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PARTICIPANTS

Sijmen de Vries, MD – Chief Executive Officer

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Thank you very much, Lucy. Good morning, ladies and gentlemen. And before I do that, I would like to point you to this slide showing forward-looking statements. Because I will be making some forward-looking statements of course during this presentation. And the results, actual future results may actually differ from that as you well know.

So what are we doing? We're building this global rare disease biopharma company at Pharming. And we do that you see on the slide here with three pillars. First and foremost, we have our lead product from our own research platform RUCONEST® for the treatment of acute attacks of hereditary angioedema. That is creating significant revenues, of course, very mainly in the United States market and it's still growing after 10 years in the market. You see the results here on the slide after nine months of this year more than US$227 million were sold.

And you see on a quarterly basis the product keeps growing. It means there's more physicians prescribing the product and there are more patients using the product all the time. It means also that, and I'll come to a little bit later, RUCONEST® has a very special place in this market, because it is actually providing the missing protein C1 esterase inhibitor that's causing this disease.

The second pillar you see there is the recent launch last year in April 2023 of our new product Joenja®, which is a product we in-licensed from Novartis for a rare disease, an ultra-rare disease and primary immune deficiency called APDS, activated phosphoinositide 3-kinase delta syndrome. And you see that we have been able to get significant revenues out of that in this year as well. You see almost US$32 million in the first three quarters of this year.

It's a new disease that was recently discovered. So we have a lot of focus on patient finding. I'll talk a little bit about that later. And we are building out our commercial presence whereas RUCONEST® is virtually only U.S. marketed. We're building out a big global presence with Joenja®. And that's why Joenja® is a very important pillar to build this global operating rare disease company.

And on the right-hand side you see the third pillar that is the further development of the pipeline. First and foremost, some new indications for Joenja®. We started a Phase II trial in a primary immune deficiency. I'll come to that later. And we have a BD focus on getting clinical stage products to actually bring into our commercial infrastructure and leverage our capability of developing and bringing to the market new products. And we're looking for rare disease opportunities in primarily immunology, hematology, respiratory and gastroenterology. So we're really on the hunt for new assets to build further into our infrastructure.

And here's a visual depiction of the pipeline. You see there are two products in the market, RUCONEST® and Joenja®, and you see there also depicted is the geographic expansion of leniolisib, into the markets further afield from the United States and the United Kingdom. And of course, the second indication in Phase II for the primary immune deficiency.

So let's look at the first pillar now in some more detail at RUCONEST®. So we're talking about hereditary angioedema, and hereditary angioedema, as I said before, is caused by the fact that these patients have insufficient C1 esterase inhibitor or not functioning C1 esterase inhibitor. And that causes the attacks of the swellings. And there's three main pathways involved here, as you can see on this chart. And you see that C1 esterase inhibitor, you see everywhere these red symbols work on all those three pathways. And I think that's important to note, albeit that the central pathway that you see there, the bradykinin/kallikrein axis, is a very important one for the symptomatology of treating the attacks or for prophylactic treatments.

But it means that, if you want to cover this disease in its entirety, you need to be able to actually work on all those three axes. And that's exactly the point with the lots of competitive products now on the market. And that's good news for the patients because it means that there is a lot of prophylactic therapies available. The majority of U.S. patients are on prophylactic therapies. But all these prophylactic therapies are, so-called, targeted therapies and they mainly address that central axis, the bradykinin/kallikrein pathway. That means that a lot of patients benefit actually from prophylactic treatments, but it also means that there's always breakthrough attacks.

So it means that all the U.S. patients need to have rescue therapy at hand, when they are under prophylaxis. And it means also that patients that are using a targeted therapy for acute therapy also suffer from redosing or from slow resolve of the attacks. And that means that RUCONEST® takes a very special place, because RUCONEST® covers all these three axes, and RUCONEST® is therefore mainly used by patients who have a very high frequency of attacks.

And there's a special group there that is called the so-called, normal C1 or type 3 patients, a newly discovered group of hereditary angioedema patients that are very, very frequently attacking and have very severe attacks generally speaking. And those are not well responding to all the targeted therapies. And that's the place where actually RUCONEST® serves these patients. It's a small group of patients relative to the total market. But they are very high users, hence why we have a good market share here in terms of dollars of the market.

