Pharming Group N.V.
24th Annual Needham Virtual Healthcare Conference 2025 - Presentation

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PARTICIPANTS
Fabrice Chouraqui – Chief Executive Officer
Anurag Relan, MD – Chief Medical Officer

John Gionco – Analyst (Needham & Company):
Good morning, everyone and welcome back to the 24th Annual Needham Healthcare Conference. My name is John Gionco. And I'm a Member of the Biopharma Research team here at Needham.

And so for our next session, we have Pharming Group for a presentation and Q&A. And it's my pleasure to introduce the company's President and CEO, Fabrice Chouraqui, as well as the company's CMO, Anurag Relan.

So before I turn it over for the presentation, I want to quickly inform our audience that if you'd like to submit questions, you may do so via the Q&A text box on the webcast player. And we'll address them after the presentation.

With that, Fabrice and Anurag, it's a privilege to have you here today and thank you very much for joining me.

Fabrice Chouraqui – Chief Executive Officer:
Thank you very much, John. And thank you so much for having us as part of this 24th Virtual Healthcare Conference. So, I'm Fabrice Chouraqui. I'm the new CEO of Pharming and I'll be joined on this call by Anurag Relan, who is our Chief Medical Officer. In this call, we'll be making forward-looking statements that are based upon our current insights and our plan. And as you know well, this may differ from future results.

I must say that I'm very excited to be joining Pharming. Over the years, I've developed an experience across the business spectrum from pre-clinical research to clinical development and then commercial leadership, business development and capital formation. And in light of this experience, I'm really impressed with the development of Pharming over the past decade and also the very significant growth prospect.

RUCONEST® has become one of the cornerstone on-demand treatments for HAE and Joenja® is already approved and launched in the U.S. for the treatment of APDS, with a significant number of patients already on treatment and it is due to be launched in other countries. And with the recent completion of the acquisition of Abliva, this is another steppingstone actually in the development of the company and we'll talk about this.

So at Pharming, we have a very clear vision. Our ambition is to develop a leading global rare disease company with a diverse portfolio and presence in large markets that leverage a proven and efficient clinical development, supply chain and commercial infrastructure. Our 2024 results are a good illustration of the solid foundation that we've built to realize that vision.

As you may have seen, full year 2024 revenues increased by 21% to US$297 million with operating profits and positive operating cash flow in the last two quarters of 2024. RUCONEST® grew by 11% in 2024 to US$252 million and 9% in the last quarter of the year, driven by a continued increase of the new patient enrollment and the sustained expansion of our prescriber base, which is a testimony, in my opinion of RUCONEST®'s unique profile and valuable position for a specific population of patients.

Joenja® revenue increased by 147% to US$45 million. We've already identified more than 240 APDS patients in the U.S. and close to 900 worldwide. At the end of 2024, we had 96 patients on paid therapy in the U.S. and 188 on treatment globally. And as you will see in a few minutes, the drug is still in its very early stage of its life cycle with many well identified growth acceleration opportunities in the near-term. With the VUSs, with the pediatric label extension and also with the launch of the drug in key markets outside the U.S., starting with the UK this quarter.

Our pipeline continues to expand and it really provides significant growth prospect beyond RUCONEST® in HAE and beyond Joenja® in APDS. I believe that we now have two assets with US$1 billion sales potential. Joenja® as a whole if you consider the entire life cycle and KL1333, which was part of our acquisition of Abliva.

For Joenja®, we have two ongoing studies in PIDs with immune regulation and CVID. These two indications are much larger prevalence than APDS and Anurag actually will elaborate on those in a few minutes.

KL1333, which as I said is coming from the recently completed acquisition of Abliva, is also a significant growth potential asset currently in a registrational trial, a Phase II trial for primary mitochondrial disease which is a well characterized genetic disorder which affect more than 30,000 patients in the U.S. and in the top four markets in Europe. So before I let Anurag tell you about these very significant pipeline opportunities, what I'd like to do is to elaborate on the near-term growth opportunities that will continue to fuel our momentum.

