Pharming Group N.V. Oppenheimer 34th Healthcare Life Sciences Conference - Presentation

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PARTICIPANTS

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Hartaj Singh – Analyst, Oppenheimer & Co. Inc.

Hartaj Singh – Analyst, Oppenheimer & Co. Inc.:

Great. Thank you, David, also for always making this so easy. Very happy to welcome Sijmen de Vries, who's President and CEO of Pharming. And actually, is probably one of the people I've known the longest in my career in Wall Street, somewhere between 15 and 20 years. And always a pleasure hanging with Sijmen, who's also just a phenomenally interesting and erudite person. He's going to present Pharming Group to us in a presentation. We'll leave some time for Q&A, right to the end, five to 10 minutes. So with that, Sijmen, please take it away.

Sijmen de Vries, MD – Chief Executive Officer:

Thank you very much, Hartaj, for that very nice introduction. Ladies and gentlemen, good afternoon, or good morning, wherever you are. And before I take you through the Pharming story, I would like to point you to this slide on forward-looking statements, as you know, because we're as public company and this presentation may contain forward-looking statements that are based upon our assumptions and plans and may not become reality, as we all know.

And without further ado, I would like to go forward and explain to you the Pharming story. So we're really building this leading global rare disease biopharma company. And we do this on the basis of three pillars, as we define them.

The first, on the left-hand side, is this foundation that we have in RUCONEST, which is our recombinant C1 esterase inhibitor that is approved for the treatment of acute hereditary angioedema attacks. And that product has been on the market in – this is mainly a U.S. business – It has been on the market in the U.S. since end of 2014. And we were very proud to actually issue a press release at the beginning of the year where we could report that we significantly exceeded our guidance of low single-digit revenue growth, because we grew the product in 2023 by 10%, up to $227 million. Net sales are expected for the year 2023.

And this is an asset that we believe will continue to support our business in a very considerable period of time going forward. I'll explain that a little bit later, why, despite all competition coming onto the markets as we see it currently happening.

Second pillar is our in-licensed compound from Novartis, Joenja branded for APDS, a rare, newly discovered immunology disease. Joenja was approved by the FDA in March 2023, and we already booked revenues, or expected revenues about $18 million in the first nine months on the market. And this is also a rare disease. It is about 1.5 per million. And therefore, this is a very newly discovered disease.

Regulatory reviews are ongoing with the compound in Europe, Canada, Israel and Australia. And of course, since the label is 12 years and up, it actually has pediatric trials as well, and also has a small Japanese clinical trial going on. And I will come to that later.

Then, on the right-hand side, because we have the commercialization infrastructure in the U.S. and in Europe, and we're panning out over these other markets, we're not only developing leniolisib for a second indication, which we announced as immunodeficiency with immune dysregulation beyond APDS, I'll come to that a little bit later. But also, we're really focusing on in-licensing or acquiring additional late-stage or clinical stage programs, focusing on immunology, hematology, respiratory or gastroenterology for rare diseases. This is really how we see the growth of Pharming going forward to become that leading global rare disease company.

And at the moment, the pipeline, looks like this. RUCONEST in the market, Joenja (leniolisib) in the market. Leniolisib on the regulatory review, leniolisib in pediatric and Japanese trials, and leniolisib just about to start a Phase 2 dose finding study for that new indication. And last but not least, we also have an early-stage preclinical program, a gene therapy forhereditary angioedema.

Let's take a first look at RUCONEST, why this is such an important, and will continue to be such an important support for our business. RUCONEST targets the root cause for hereditary angioedema. That is actually the missing ability to make properly functioning C1 inhibitor. You see on this slide that there are three basic pathways here that can lead to a hereditary angioedema attack. And you see the red signal C1 inhibitor, is everywhere on the slide. So basically speaking, C1 is the missing protein. You correct it with an adequate dose of C1. And in the case of RUCONEST, patients are injecting themselves, slow IV. They do that at home when they feel an attack coming. And basically, that is the story, how you treat hereditary angioedema.

