Pharming Group N.V. 1Q 2024 Results Call

May 8, 2024

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Operator: Good day and thank you for standing by. Welcome to the Pharming Group N.V. Q1 2024 results conference call and webcast. At this time all participants are in a listen-only mode. After the speaker's presentation there will be a question-and-answer session. To ask a question during the session you will need to press star one on your telephone. You will then hear an automated message advising your hand is raised. To withdraw your question please press star one and one again. Please be advised that today's conference is being recorded. I would now like to hand the conference over to your speaker today Sijmen de Vries. Please go ahead.

Sijmen de Vries, MD – Chief Executive Officer:
Thank you very much, Sandra, and welcome, ladies and gentlemen, to our first quarter results conference. Next slide, please. I'm here with my three colleagues, in order of speaking, Stephen Toor, our Chief Commercial Officer, who is joining us from our New Jersey office; Dr. Anurag Relan, our Chief Medical Officer, joining us from our US office as well; and Jeroen Wakkerman, our Chief Financial Officer, who's based with me here in Leiden.

Before I do that, I would like to point out on the next slide, the forward-looking statement slide. So we will be making forward looking statements today in our presentation and those are based upon our current plans and – and insights of the situations of the current market circumstance. And of course actual results may differ from these forward-looking statements. So you cannot necessarily rely on those. So having said that, I would like to go through to slide five.

Yes, and here we are. We're building this leading global rare disease biopharma company. And we do that based on three pillars and this is a very familiar slide for you. We've been here before. On the left-hand side, the foundation of our company, the product RUCONEST® that comes from our own research and has already been on the US market for almost ten years. It was approved in July 2014. Recombinant protein replacement therapy for hereditary angioedema attacks. And as you can see, we are still, you know, growing this product and, you know, we had an 8% growth versus last year this quarter. Good growth last year as well. And we see increasing numbers of prescribers and patients. And there's many options for these patients available but RUCONEST® continues to play an important role and we expect it to be continuing for the foreseeable future. And Stephen will talk a lot more about that in his part of the presentation.

Next you see there Joenja®, the product we in-licensed from Novartis for the treatment of APDS, an ultra-rare immune disorder, a new disease that was only discovered ten years ago and we

already have the first disease-modifying drug on the market that we launched now a year ago. We are seeing a very successful introduction of the product in the US market. Stephen will allude to that as well. You know, we're very proud that we can actually, record US$9.6 million sales in this quarter, a good growth versus 4Q of last year. And you see here if you add both numbers, we realized nearly US$28 million of sales for this product in the first 12 months on the market. It's a newly described and also rare disease and there's a very strong focus there for patient finding. Both Stephen and Anurag will talk about that and how we go about that to find those patients. We're also very pleased to see that very recently we got a second approval in Israel at the end of April 2024. We have a lot of regulatory reviews ongoing and a lot of trials ongoing and Anurag will talk about that a lot more.

And on the right-hand side the possibility to leverage our commercialization infrastructure both in the US and outside of the US by not only, finding new compounds to hunting for clinical stage or later stage compounds to in-license or acquire to actually leverage, but first and foremost we have a very interesting opportunity in leniolisib to develop it further for a second indication for primary immunodeficiencies with immune dysregulation beyond APDS where we are in the final stage of preparing a Phase II dose-finding study. And in addition, we're working on a third primary immunodeficiency indication in earlier stage at this point in time. And Anurag will talk about that a lot more.

And on the bottom of the slide, you see that we have a total revenue guidance out between US$280 and US$295 million for this year, you know, driven of course by Joenja® but, the foundation is of course RUCONEST® underneath that.

And then you see the next slide look at more in detail because we're going to talk a lot about the potential for Joenja® today. Joenja® for APDS is the first stage where we are currently now in a market with a 12+ indication in the US where we already found a significant portion of the identified patients on paid therapy where we have a lot of ongoing search for patients and so-called variants of uncertain significance mutations. That's ongoing. The next step, and where you're already seeing and that's an interesting observation of almost US$1.1 million of sales in this quarter already outside the US. So in other words, we're starting to work on the global expansion of the product and on the – and the pediatric study will further boost that to get a full label and full geographic coverage for Joenja® in APDS. And then as I said already earlier, the bigger indication that we are starting a proof-of-concept trial in the not-too-distant future for the bigger indication of PIDs with immune dysregulation with similar symptomology to APDS.