Let me start with RUCONEST® in HAE. RUCONEST® has established itself by now as one of the cornerstone on-demand treatments for HAE attacks. As you probably know, HAE is caused by the deficiency or the dysfunction of the C1-esterase protein which is a protease inhibitor involved in the regulation of the inflammation and immune function.

As you can see on the slide, there are three inflammatory cascades involved in the development of an HAE attack. And the C1-esterase inhibitor represented here by the red marker, blocks many enzymes across all of the three pathways. And that's very unique. Other on-demand treatments are effective by blocking a single point in these cascades. And patients who don't respond to these targeted therapies can often benefit from RUCONEST® since it works really comprehensively across all these systems, which makes actually the value proposition very distinctive.

And that mechanism of action actually explains the unique efficacy profile of RUCONEST® regardless of the type of HAE. I mean, data shows that 97% of attacks are addressed in a single dose of RUCONEST® and 93% of patients achieve a sustained response for at least three days after an injection of RUCONEST®, which is well beyond what is often possible with other treatments. And as you see on these pictures, severe HAE attacks are highly debilitating when they occur on external tissue and they are even life threatening when they occur in internal organs. And so RUCONEST® rapid onset of action and fast onset of relief give these moderate-to-severe patients with the reliability that they need to better plan and control their lives.

Let me now elaborate a bit on Joenja® which we launch in the U.S., now two years ago. So APDS, it's a rare primary immunodeficiency, which is caused by a genetic defect that leads to PI3Kδ hyperactivation. And this results in the misfunctioning of the immune system and it is characterized by frequent and severe infections as well as a wide array of immune dysregulation. APDS is a progressive disease that leads to early mortality and about 25% of patients die before the age of 30.

So Joenja® is the only approved disease modifying treatment for APDS. It addresses the root cause of the disease by normalizing the hyperactive PI3Kδ pathway, which allows to address both the immune deficiency and the immune dysregulation. Joenja® is now approved in the U.S. as I said, but also in Israel, in the UK, and in Australia. There's ongoing regulatory review in the EU and in Canada and we are about to file in Japan.

I think that Joenja® is a good example of an asset with a clear stream of growth catalysts in the near and long-term. In the U.S. after an initial bolus of patients, we are now working to identify and enroll new patients before we capture two well defined opportunities that will be coming in the next 12 months. First, the reclassification of patients with Variants of Uncertain Significance so called VUS, and second, the label expansion to the pediatric population. So let me walk you through these two opportunities that will fuel the product growth in the short-term.

So let me start with the VUS. The challenge in diagnosing APDS occurs when the result of a genetic test shows a VUS. And this happens because the variant is novel and there is in a sense, not enough information to find out if the DNA sequence on the affected gene is disease causing or not. In fact, there are already over 1,200 patients in the U.S. alone who have received an inconclusive test, so a VUS test result.

And so because of that large number, we have been supporting a project to help gain additional insights in these VUSs. And the study, which will be published soon in a peer review journal has shown that a proportion of these variants lead to PI3Kδ hyperactivity and as such should be reclassified as APDS. So the next step in the process is for the genetic testing labs to review the data that will be published, reclassify those patients and inform their doctors. And these efforts will ultimately lead to the identification of many new APDS patients in the second part of the year.

Now, beyond this VUS opportunity, we are actually about to file for an extension of our label to the pediatric population, where we have an active clinical program with recent data to support the regulatory filing. As you probably know, APDS symptoms begin at a very young age and more than

25% of the patients that we have already found are below the age of 12. And since the disease is progressive, it is obviously important to be able to treat before.

So last December, we were very excited to report the top line results from the first clinical study with APDS for children age 4 to 11. And the study demonstrated benefits across the two co-primary endpoints, which was consistent, with what we had observed in the adult APDS population. And this is actually very significant finding for clinicians. And the data will actually be presented at CIS, which will occur next month, in May. So we are now working on the regulatory filing to the FDA, which we expect to complete in the second part of the year. And so this new indication should result in another expansion of the addressable population and should come in the first half of 2026.

