's an open-label study. But I think you should more think about, and Anurag correct me if I'm wrong here, but by the end of next year is probably a more likely thing that we will have insights and can actually formulate how we are talking about with regards to the following Phase III trial.

And secondly, we don't necessarily always give detailed information on regulatory interactions because they can be a little bit unpredictable. But you're right, you have seen that we are anticipating that we have got regulatory action in 2025 from those and not necessarily in 2024.
So basically, yeah, that is correct. I hope I answered those questions.

Simon Scholes: Okay, yeah. That's fine. Thanks very much.

Sijmen de Vries: Okay.

Operator: Thank you. As a reminder, to ask a question, please press star one-one on your telephone and wait for your name to be announced. As there are no further questions, I would now like to hand back to Sijmen de Vries for any closing remarks.

Sijmen de Vries: Thank you very much. And thanks, ladies and ladies and gentlemen, for attending our conference. As you've seen, we've posted some stellar results for both the second quarter and the first half of this year.

We illustrated to you that we are very confident that RUCONEST® will be an important driver for our financials for the coming years to come, given the fact that we serve this very unique patient population despite expected competitive entries. We also showed you that although, indeed, as you heard, the growth for Joenja® is continuing this year, it is not going to be linear from Stephen, but that we have a big bolus of patients expecting to come online in the United States from beginning of next year onwards because of the expected outcomes of the VUS, which will, of course, being an important growth stimulus for Joenja® in '25 and '26.

You also heard that we expect that we get a positive discussion with the Europeans in the first quarter of '26 and that we are working very hard on getting our pediatrics and our Japanese trials worked out and so that we can actually submit to the Japanese authorities and enter the second biggest market in the world and have another at least 25% bolus of additional patients under the age of 12 available for commercialization, both at that point in time, of course, in the US and the rest of the world and the European Union where we expect to be on the market by then.
And then you heard, of course, how we are going to build a pipeline and a product by starting with a Phase II study for PIDs with immune dysregulation as a second indication for Joenja® imminently. And we are, as of course waiting for regulatory feedback for the start of a third indication, also a Phase II trial, that we expect to start in the not-too-distant future.

And last but not least, about the intensifying efforts to in-license or acquire new opportunities so that we can broaden our portfolio in rare diseases and build this global rare disease company.
So thank you very much for being here. And we look forward to updating you on our next occasion at the end of October when we have our third quarter results. Thank you very much.

Operator: This concludes today's conference call. Thank you for participating. You may now disconnect.

[END OF TRANSCRIPT]