So having given you this introduction, I would like to now hand over to the next speaker, to Stephen Toor our Chief Commercial Officer. Steve, over to you please.

Stephen Toor – Chief Commercial Officer:

Thank you Sijmen. Hello everybody. If you could go to the next slide, please. The key features of RUCONEST® remain the strengths that have continued to underpin commercial success over the last ten years since launch. Those unique product attributes and exceptional customer service and execution by our customer-facing teams is why RUCONEST® continues to remain a strongly relevant part of the conversation in the HAE community. Now that remains the case despite the transformation of the treatment landscape with the prophylactic launches and genericization of Icatibant. And it will continue to remain the case in the face of oral acute competition in the coming

years. HAE patients using RUCONEST® generally have a more severe course of disease and they need a virtually guaranteed and fast efficacy that stops an attack in its tracks. RUCONEST®'s unique product features and the mode of administration deliver that in a way that current and future options can't. As you know, 2023 was a strong year with solid growth in prescribers, new patients and sales. That success was in spite of the market-wide event related to reimbursement for government patients in Q1 23. And in Q4 24 we've seen less of an impact as the patient's out-of-pocket responsibility almost halved. The strength of leading indicators has continued into this year and we've had a strong Q1, up 8% on prior year and we exit Q1 2024 on track to achieve the revenue guidance which, as previously discussed, is seen to be low-to-mid single digit growth for RUCONEST®. If you can go to the Joenja® slide, please.

As you know, we were strong out the gate with the launch of Joenja® with patients fully reimbursed within days. And that momentum built through year one and it continues into 2024. So we now have 83 patients fully reimbursed with five more being processed with 15 newly-diagnosed patients in the quarter taking us past 220, close to half the number of patients the literature suggests are out there. Although we believe there are more. And we have over 50 more diagnosed patients who we're working with their physicians to enroll into our program. Plus of course 50+ pediatric patients who are diagnosed who could potentially go on Joenja® treatment when the pediatric label expansion is approved. So all this means we exit Q1 just below US$10 million in sales and 21% up on prior quarter. As we discussed in March on our 2023 full year call, as we convert the caseload identified at launch, our focus moving forward remains finding new patients. And given APDS is an autosomal dominant condition, this means testing families to uncover additional patients with this progressive disease so they too can benefit from management and treatment. And we're also working to resolve VUSs for the many patients who have these results which Anurag will discuss further. And with RUCONEST®, the results for the quarter are in line with our financial guidance for the year. If you can go to the next slide, please.

So our US teams continue their patient-finding, education and genetic testing efforts to build the APDS patient base. At the same time, we remain laser-focused on RUCONEST® execution. And while at different stages in the commercial cycle, both RUCONEST® and Joenja® are critical to our growth. Now, I've already covered the US here that you see on the first pillar. For ex-US alongside the US launch we continue to build our capabilities in preparation for launches in the EU, UK, Japan and Australia and other Asia Pacific countries. Our ex-US teams are focused on both educating, finding potential patients, testing and diagnosing and continue to build that patient funnel all in readiness for the steady flow of launches that we have in the coming years. And so far, we've identified over 800 patients in those key launch markets. And we also see multiple years of growth ahead for Joenja® with initiatives such as family testing and VUS validation that should contribute modest additions to patient numbers in 2024. We expect those initiatives though to have a more significant impact in 2025 when we see a potential for a few hundred patients to be on Joenja®. And altogether the APDS opportunity as you know is at least 1.5 patients per million or approximately 2,000 patients in these key markets of which we've already found a large number. And while the ex-US prices are expected to be lower than those in the US, the overall APDS opportunity is still significant. So while much of our organization is focused on Joenja® for APDS, we're also, as you see in the final column, focused on developing leniolisib for additional indications. So this is a good moment to hand over to our Chief Medical Officer, Anurag.