So, as you can see, we have really two well defined growth catalysts in the near-term with the VUS and the pediatric expansion. In addition to these, we'll be launching Joenja® in seven key markets outside the U.S., meeting with the UK this year, followed by Australia, the top key EU countries, Germany, France, Italy and Spain, and then Japan and Canada. The drug is accessible through access programs across the world. And we may also decide to work with partners in some regions to ensure that we maximize the sales potential in a cost-effective fashion. And all of this will fuel significant growth in the near-term.

In the long-term, Joenja® has the opportunity to become Pharming's first US$1 billion asset with two new indications with much larger prevalence.

And so now I'll hand over to Anurag who will tell you more about the rational for these two new indications, which we expect will be very significant growth opportunities. Anurag?

Anurag Relan, MD – Chief Medical Officer:
Thanks, Fabrice. So in addition to these near-term opportunities in APDS that Fabrice has talked about, we are developing leniolisib for primary immune deficiencies. And actually if we go to the next slide, there we go. So we're developing leniolisib for primary immune deficiencies with immune dysregulation. What you see in the diagram on the right is a subset of all primary immune deficiencies.

APDS in fact is one such example of a primary immune deficiency with immune dysregulation. And we have now started two more programs in this area. And the rationale to study leniolisib here is based on the critical role that PI3Kδ plays in lymphocyte regulation. And as you can imagine, because it plays such a critical role, the patients that are being studied here actually have a similar clinical manifestation to APDS patients and likewise a large unmet clinical need.

And therefore, the strategy is quite straightforward and is to modulate PI3Kδ activity to address the clinical manifestations of immune dysregulation, specifically the lymphoproliferation and the autoimmune manifestations that these patients have. And as I said, we have two programs now going on. The first is a group of patients who are genetically defined and they have symptoms, again, similar to APDS patients and these genes are linked to PI3K signaling. This is a study that we started back in October of last year. This is a study including 12 patients who will be treated for 20 weeks in a dose finding manner. We have received FDA fast track designation for the study and this is being conducted at the NIH.

In addition to that, just in the last couple of months we started an additional program in patients what's known as common variable immune deficiency. These patients also can have immune dysregulation manifestations and this represents a much larger group of patients. This study was started in February and this will be a multi-center study that I'll talk a little bit more about in the next slide, but this will include 20 patients who are treated for 24 weeks.

And here you can see some details about this study. Again, it's a study going on in the U.S., the UK, as well as in countries in Europe. These are patients who have a diagnosis of common variable immune deficiency, as well as manifestations of immune dysregulation. It's a safety and tolerability study, and it's built along the same lines as the APDS program as well as the other study I mentioned, where patients will be starting at a low dose and escalated from 10 mg to 30 mg and eventually to 70 mg. These will be patients who are treated for a total of 20 weeks. And the goal here, as with the other Phase II study, is to inform the dose and design for a Phase III program.

But we're quite excited about both of these programs because there's a significant unmet need. And again, the biology here is quite clear in terms of the role of PI3Kδ in terms of manifesting these clinical features of immune dysregulation.

If we go to the next slide. We can talk a little bit about our third program in our portfolio, which was just acquired via the completion of the Abliva acquisition. And this follows the strategy that you heard Fabrice outline, namely to develop a global rare disease company with a diversified portfolio. And the program is with a molecule called KL1333. It's being developed in a condition called primary mitochondrial diseases. These are rare disorders where there's impaired mitochondrial energy production. And because these patients have dysfunctional mitochondria, they have features that are actually quite consistent with that, including severe fatigue, muscle weakness, and unfortunately, reduced life expectancy. And because of all these same features, they also have a significant impairment on their quality of life.

KL1333 is positioned to become a unique molecule in the treatment of mitochondrial disease. There's a novel mechanism of action that specifically addresses the underlying disorder by increasing NAD+ levels. And there's a number of patients who are already diagnosed with the condition. And we have a pivotal study ongoing with a positive interim analysis that I'll review for you in the next slide.