And you see there that these patients, for instance, the new oral products that come on the market, one of the new oral products that is coming to the market is actually tested in the patient population that is responsive to that icatibant/Firazyr, which is the main product working on the central pathway. And that product has an exclusion criterion for patients not responding to that icatibant. And that's exactly where RUCONEST® is served. So RUCONEST® serves those patients that are not responding to icatibant, whereas these kinds of therapies are serving patients that are responding to icatibant. Hence, we think that RUCONEST® will continue to have its place in the market in this special segment of patients, because those patients really need a product like RUCONEST® that works on all axes.

And basically here you see a slide that summarizes this. We're the only protein replacement therapy here on the market and continue to grow the product. And patients are feeling very, very comfortable with actually dosing themselves with the slow IV injection that RUCONEST® is. So it's not a product that works like convenient like a pill, but it's a product that you rely on for your efficacy. And we are very, very confident that RUCONEST® will continue to have its place in the market, and will serve those patients that are really needing the efficacy that RUCONEST® has.

So let's switch to Joenja®, leniolisib. As I said before, we in licensed this product from Novartis back in 2019 when it was in the pivotal trial. It's a PI3 kinase delta inhibitor and it actually brings back the PI3 kinase delta enzyme, which is hyperactive in the disease called APDS, to a normal level. So it doesn't stop the PI3 kinase delta as you would be familiar with in oncology. But it actually modulates it back to a normal level. Hence why the immune system that is actually being dysfunctional in APDS can basically be coming back to a normal balance and create immune cells that are actually functioning. Because that is the issue.

APDS patients don't make functioning immune cells and the immune system is overstimulated. So they have a lot of overstimulated lymphoid tissue that often leads to lymphoma. And that's why this disease is a disease with a significant excess mortality. In fact, we were seeing the first publications coming at this point in time. And it seems to be pointing in the direction of 30% mortality by the age of 30 in excess of normal mortality caused mainly by lymphomas as one of the ultimate clinical symptoms of this disease.

It's the first PI3 kinase delta inhibitor that was actually approved in a double-blind placebo-controlled trial. And it has a very benign safety profile. We have in fact patients that have been using Joenja® for more than eight years now and continue to be on the drug and continue to have increasing benefits and an increasingly normal immune system. And of course, it's a new disease, so we don't know much about further long-term effects for the disease. The numbers are very small still, but we keep following this, of course, and we'll be reporting into the future about the long-term beneficial effects for the disease. But so far the open-label extension points to the fact that the longer you use Joenja®, the better, the symptoms actually disappear.

And it has a significant potential. It's an ultra-rare disease. The literature says about 1.5 patients per million population. So we calculate with about 500 patients in the United States. We already found approximately half of those. Of those 25% to 30% are pediatric patients under the age of 12. And the label currently is 12 and older, so they're not yet reachable. But of those that are directly eligible, something like 150 or 160 patients. We reported already 93 of these patients on therapy by the end of the third quarter. And we continue to find those patients.

And there is an important aspect here, because it's a new disease and I will come to that a little bit later. For every new patient we find, and we have an extensive genetic testing program, we find about four or five patients with a so-called Variant of Uncertain Significance and that represents a very significant pool for expansion further and then actually further clarifying the disease. Globally, where healthcare systems are often more centralized than in the United States. For instance, in a market like France, we found more patients than on a per population basis.

For instance, in France we have already found 1.1 per million patients, because it's well centralized healthcare system, countries like here in the United Kingdom, it's also a little bit better in terms of the centralized healthcare system and also more relatively more of these APDS patients have been identified. But it is still a lot of work to do to actually find those patients, of course all around the world. But you see, we're well on our way. We found almost 900 of those probably 2,400 patients that we expect in the markets where we are planning to commercialize. And of course, that is excluding the Variants of Uncertain Significance here as well.