Anurag Relan, MD – Chief Medical Officer:

Thanks Steve. Next slide please. As you mentioned Steve, we've got a strong launch of Joenja® in the US. This reflects both the unmet need and the clinical experience with Joenja®. And to review, Joenja® is approved for the treatment of APDS in adult and pediatric patients 12 years of age and older. And this approval was based on data from a randomized, placebo-controlled study that showed Joenja® met both primary endpoints with significant benefits also seen in the secondary and other exploratory endpoints. Importantly what we've seen across the development program is that Joenja® is proven generally safe and well-tolerated. And this data has been seen not only in the randomized study but also in the ongoing long-term open label extension study. In that study, we also saw benefits with patients being able to reduce or discontinue their use of immunoglobulin replacement therapy. And we also saw reductions in infection rates over time. We continue to share this data on the long-term use of Joenja® from these studies as well as from post-marketing experiences. Next slide.

As with many rare diseases patients have a long journey to reach a diagnosis. We have several efforts now ongoing to help patients get a correct diagnosis quickly. The first set is around medical education to raise awareness about APDS and shared data on leniolisib. For example, recently we've shared information about the seriousness of APDS by publishing data on early mortality and the frequency of lymphoma in these patients. We've also been discussing, for example, the frequency of bronchiectasis, a lung complication that is often seen in these patients at a young age, to help doctors be able to recognize the types of symptoms that APDS patients may have, and to be able to perform a genetic test which is actually the only way to make a diagnosis.

Now, to make that diagnosis we've made the genetic testing available through a sponsored no-cost testing program. We also have assistance from genetic counsellors to be able to help patients and physicians interpret the results and we're working closely with these patients and their doctors to also help perform family testing because as an inherited disease we know that there are more patients than the patients that we've uncovered so far. We found in fact that most patients have not had proper family testing such as testing of parents or siblings to ensure that all of those members of their family can also receive the correct diagnosis. We have several programs now in place to help assist with that type of effort.

And as you've heard us talk about several times now, getting the genetic test is important for these patients but also interpreting the result is critical. And unfortunately many patients after they get a genetic test, can get a result called a variant of uncertain significance. What this means is that these patients have a variant or a mutation that hasn't been previously described. And what we found is that there's a significant number of patients who have actually already received a VUS test result. Just in the US alone 1,100 such patients. We're working closely now with a number of groups to help curate all of this data and put that into a single central database. And on top of that, what we need to do is perform further testing to determine whether that variant is disease-causing or not. Recently we've been able to start a functional testing program whereby patients can get access to a functional test and that can help them determine if they have APDS. And we're seeing already the results of those in the first quarter where patients who had a VUS result got a functional test and then eventually got a diagnosis of APDS. Some of whom are already on Joenja® now.

And to address this problem more firmly and more completely, we also have a large study called a MAVE study which will allow us to determine all possible variants. And we're expecting that this is

going to read out and by the end of the fourth quarter to be able to answer the question of which patients who have a VUS actually have APDS. Next slide.

In addition to the work that we're doing with Joenja® in the US, we have several projects to bring Joenja® to patients in other countries and to younger patients. We have an application under review, for example, in Europe and we're waiting now CHMP opinion. We anticipate being on the May agenda for a CHMP opinion so that will be later this month. We also have completed enrolment in our Japanese clinical study and we're working with the regulatory authority there to determine the filing strategy following the completion of the clinical trials that are ongoing. And then we have two pediatric studies. The first is children ages four to 11 and enrolment is completed there. And then we've an ongoing study that you see on the right for children ages 1-6-year old using granules and we had the first patient dosed last year. And enrolment is continuing there. Considering all of these clinical trials as well as the expanded access and Named Patient Programs, we have 138 patients receiving Joenja® through these various programs. And as you heard from Sijmen, we also received recently the marketing authorization in Israel. We have a number of reviews ongoing including in the UK, Canada and Australia. And we're expecting regulatory action on those reviews in the course of 2024 and 2025.