Patient recruitment for the second wave of this pivotal study is to begin shortly. And we anticipate readout from the pivotal study in 2027, with potential FDA approval by the end of the following year. And again, this is a rare disease with a significant unmet need. No approved therapies. It builds on our strategy and portfolio where we have expertise in developing and commercializing rare disease drugs. And we're able to also leverage the concentrated centers of excellence and strong advocacy groups that exist for these mitochondrial patients.

Now on the next slide we can see some details of the clinical program. And this is again a pivotal study that's ongoing. The first part of the study or WAVE 1 was fully enrolled and this included 40 patients across six countries. And there was an interim analysis conducted at the 24-week time point that concluded in the third quarter of last year. And on the right, you can see some of the details of that interim analysis. Specifically, there was a positive futility analysis achieved with both

endpoints having passed futility. And what that means is that there were differences favoring the active arm versus placebo for both endpoints, such that if the trends continue, we expect a successful result at the completion of the study.

The Data Safety Monitoring Board also recommended continuing the study, without any changes to the study design, worked into the dosing regimen. They confirmed that with 180 patients we should be able to achieve the desired level of power. And the goal now is to begin WAVE 2 as quickly as possible here shortly with 180 patients total who will be treated for 48 weeks. And we expect again the readout from WAVE 2 or the entire study to occur in 2027.

And with that I'll hand it back over to Fabrice to wrap things up.

Fabrice Chouraqui – Chief Executive Officer:
Thank you, Anurag. So I think you've seen over the past 20 minutes that we build, I think, a solid platform for sustainable growth and value creation with the aim to develop a leading rare disease company. If you consider our priorities in the near term, we have three priorities. I mean the first one is about growing our commercial portfolio. So, it's really to maintain the momentum that we are seeing on RUCONEST® thanks to its specific positioning within the on-demand treatment market.

It is to continue to grow Joenja®, identify and enroll new patient on APDS, fully capture the opportunities provided by the U.S. and the expansion to the pediatric population and then expand beyond the U.S. in a targeted way starting with the UK this year. Now, we continue to invest in our long-term growth with a high value pipeline as you've seen.

I think we have two potential very interesting new indications for Joenja®, which clearly could propel the drug to a whole new level. And the acquisition of Abliva, which is in a pivotal stage which we have seen already actually some results from an interim study that brings actually another asset we see with revenue potential.

And last but not least, is obviously to ensure that we build a highly efficient organization where we do best, what matters most and where we create actually a scalable infrastructure to prepare for future portfolio development.

We have communicated revenue guidance of US$315 million to US$335 million that illustrate actually this momentum. And obviously we look forward to updating you on our progress as we move along the year.

So let me pause for now, and I'll hand over back to you, John, and would be very happy to take any questions.

John Gionco – Analyst (Needham & Company):
Great. Well, as Fabrice and Anurag, thank you very much for that great overview of Pharming. And again, just as a reminder for the audience, if anyone has any questions at any time, you may log them via the webcast player and I'll be sure to address them.

But maybe just to get things started, Fabrice, you've obviously been in the CEO seat here for a short time. Just wanted to get a sense how the transition's kind of been going since you've come aboard? And, I know you kind of highlighted at the end there, some of your priorities for the company moving forward. But from a prioritization standpoint, maybe in 2025 specifically, just wanted to see, what you think, it will be of most focus from a commercial standpoint, as well as R&D standpoint?

Fabrice Chouraqui – Chief Executive Officer:
Cool. No. Thank you, John. Obviously, very excited to be joining Pharming. It's been now a bit more than a month. As I said, very impressed with what the company has achieved in the past decade. I don't think there are many biotech companies who've been able to develop a drug end to end and successfully commercialize it and then launch successfully a second asset and then complete an acquisition with a very promising asset and which is now actually as of today two-potential-billion-dollar opportunities in our pipeline.

So this is very, very exciting for the future. In terms of priorities, I think that it is very clear. I mean, short-term, is very much to continue to the momentum that we see with RUCONEST®. The drug has been in the market for ten years. It is well entrenched in a subcategory of patients in the well-defined on-demand treatment market. And we've seen last year, you've seen the numbers that actually the drug continued to grow very steadily with more doctor's quarter-on-quarter prescribing the drug and more patients on the drug.