And last but not least, you already see that 164 patients were reported on treatment in either early access programs, clinical studies, or on the named patient basis, because that is already happening outside of the United States. There is some of these early access programs and named patient programs where our patients are being treated. And that is partly paid and partly unpaid early access programs.

And then you see on the right-hand side the new indication, as I was alluding to, that's about 7 per million. And that is actually a primary immune deficiency with immune dysregulation as well, like APDS, same type of symptom complex and although it is now related to well-known mutations. And I will come a little bit later about to talk about that in more detail.

Let's first have a look at our patient finding strategies and activities that we have in the market. Of course, there's a lot of medical education ongoing. So we attend a lot of congresses, mainly immunology congresses, but also other congresses, because these patients can be hiding with pulmonologists because they have recurring severe pneumonias, for instance, and then very quickly develop a lymphoma, in which case there's also patients to be found sometimes with a hematologist, but also they can have unexplained gastroenterology problems where basically their gastric tract is blocked by enormous lymphoid tissue and have unexplained GI problems and therefore they can be hiding with a gastroenterologist as well.

So we work really on the tertiary centers to find those patients. And one of the things we do in the United States to find those patients is offer free genetic testing. And that is how we have found quite a few patients already. Like I said, for every patient we identify, we find about four or five of those VUS patients that form a significant pool for further patient identification.

Then we of course, go into family testing. We have found mainly patient zero's, so to say, and because it's a dominant autosomal mutation, by definition, there will be family members that will be affected. And we keep finding that as well. So we go into systematic family testing as well. And that's not an easy thing to do in a big country like the United States. But we have started that in all earnest and the first patients have been identified and actually in that fact.

And then we come to a huge pool of potential new patients, as called the VUSs. And we have found about 1,200 VUS patients. And we have a number of initiatives going on to actually clarify the full extent of the disease i.e., which of those VUS patients represents APDS patients and which do not. And that is a very important aspect, because you only want to treat people with patients with a hyperactive PI3K delta pathway with Joenja® and not anybody else.

Now, we're doing a couple of approaches here. First of all, we work on individual batches of patients, but the biggest effort that we currently have is so-called MAVE. It's multiplexed assay of variant effect. It's an in-silico activity that's ongoing and that's just about to be completed by the end of this year, which will clarify the entire relevant gene and which will clarify all the mutations that are pathogenic.

And the expectation is, normally speaking, that. And we already got some early numbers from small batches of patients that we have tested that about 20% of those patients are to be expected to be positive for APDS. That means that we will be looking at probably a doubling of the patient pool in the beginning of next year, and that will be the next growth engine for Joenja®.

So when you look towards Joenja®, you see that we have now reached the majority of the patients that are actually eligible. Going forward, in 2026, we expect in the VUS pool to actually double the patients in the United States. So we can actually recruit patients out of that new pool. And then subsequently, of course, the next expansion is the pediatric studies that will come online. And you see that here depicted in this slide, as well as the geographic expansion that we are working on.

So that means that in 2025 is the VUSs, and 2026, it's also the VUSs, the pediatric studies and the geographic expansion will start. You see, in Europe, we have the CHMP that we expect to bring the last remaining question to in January 2026. And therefore, it means that we expect to get a positive opinion from the CHMP because the positive clinical benefit and safety has already been concluded. We have one outstanding CMC request that means that we will expect to actually enter the first European markets, Germany, by mid-2026. For the UK, this country we were already approved and expect to be able to get into the UK market in the second quarter of next year.

Japan is an important aspect in the geographic expansion. We also expect to bring the file into Japan in the not-too-distant future and also look to come into the Japanese market in 2026. And then the periodic studies, of course, as I was already alluding to one of them, the main one, the four- to 11-year-olds, is almost finished and will be reporting soon. And therefore we can bring the file to the FDA and to the EMA as well. And therefore we expect there, like I said earlier before, in 2026 we will also be able to serve those patients under 12. And of course it's a genetic disease, so the earlier you treat them, the better it is of course before permanent organ damage is being done by the disease.