And then we're very excited also about the possibility of using leniolisib outside of APDS, and I'll be talking a little bit more about that now. In the next slide you can begin to see through our work in APDS we have a better understanding of the broader PID landscape. Now, what we see is that there are a large number of PIDs. Obviously, these PIDs have an increased risk of infection but we also see there's a subgroup of PIDs that have not only this phenotype of increased risk of infection but also have this immune dysregulation phenotype. And what I'm referring to here is this concept where there's abnormal lymphoproliferation and frequently autoimmunity. APDS of course is an example of such a primary immune deficiency with immune dysregulation.

In the next slide I'll talk a little bit about this first program where we're already moving forward on a second non-APDS PID indication. Again with encouragement from experts across the world suggesting that we should study leniolisib in these populations.

And what these experts are telling us is that there are many patients with clinical features similar to APDS that have similar disordered PI3Kδ signaling but don't necessarily have the PI3Kδ genetic abnormality that we see in APDS. And that signaling not surprisingly leads to the clinical manifestations that you see on the right. And you see that these are very similar to the types of things that we see with APDS. Mainly we see abnormal lymphoproliferation, so large lymph nodes, large spleen. We see this also in the gut. On top of that there's the problem of autoimmunity, again signaling the abnormal dysregulation in these patients' immune system. We see GI disease, lung disease, and frequent infections of course. Then unfortunately, these patients also have a predilection towards developing early lymphomas. So there's clearly a high unmet need here, and not surprisingly given that there is abnormal signaling and that the symptoms you see there on the right are similar to APDS, the treatments that are being applied for these patients such as rapamycin, an MTOR-inhibitor, or other immunosuppressive agents have also been applied in this population. So overall we see that there's a strong basis to study leniolisib in this group of patients. And you see some of the genetic abnormalities that are mentioned there, including the condition

called ALPS caused by an abnormality in the FAS gene, CTLA4 and PTEN. And on the next slide you can see a little bit about the work that we're doing to advance this program.

And we're working closely with team at the NIH and this includes Dr. Rao, who led the APDS clinical trial program at the NIH, and Dr. Uzel who actually was part of the team that led to the discovery of APDS ten years ago. And we're starting this Phase II proof of concept dose-finding study. We're starting at doses that we used in the leniolisib development program for APDS also. So starting at the 10mg dose. And as I mentioned we're using patients that have a number of abnormalities including those listed there. The primary goal of course is to look at safety and tolerability and we're also going to be looking at pharmacokinetic measures and various efficacy measures. And patients will receive doses for a number of weeks and escalate as they progress through the program. And the goal is to be able to pick the best dose regimen for the Phase III study.

And if we go to the next slide, we can see some of the populations that have already been characterized with these various genetic abnormalities. And you can see here several large cohorts with each of these different genetic forms of primary immune deficiency. And these large cohorts together tell us that there's a treatable population of approximately five patients per million across the world here. So when we put all of this together you can see we're very enthusiastic about the potential of Joenja® in APDS as well as beyond APDS in these various abnormalities that have clinical features that are similar to APDS. And with that, I will turn over to my colleague Jeroen to talk about our financials.

Jeroen Wakkerman – Chief Financial Officer:
Thank you very much Anurag. Next slide please. In the first quarter of 2024, the revenue has increased by 31% to US$55.6 million, and that's a comparison to first quarter of last year. And this is driven by both the US commercial launch of Joenja® and revenue growth of RUCONEST®. RUCONEST® revenues increased by 8% to US$46 million compared to first quarter last year and Joenja® revenues were US$9.6 million and that's a 21% increase compared to the fourth quarter of last year. So overall we're well on track for 2024 to hit our total revenue guidance which is between US$280 and US$295 million or 14-20% revenue growth.

Looking at gross profit it increased in line with the sales increase. Gross margin dropped slightly and that was because of a non-recurring inventory impairment of just over US$2 million. Looking at OpEx, it went up compared up to last year's first quarter but went down if I compare it to Q4 last year as we already indicated at the time. So this increase versus last year was planned and we are increasing the OpEx to support the launch of Joenja® in the US but also preparation for the launch outside of the US.

The operating loss because of the increase in OpEx increased from US$13.7 million to US$16.3 million in the quarter and net profit remained fairly stable, increased by US$0.2 million and that is compared to the operating loss is due to better net finance results in the quarter. Our overall cash and marketable securities position went from US$215 million to US$203.5 million so a reduction of $11.5 million and that is on the back of mainly negative net cash flow from operating activities of US$7.6 million.