So a very healthy situation, and I don't see this changing, despite new entrants. I've worked in many categories, highly competitive categories. But clearly and when you have a drug like RUCONEST®, which has a very unique value proposition for a subcategory of patients, it tends actually to benefit from the market growth.

When it comes to Joenja®, as I said, we have two very clear opportunities in the short-term. The VUS and then the pediatric expansion. And that will fuel the drug or the growth of the drug, which is still today in a very early stage of its life cycle. More longer term from a pipeline perspective, we have really two important opportunities with Joenja®, with the new indications for PIDs with immune dysregulation and with Abliva.

Here we have a program for mtDNA mitochondrial disease, which clearly for which you have real unmet medical needs and for a significant number of patients as a rare disease. As I said, more than 30,000 just in the U.S. and in the top four EU countries.

So that's really the commercial priorities, and we are in full execution mode. And obviously, the goal is to continue to grow organic growth, but also inorganic. And we'll obviously continue to look for value accretive opportunities, although in the short-term the integration of Abliva is the priority.

John Gionco – Analyst (Needham & Company):
Right. So, and I guess just to confirm that then, BD has been an aspect of Pharming in the past, and obviously, I believe the Abliva acquisition in December is an example of that. So is it fair to say that then you should expect a bit of a lag, in terms of potential BD expansion, in the next year or two?

Fabrice Chouraqui – Chief Executive Officer:

I mean, again, we'll be opportunistic. But I think, when you want to grow, you need to make sure that you can build an efficient and scalable organization. And so, yes, to your point, I think now we have some homework to do. We have some very well identified, growth opportunity in the short-term. Let's realize them. We have some work to do with the integration of Abliva and, the ongoing, lifecycle management of Joenja®, but we will continue to identify opportunities, and it's all about actually long-term value creation.

John Gionco – Analyst (Needham & Company):
Right. And so you mentioned about being a scalable commercial company. For each of these indications, do you have an individual salesforce, or are there synergies between your products and the people who are marketing them?

Fabrice Chouraqui – Chief Executive Officer:
And nowadays I would say, I mean, when you think about the commercial organization, it's more than salesforce. And actually the bulk of resources often are outside purely the salesforce. And here, this is where you can leverage, established capabilities. So you take market access, which is paramount, and together with, patient services, to ensure pull through and any dropouts. I mean, these are capabilities that the company has built over the years. So as we expand our portfolio, the goal is, again, to leverage those capabilities and minimize new FTE expansion.

John Gionco – Analyst (Needham & Company):
Right. And so now moving on to RUCONEST®. You mentioned that the HAE market is highly competitive. And you kind of touched on some of the differentiating characteristics of RUCONEST®, that might insulate it from new products coming on the market, especially with the coming up of orals, for HAE both in the on-demand and prophylactic segments. Just curious, if you could provide a little bit more color on, what you think about them coming in and how RUCONEST® could benefit from that?

Fabrice Chouraqui – Chief Executive Officer:
Well, thank you for the question. I actually I've already met a number of prescribers being on in the field. And I was very impressed with the feedback I got from doctors. I mean, some telling me how much RUCONEST® is transformative for the life of their patients. And clearly, can see that the drug is being used for really moderate to severe patients who have more severe attacks, more frequent attacks, patients that require reliable products, reliable and high efficacy treatment.

And so, yes, I mean, I think the drug has positioned itself given its unique profile. I think it's good to see more treatments coming that gives more choice actually to clinicians and to patients. But when it comes to reliability and high efficacy, I believe that RUCONEST® is well entrenched and in a sense could actually, as I said earlier, could gain actually from new entrants. Because when you have new entrants then doctors pay more attention on whether their patients attacks are controlled or not and they are more likely actually to switch them to a high efficacy drug, whereas when they are very used to a treatment, they are not necessarily paying the same attention.

So, I see even opportunities for RUCONEST® in the years to come and I see the drug continue to maintain its momentum.