Now, there are other products on the market, a lot of prophylactic products on the market, and also acute products on the market that actually target one of those pathways in the middle. And that is mainly the kallikrein independent pathway, as you can see there. So that actually is helpful for symptomatology. But it's not the whole story, and that's what you see. The difference between RUCONEST and those products is called breakthrough attacks.

In any sort of prophylactic therapy, there's up to significant numbers of breakthrough attacks, or significant numbers of patients actually suffering from breakthrough attacks. As is the case for those acute medications that only target that pathway, they suffer from significant redosing that is needed to actually deal with one attack.

And if you look at the next slide for RUCONEST, you see then what I mean, that is actually, we treat the root cause. And if you look at the right-hand side, 97% of the patients that treated the attacks with RUCONEST, just needed one dose. And that is actually very close, as close as you can come to 100% efficacy, of course, with a compound like this. Basically speaking, and that is exactly what the story of RUCONEST is, We serve the severe end of the market, where people have high frequency attacks and severe attacks, and they rely on RUCONEST as their ultimate product, which will actually help them to stop the attack and basically deal with and manage their disease Which is in slight contrast to a lot of products that we see that are used both for prophylactic and for acute therapies, where breakthrough attacks are quite frequent or redosing is quite frequent, up to 40% in most cases.

RUCONEST really serves the patients in that part of the market that is not driven necessarily by more convenient products, such as subcutaneous injections or oral products, but they need the efficacy of RUCONEST these patients. They don't have a choice, basically, and they failed all of those previous therapies. We think that RUCONEST, therefore, with no other C1 inhibitor on the market, that is actively marketed, is the answer here in this case, for those patients that need the efficacy of RUCONEST, and they are suffering at very high frequency from hereditary angioedema attacks.

And you see here that RUCONEST still continues to make inroads in the market. The basis for our growth was a continuing growth of physicians prescribing RUCONEST, and then strong growth in patients using RUCONEST. We are quite confident that RUCONEST does not only help with treating the breakthrough attacks that are occurring of the other therapies and where you have that different mode of action, but that RUCONEST also continues to serve those patients that need the efficacy of RUCONEST.

So that is with regards to the hereditary angioedema product, RUCONEST. And I would like to now quickly show you the new compound – Joenja, for APDS.

What is APDS? APDS stands for activated phosphoinositide 3-kinase delta syndrome. As you can see here, discovered only 10 years ago for the first time and estimated to have a preference of about one and a half patients per millions of population. That equates to about 2,000 patients in the markets that we are planning to commercialize Joenja, in the future. To date we have already identified more than 840 of those patients, and identified, I mean they have been confirmed by genetic tests.

And this is a disease that, like I said, only described recently, and has very widely signs and symptoms, but always is going down a spiral, a negative spiral. And the good news is that the disease can be tested according to commercially available test, which is a genetic panel, a test for about 600 genes.

Now, as you can imagine, since it is a failure of the immune system, it's an immune deficiency with immune dysregulation. It has many aspects on these mostly young people, as you can see here, if you summarize this slide, you can see that these young people live a life that is going on a downward spiral and is associated with physical, mental and big social problems such as that cannot function in normal life and has a very heavy treatment burden so far, and eventually ends unfortunately with a very much shortened lifespan.

And why is that? Because if you look at the symptoms of this overactive pathway, it basically creates the immune disbalance and the immune dysregulation and you see the symptoms there on the right-hand side. And that starts at very young age already with consistent and severe infections, both viral and bacterial, lymphoproliferation, Some of these kids have lymph nodes, the size of golf balls in their neck, for instance, lymphadenopathy, splenomegaly/hepatomegaly, and of course, if you have bad lymphoproliferation in your gut, it leads to really serious enteropathies.

But also because of the immune dysregulation it leads to autoimmunity of all sorts. And very early on in life, often because it consists of the severe recurrent infections, leads to bronchiectasis, so permanent damage to the lungs. And the worst outcome of this whole thing is in a very high percentage of patientsthis can lead to the malignant proliferation – lymphoproliferation, i.e., lymphomas, which of course, patients in their early twenties have a very bad outcome and a very

high mortality, up to 50%, we think at this point in time.