On the next slide we see the revenue breakdown by product and geographic segment and just focusing on Joenja® for the first quarter we saw an US$8.5 million revenue in the US from US$7.8

million Q4 last year. We see US$1.1 million outside of the US and that was US$0.3 million in the fourth quarter and this is sales from Named Patient Programs. And if you look at the overall part of Joenja® in the total revenues at US$9.6 million, that's now 17% of total sales, and obviously last year was nothing. And we expect that share to go up going forward.

On the next slide some more perspective on the OpEx. As I said, the OpEx went down from last quarter by around US$10 million and the OpEx really reflects the continued investment in Joenja® in the US and the launch preparation ex-US. We also increased investments to expand the leniolisib franchise. So think about the pediatric trial and new indications that we are working on that Anurag mentioned. And we also increased payroll cost and that is because of the general business growth. With that I would like to hand over to Sijmen for the outlook for the remainder of the year.

Sijmen de Vries, MD – Chief Executive Officer:
Thanks Jeroen and yes, I'm happy to present you with the next slide, the outlook for 2024. As you heard in the beginning, we gave guidance and we continue to give guidance between US$280 and US$295 million for revenues for this year which means between 14% and 20% growth with quarterly fluctuations as expected. For Joenja®, you heard about the continued progress in finding the additional APDS patients in the US market, the patients that are already identified, but also this is supported by the systematic family testing that we have embarked upon and the first results of the VUS validation efforts. And subsequently converting those patients to paid therapy. Albeit you also heard from Anurag that the MAVE experiment which will provide the definitive answer of the full definition of APDS will report at the end of this year. So in other words, we expect a significant inflow of patients in the US from that experiment, with more than 1,100 patients currently diagnosed with VUSs.

Then you heard about the increasing ex-US revenues from the commercial availability through the Named Patient Program which we expect to continue to increase during the remainder of this year. The clinical trials, the pediatric trial and of course the Japan trial continue. We also expect regulatory action this year from the various jurisdictions where we have regulatory files that are under review. We're very excited of course and expect in the very near future to be able to announce that the Phase II proof of concept clinical trial in PID with immune dysregulation will be started and to significantly expand our commercial potential of leniolisib which you heard Anurag outlining the details about.

And then last but not least we have an active business development group that looks for primarily in-licensing opportunities but also we look at acquiring opportunities that are in clinical stage of development or later, and, you know, in those areas that are mentioned here on the slide, immunology, hematology, respiratory and gastroenterology preferably. So in other words we have a very busy remainder of the year ahead of us and we look forward of course to updating you on that later on. But let's switch over now to the operator first because there may be some questions that we happily answer. Over to you, operator.

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 questions please press star one and one again. We will now take the first question from the line of Christian Glennie from Stifel. Please go ahead.

Christian Glennie (Stifel): Thank you. Thanks guys, for taking the question. Three questions please. The first one would be on Joenja® in the US. Just to understand a bit better the sort of potential moving parts here in terms of patient numbers. You talked about 83 being on treated therapy as of 31st March but that compares to 81 at the end of December. So just a net two additional but maybe there's some additional patients there that have come on but then some have dropped off. And then maybe some comment around the duration of treatment that you've seen so far given that you'll now have some patients potentially who've been on it since it was launched 12 months ago. So just a better understanding of the patient dynamics there and what to expect through the rest of the year.

Sijmen de Vries: Steve would you be so kind?

Stephen Toor: Sure, thanks Christian. Good morning. Yes, we were 81. We added four group patients in the quarter. There were two though that dropped out. One was post-transplant. Unfortunately, that patient passed away unrelated to Joenja®. And then secondarily, a patient with an unknown adverse event. So the net of that is 83. We also diagnosed or had diagnosed 15 more patients during that quarter, and those are currently being processed obviously and will be additive to the current patient load. So as things stand right now, our outlook is much the same as Sijmen said, you know. We're on track to get to where we need to by year-end.