John Gionco – Analyst (Needham & Company):

Yes, I mean obviously last year you showed double-digit growth in revenues for RUCONEST®, so obviously patients are seeing the benefit from it as well as physicians and definitely looking forward to see it grow in the coming years.

Fabrice Chouraqui – Chief Executive Officer:
If you take actually, if I may actually, you take another disease area like MS. I mean MS, 10 years ago was an injectable market. Orals came, I mean subcutaneous treatments remain actually used very significantly, orals created their own space. I actually launched one of these very successful orals and then a drug like Tysabri, which has a very specific profile actually kept being used significantly because of its different profile, because an IV drug. And so, and I've seen that in other categories as well where actually, new entrants allow to grow the markets, but at the end of the day it's very much about your positioning and the value prop, your valuable position for a specific segment of the patient population.

John Gionco – Analyst (Needham & Company):
Right. And especially in the HAE market, when patients go on a particular product and they like it, there is tendencies to stay on that. And the familial aspect of the disease as well definitely plays a role in that. So moving on to Joenja®, I believe you mentioned you guys have identified about 1,200 patients, with the efficiencies that you're trying to gain in patient identification and the expansion into the pediatric setting. Do you guys have a number in mind in terms of how large you can grow that segment?

Fabrice Chouraqui – Chief Executive Officer:
We haven't shared a number. I mean what we are sharing every quarter is the number of patients on paid treatments in the U.S. will continue to do so. As I said, after an initial bolus of patients, we are now working to identified and enroll new patients months after months. I believe that because of the VUS, we'll see an acceleration of that with a number of VUS patients being reclassified.

And then next year we'll have actually the pediatric label expansion that will kick in. So well, staggered opportunities on top of the continued increase of enrollment of normal APDS patients and obviously also the geographic expansion. So no number to share at the present time, but clearly an acceleration of patient enrollment to be seen in the second part of the year.

John Gionco – Analyst (Needham & Company):
Great. Yes. Well, we're definitely looking forward to getting those updates then. And maybe if you could just from a pricing and payor coverage perspective, what does that landscape kind of look like for Joenja®?

Fabrice Chouraqui – Chief Executive Officer:
So it's for Joenja®, it's about half commercial and Medicaid and the team has done an amazing job. I was very impressed actually to see the work that they've done. And so clearly payors are not a barrier actually for Joenja® prescription, I mean it's a highly debilitating disease, it's a progressive disease, and therefore the value proposition of the drug is very clear. So on the payor side, I think we've seen a very good endorsement of payors in the U.S. and that has not been actually an issue whatsoever.

In the rest of the world, we expect to see the final guidance from NICE, the UK payors, anytime soon. And then we are also actually working with payors in Australia now that the drug has been approved.

John Gionco – Analyst (Needham & Company):
Great, good to hear. So we do have a few minutes remaining here, maybe for Fabrice, if you want to end us with any aspects of the Pharming story that you think might be misunderstood or underappreciated at this time for the company in 2025 and beyond?

Fabrice Chouraqui – Chief Executive Officer:
Well, thank you for the opportunity, first of all, to speak with all of you. I must say, I'm very impressed that Pharming over the past 10 to 15 years was able to really build a very effective infrastructure in clinical development, you heard Anurag, in supply chain and in commercial, in the field of rare disease. And so the goal now is to leverage this platform, make it scalable so the company actually can grow to new heights. We have very clear opportunities in the short-term that would allow us to maintain our momentum.

Our guidance, I think, is a good illustration of this, the guidance for 2025 and then in the mid run, you've heard from Anurag some very clear pipeline opportunities. So, I think everything is there to realize our vision to become a leading rare disease company. And personally, this is why I joined Pharming and I'm very impressed with the fundamentals and the clear opportunities lying ahead of us.

John Gionco – Analyst (Needham & Company):
Great. Well, Fabrice and Anurag, again, thank you very much for joining us. It was a pleasure to hear about the Pharming story and looking forward to all the updates to come in the near future.

Fabrice Chouraqui – Chief Executive Officer:
Thank you so much, John.

Anurag Relan, MD – Chief Medical Officer:
Thanks, John.

[END OF TRANSCRIPT]