In other words, it's a downward spiral. All because the PI3-kinase delta pathways are overstimulated, and basically does not form any sort of functioning immune cells. It is overstimulating and makes too many immune cells, but none of the immune cells are functional and therefore the immune system is not functioning.

What does Joenja or leniolisib do? It basically brings back the balance and allows the immune system to start producing functional cells, rather than only these cells that do not function when you have a hyperactive pathway. Joenja really modulates back the PI3-kinase pathway to normal levels, such that the immune system can gradually build itself up.

And that's exactly what we saw in a clinical trial. And you all think PI3-kinase delta, those products may have very bad side effects. That is the other piece of good news. Not only was Joenja approved in a randomized placebo control trial in patients with APDS, 30 patients were treated for 12 weeks and followed up for 12 months after that. But also there were no different side effects in this trial other than those in placebo. And even better, because we did a lot of long term follow up. We followed patients, when we submitted to the FDA, were followed an average of two years and maximum of five years. And of course, they continue to be on drug, all of them at this point in time. So we are already two years further down the line.

But we see that not only does the tolerability stay the same, so very benign tolerability profile, but also the efficacy and the parameters continue to improve in those patients with the longer the duration that they use the drug. And those results were published from the long term follow up last year and were presented last year.

It means that basically you have a drug that stops the negative spiral that corrects the immune system and makes the immune system function again. And it is an oral product, so they take two tablets a day, these patients, for the rest of their lives, and normalize the immune system and have a very – as a token of, you see that a lot of patients are already on drug. We reported 92 of those patients enrolled, 81 were on paid therapy already by the end of the year.

And there is, of course, a significant adherence, because all of the patients that were on the original trial and were already enrolled are still on drug and continue to be on drug. And like I said, some of them have been for around seven years already.

Now, of course, what are we going to do next with this product? So we're looking beyond the FDA approval. We're waiting at this point in time for the CHMP opinion for Europe that's expected this quarter. Subsequently, we will file with the United Kingdom authorities, and we can do that on the basis of either the FDA approval or the EMA approval, because they have a mutual recognition procedure in place there now.

I was already alluding to the fact that we roll out to Japan. So, we have agreed a small study, a three-patient study that is almost completed, and then we expect therefore to submit the Japanese file by the end of this year. We have the Australian, Canadian and Israeli submissions under regulatory review and expect approval there in the first half of this year.

And important, of course, because as I already alluded to earlier, this is a genetic defect, it's a

dominant mutation, that the pediatric studies are very important. And of course, the majority of the kids we find in the pediatric study from four- to 11-year-olds, has almost completed enrollment and we will be submitting those results to the FDA and subsequently to the EMA in the not too distant future.

Of course, there's a pediatric for the small, pediatric study for the small kids, which is the minority of the pediatrics that has also started dosing, we have a named patient program, because we have a lot of incoming requests for treatments in many markets in the Middle East for instance and in Southeast Asia. So, we have a named patient program ongoing already with the product.

And like I said, we started the second indication development for PIDs with primary immune deficiencies, with immune dysregulation. And we expect the Phase 2 dose-finding study to start in the second quarter of this year. The main challenge that we have ahead of us is disease education. It's a new disease. So, we need to educate on this disease and we are very active doing that, we do a lot of publications and attend all the relevant congresses, but we also need to find the patients in the markets.

Now, we have found, as you can see, we have already found more than 840 of those patients in the market where we are actually going to commercialize. However, in the United States there's a bigger challenge, because it's a lot more decentralized healthcare. And we have found of those 840, just over 200 in the U.S., and in the U.S. we're very active with offering genetic testing program, that we actually offer to those patients that are suspect. It's called navigateAPDS that are suspect for the APDS diagnosis. So, we go to the immunologist, we go to hematologists, we go to gastroenterologists, and we go to the pulmonologists, because that's where the patient can hide according to their symptoms, mostly, of course, with the immunologists, because they have a primary immune deficiency and offer those free genetic testing kits for those to actually figure out whether they have the disease.

And then, of course, on the right hand side, once we found the patients, we are now starting family testing by directly sending our genetic counselors and our clinical educators to those patients to actually tell them about what kind of disease they have, and that they should actually maybe talk to their family members about who may have less than perfect health, to actually tell them what disease they have and what medicine they now have, and that they should offer free genetic testing to their family members as well.