Sijmen de Vries: I think you're referring to that – thanks Steve for that. I think, you know, as with all these sorts of ultra rare therapies, you will see of course especially at the beginning you'll see some lumpiness in the sales, right. That's why we say quarterly fluctuations Christian.

Christian Glennie: Yep, okay, thank you. And then have you got a – I mean, is the working assumption that the majority of patients continue to be on therapy or have you got an average duration of treatment that you can quote at the moment?

Sijmen de Vries: I think you're right. I mean, people stopping therapies is far and few between that we see, right. Anurag, do you want to say something about that?

Anurag Relan: Yeah, thanks Sijmen and hi Christian. Yeah, we see continued very high compliance with the product. We've seen that rapid clinical development program and we see infrequent discontinuation.

Christian Glennie: Okay, thank you. And then the second one would be on leniolisib or Joenja® in Europe flagging ongoing review with the EMA and obviously expecting a CHMP. Just wanted to try and understand a little bit as much as you can tell what some of these issues could be or relate to. Do you have any outstanding issues there? And when you say you expect to be on the agenda for May, that's not necessarily the same thing as being up for an opinion in May. I just want to clarify what your expectation is for the May committee.

Sijmen de Vries: Anurag, would you be happy to answer that question?

Anurag Relan: Sure. So we do expect to be on the CHMP agenda for their meeting at the end of May on the MAA. So that's our expectation. Of course, we will wait for the CHMP feedback to confirm that.

Christian Glennie: Okay. So, we should be expecting, that's your expectation, Joenja® will be up for an opinion at the meeting in May.

Anurag Relan: That's correct.

Christian Glennie: And then just finally on the named patient rollout. Obviously 1.1 million you said that will continue to grow. Can you give us a sense for the growth there through the rest of the year and also, you know, kind of the number of patients and sort of the prices that you're getting for these patients? Thank you.

Sijmen de Vries: Steve, would you like to comment on that?

Stephen Toor: Certainly. So the prices are generally in line with the US price. Sometimes with a slight discount to that. So generally in that ballpark though. In terms of numbers we don't necessarily forecast NPP out just because that's driven obviously by the doctor and their discussions with both the patient and local authorities in country. But we would expect to see as the product becomes better known and the effect that the positive effect on patients becomes more widely understood that as we await approvals more patients do benefit from that. But there isn't a specific target as such. It's very much doctor-driven, Christian.

Christian Glennie: Okay, thank you.

Sijmen de Vries: Thank you Christian.

Operator: Thank you. We will now take the next question from the line of Sushila Hernandez from Van Lanschot Kempen. Please go ahead.

Sushila Hernandez (Van Lanschot Kempen): Yes, thank you for taking my question. Also one on Joenja® and patient-finding. You say that there are 15 diagnosed patients in Q1, so how many of these patients do you expect to be converted to paid patients? And also on operating expenses, are these the levels that we can expect throughout the year or are you foreseeing any increases or decreases compared to this quarter? Thank you.

Sijmen de Vries: Okay, so may I suggest Stephen that you answer the first one? Is that alright?

Stephen Toor: Yep, absolutely. So thanks for the question. We expect the majority of those patients, if not all of them, to be converted onto paid therapy. We have not as yet had a rejection, so I would expect in the course of business that all those patients to come online.

Sijmen de Vries: Would you like to comment on the operating expenses Jeroen, what we expect for that?

Jeroen Wakkerman: As I said last year on the OpEx where it was in the Q4 it was US$73 million, that we expected it to go down. It has gone down now and I would expect it to be slightly up in the next quarters because we keep investing in Joenja® both in the US and ex-US. And so, I don't expect a sharp drop or anything in OpEx in the next few quarters.

Sijmen de Vries: Does that answer your question, Sushila?

Sushila Hernandez: Yes, thank you.

Sijmen de Vries: My pleasure.

Operator: Thank you. We will now take the next question from the line of Joe Pantginis from H.C. Wainwright. Please go ahead.