And then of course, we started the Phase II for the PID indication, the new indication, and that is basically the same symptom complex, as I was already alluding to earlier. As in APDS, it's just a bigger group of patients and they are suffering from well known, they have well known mutations like CTLA4, ALPS-FAS and PTEN for instance, to mention three of those. So they're well identified and there's no treatment for these patients as well. They also suffer from a hyperactive PI3 kinase-delta pathway.

That's why we decided together with NIH, who were also important in developing APDS and the experts of APDS, to start this Phase II dose finding study. The first patient in the meanwhile has been dosed. It's a 12-patient study where we look actually for safety and we look for early signs of efficacy. So if we fast forward by 12 months, we can have the first indications of efficacy in this

indication. We will have the information that we need to actually design the Phase III trial and we can work on further of expanding the Joenja® franchise.

And then you already saw it in the previous slide as well on the bottom there. We have also defined another PID that is even bigger than this and we are currently in the final stage of discussing it with the regulatory authorities about what the Phase II trial of that new indication looks like. And we will, of course, update you as and when we have more details on that indication and on the Phase II trial that is designed for that new indication.

So in other words, Joenja® is an important growth driver, has been an important growth driver for the company and continues to be an important growth driver for the company. And you see that depicted here on the financials. The growth of RUCONEST® and Joenja® together, if you look on a quarter-by-quarter basis made the company grow by 12%. You saw that the gross profit increased as well versus last year third quarter and that operating expenses increased. But you also noticed here that we delivered a profitable third quarter. If you look at the gross profit compared to the operating expenses, you see that we had a small profit of US$4.1 million, which is an improvement over last year.

So we also have been investing a lot of money into the launch of Joenja® and we continue to do that of course. But the growth of the sales of the two products together means that the company is turning into the direction of profitability again. And you see we have a continued cash, a nice war chest to do small acquisitions and/or in licensing without having to go to the market to do so.

And here if you look at the nine months versus the nine months last year, you see the same growth and actually it's even 25% here compared to last year, the first nine months driven, of course, by continued strong growth of RUCONEST® and a growth of Joenja®. And there you see that we're also still bringing in a small loss, but the numbers are improving and we expect the company to turn into profitability in the not-too-distant future.

And that's the financial guidance that you see on this slide here. We are expecting to bring in, and we said at the beginning of the year, continue to be guiding on that. We are bringing in revenues between US$280 million and US$295 million. And we see that, we expect Joenja® to continue to grow because most of these patients and the vast majority of patients in fact stay on therapy. We hardly have any patients leaving the therapy.

As I was already earlier alluding to we have up to eight years patients that are using Joenja®, and very importantly the growth of the operating expenses associated with the launch of Joenja® and the preparations for the launch of Joenja® and the clinical programs that we have, has been flattening out, and we expect no big growth in operating expenses going forward either.

So, if we look at the outlook that we gave for 2024 that is unchanged. You see the revenue expectations here between US$280 million and US$295 million, the continuation of those efforts of finding those APDS patients. I hope you understand that it is very important to keep a look at the VUS results that will be coming in the not-too-distant future, because that represents a potential doubling of the patient population of Joenja®.

We see also, and you see that also when we have our detailed finance reports that we're getting increasing revenues outside of the U.S. from those named patient programs and those paid early access programs that are building a nice pool of patients outside of the United States. We are working on finalizing the pediatric trials, of course, because that is another 25% to 30% of patients that becomes directly available. And of course, working on getting access to the second biggest pharmaceutical market in the world in Japan. And we will be reporting on that. We also have the regulatory activities ongoing in the European Union, Canada and Australia. And very important to start that potentially huge inflection point for the company going forward, that Phase II in the new primary immune deficiency.

And then last but not least, we can handle more products. So our business development group is very, very busy and we have a lot of continuing discussions ongoing, sometimes in early phases, but almost always there is something that we are taking a very close look at, and we hope to bring a new asset, either in-licensed or acquired into the company to further expand and accelerate the growth and leverage our commercialization infrastructure even more.

So thank you very much for that. I see, I have 30 seconds left. I'm sorry, 30 seconds left for questions. So if you may have any questions. There's only 25 seconds now. Thank you.

[END OF TRANSCRIPT]