Because that as, given that it is a dominant mutation, and there will be, of course, quite a few of those patients that will have family members that need the product as well. And so far there has not been the United States, there's no systematic family testing going on. We have 81 patients we have on the product, we only have found one case of a family member. There's still a lot to go there to find. So, there's a lot of work going on in that respect.

And then with the genetic testing comes another big opportunity for further patient finding, because most of the tests actually, because it's a new disease and it is still a very narrow description of the disease, most of the tests come back with a so-called Variant of Uncertain Significance or VUS. That means that variant is in the relevant gene, the patient has the phenotype, but that specific mutation has not been linked formally to the hyperactive pathway. Therefore, you need to basically link it, and therefore you have to do a lot of work.

First of all, there's mistakes in the databases. So, we figured out some of the variants already by correcting that. And secondly, we're doing functional testing. So, each of the various mutants are then basically tested. You get patient materials, you test the patient materials. We've set up a couple of labs for that because it's not an easy test to do. And then once you actually have validated this specific mutation, that mutation will be automatically be shared with – by the public database, the ClinVar database, and will automatically, not even, not only for that patient, but also for future patients, will be classified as APDS into the future. And therefore, the disease will more fully described.

And we also have a program ongoing called MAVE, where we will do this in a combinatorial way. So by the end of the year, we expect to have more clarity on those VUSs. And at this point in time, we have already identified more than 1,100 VUSs. That is not to say, of course, that, and that's still counting that number and it's not to say that all of them will have APDS, but there will be a significant percentage that should be expected to be classified as APDS in the future.

So we think there is a great opportunity for further patient finding ongoing, and it is just taking a lot of legwork, and especially in the U.S., where the healthcare is a lot more decentralized compared to outside of the U.S. In fact, outside of the U.S, in countries like Australia, Denmark, United Kingdom, France and Switzerland, just to mention a few, we have already identified well north of more than one per million of those patients confirmed by genetic tests, because there's a lot more centralized healthcare genetic testing going on in those markets. So, we're very confident that we will also find those patients in the United States going forward.

Then let me switch quickly to the next indication. Whereas APDS is very narrowly and newly defined disease, we have also now, together with the NIH, who were at the forefront of describing APDS and actually developing leniolisib for this indication. We have now identified a second indication, which means it's primary immunodeficiencies with immune dysregulation, which is just a further array into the primary immune deficiencies, where APDS is a very small one, and this will be, we expect to be a bigger one.

And here you see almost the same picture, because these patients have about the same symptomatology. It's just that they have different mutations. In this case, well known mutations, such as ALPS-FAS, CTLA4 and PTEN, that leads to a hyperactive pathway already associated with it, are treated in the same way, or managed, I should say, because they're not treated, but they're managed in the same way with immunosuppressants and immunoregulatory drugs that do not necessarily work so very well. And basically, it means that these patients also could benefit from leniolisib in the future.

So, based on the experience with APDS, we now are actually furthering into development of the PI3 with an immune dysregulation, coupled to those, to a number of those mutations that are already associated with the hyperactive PI3-kinase delta pathway, as mentioned here on the slide. And this seems to be more than threefold bigger population to treat than the APDS patients, which of course, and of course, these patients are already well known and characterized.

And like I said earlier, in the beginning, we're very excited that we can start a Phase 2 proof-of-concept clinical trial, a dose finding trial, which has been agreed with the FDA as the path forward for this compound and that's exactly what we are going to do. We are going to test in 12 patients with those genetic mutations and the phenotype. We're going to test safety and tolerability, and

of course, we'll explore some secondary and exploratory pathways with regards to some efficacy measures as well. And use tablet dosing from 10 to 70 milligrams in four, as you can see here in the total study duration of 20 weeks, and then pick the best dose regimen for Phase 3. And that will be done by the same investigators, as I was already alluding to earlier, that were pivotal for the development of leniolisib for APDS, namely at the NIH.

So, we're very excited about this prospect that we can bring the product further into and to serve the needs of more primary immune deficiency patients that have no cure or no medicine at this point in time.

So let me then quickly take you to the financials, the financials and outlook as part of the end of my presentation here.

We scored $227 million of RUCONEST sales, up 10%. You saw $18 million of Joenja sales, for totaling $245 million for 2023. We were in launch mode. We were very profitable before we started investing in Joenja and despite the high investment level of Joenja, we continued to generate some cash in 2023. So, we have a solid basis to start 2024, from which will be another year, of course, of investments. You see the revenue generation over the years. It will be another heavy year of investment, of course, because we are going to roll out Joenja further and investing in the second indication for Joenja.

And then finally, the outlook. Well, I already alluded to the revenue guidance, the successful launch of Joenja, the very quick reimbursement of the product. Already 81 of the more than 90 patients on paid therapy. We expect the further regulatory developments, of course, and we will continue to invest very heavily, of course, in the further rollout of Joenja and development for the second indication.

And last but not least, we're very actively hunting, because we have the commercialization infrastructure, both in Europe and in the USA, and are going beyond that to actually get new assets in, preferably by in licensing, but also, if necessary, by acquiring new clinical stage assets that can further leverage our commercialization infrastructure.

And this completes my part of my presentation. I think we may have still have a few minutes of question and answers, Hartaj.

Hartaj Singh – Analyst, Oppenheimer & Co. Inc.:
Yes. Thank you, Sijmen. Very comprehensive, and as you also do on your earnings calls, just really great slides with a lot of information.

Just a couple of quick questions. One is sometimes I don't think your financial profile gets highlighted enough. I was just looking here on Bloomberg just quickly, and you had a small – you've been able to maintain close to a positive net income while you've been preparing for Joenja running the trials, getting ready to launch it. You might have a slight loss this year, we'll see when you have the fourth quarter call. But as Joenja increases, you're going to be making those investments. But it's pretty impressive that you seem to be launching these products and in-licensing more products while keeping close to, if not profitable. Is that a conscious effort by the company?

Sijmen de Vries, MD – Chief Executive Officer:
Well, yes, we try to be conservative in this respect, Hartaj. However, it's also possible, of course, that if we find the right asset, that we will invest more heavily and we will then actually become somewhat of a period, maybe somewhat loss making. Because I think what really meant the message here is, we really are aiming to actually grow the top-line. And I guess, if I've seen the various research analysts reports about Joenja, they consider Joenja already, despite the fact that APDS is not fully described yet, and it is, of course, a little bit of wait and see, because it's such a new disease. They describe this asset as significantly higher potential than RUCONEST, has some of your colleagues, and I believe that if you look at it at the current pricing level and to be expected on the second indication, the same thing, it can be a multiple of RUCONEST peak sales.

So, I think that's one observation that I have, that we already are working towards a very significant top-line growth over the coming years. But it takes time, and that's the problem with this, of course, the market is always inpatient and new basically, ultra-rare diseases take time to work your way through. But given the successful launch, we've shown that we basically not only bring the product in the market within a week and actually get patients on paid therapy the next week after that. So, we know what we're doing.

But we also are really exploring a market that has a lot of potential going forward, apart from the fact, of course, if we get a successful in-licensing or acquisition, that we can have another significant inflection point towards the top-line growth. And that's really what we are focusing on to drive that top-line growth and become that company or that partner of choice also, that global rare disease company, because I think we're really developing that unique footprint as well with regards to where we are commercializing. And that's so important in ultra rare disease that you can go anywhere and not only have to focus on the U.S. market or vice versa, right, on the European market, for instance.

Hartaj Singh – Analyst, Oppenheimer & Co. Inc.:
Yep. No, Sijmen, thank you so very much. We're at the end of the time, I just want to say that, for knowing you so long, I can see all of the fun your team members are having, but at the same time, your company just keeps on executing phenomenally. So just keep it going. We're looking forward to keeping the conversation going.

Sijmen de Vries, MD – Chief Executive Officer:
Thank you very much, Hartaj. Thank you. Bye-bye.

Hartaj Singh – Analyst, Oppenheimer & Co. Inc.:
Thanks, Sijmen. Take care.

[END OF TRANSCRIPT]