Joe Pantginis (H.C. Wainwright): Good morning and good afternoon gentlemen, thanks for taking the questions. So a couple please. I just want to start at the end of your written comments today cos more on curiosity. I mean, obviously it's not impactful of your investment case but you did disclose that OTL-105 with Orchard's being discontinued. So just curious if – two things. Is there anything technical or science that impacted the decision to discontinue for the program? And are there any payments either way for the termination and will you be potentially looking for an additional or an alternative gene therapy approach for the future? Thanks.

Sijmen de Vries: Alright Joe, first no significant payments. Secondly, yes there was always a high hurdle of course involved in this. A high technical hurdle. And when you look at it, it's associated with both the ability to generate sufficient C1 inhibitor protein by means of the blood organ. That's the one. And then of course the non-toxic conditioning regimen developments. So those were the high hurdles. And then last not least but very importantly, at the time we did not have the opportunity to develop – and that's the main reason – to develop leniolisib. We were not expecting that to be able to develop leniolisib with two subsequent indications. So we're now about to kick off that Phase II study for leniolisib for the next indication. You heard from Anurag that is a very, very significant indication which is fairly nearby the market compared to also a product like OTL-105. Obviously no competition around with a long exclusivity guaranteed for leniolisib. Secondly, we are looking at an even more and bigger PID indication going further forwards. So in other words, we have a lot of opportunities now that are more nearby, more derisk without any competitive threats here. So we decided, you know, given all the things together that it is the best way forward to focus ourselves now on this with regards to our internal portfolio; and of course to continue to look for leveraging the infrastructure, the commercial infrastructure further with our active in-licensing/acquisition quest. That's a bit longwinded. I hope I answered your question, Joe.

Joe Pantginis: No, absolutely. Thank you. And then on RUCONEST® sort of a two-pronged question. How would you describe sort of the first quarter impact with regard to insurance resets that are usually expected? How much does that impact at least just for the first quarter to be able to then get back on trajectory? And secondly, how would you describe the balance, because obviously it's very nice to see, the continued addition of new physicians to the program and refill rates? Thanks a lot.

Sijmen de Vries: Yeah, of course, it's always part of the lumpiness or the first quarter's always part and parcel of that renewals of the prioritization. But let's just go to Steve to give a bit more insight in these things. Right, Steve?

Stephen Toor: Yeah, absolutely. Hi Joe. So actually the – things went well Joe. As you know we've been doing this now for a number of years, so we're able to prepare in Q4 and the prior authorization – prioritization in Q1 actually went pretty smoothly and we were – completed almost all of them by the end of February. Now, what complicated last year was some issues as you know that were external issues that hit the market for government patients. We saw that impact decline quite significantly this year as patient out-of-pockets also came down in the Medicare space. And certainly for us it was – it was a significant decline in impact. So overall I would have said Q1, while you expect lumpiness in Q1, it was pretty successful authorization period for us.

Joe Pantginis: Excellent, thanks for the details guys.

Sijmen de Vries: Pleasure, Joe.

Operator: Thank you. We will now take the next question from the line of Hartaj Singh from Oppenheimer. Please go ahead.

Hartaj Singh (Oppenheimer): Great, thank you. And thanks for the questions. I just have a couple. Really nice launch going on with Joenja®, but I just want to kind of go back to a previous question on the first quarter fluctuation. You know, two years in a row now we've had that and they seem to be pretty extreme. I mean, is it – you know, other companies they talk about, payment into government programs. There's patient assistance programs, etc., etc. I mean, what exactly happened in the first quarter where you had this, pretty large drop-off from the fourth quarter to the first quarter? It seems mostly RUCONEST® sales. And then is that the expectation going forward? Is that the way we should model this going forward in that in future first quarters, you know, on a quarter-on-quarter sequential we should expect a pretty significant decrease in RUCONEST® sales and then that'll pick up going on later? I mean, is this the way to think about it? So that's my first question. I've just got a couple of others. Thank you.

Sijmen de Vries: Yeah. Hi Hartaj. I think it's been the case right for all those years and it was aggravated last year by this special situation there. But it seems to be the case, right? Do you want to comment any further on this Stephen?

Stephen Toor: Sure. Morning Hartaj. So I think it's certainly the case that in most Q1s you've seen over the years RUCONEST® sees a slight decline due to the reauthorization of most of our patients in that period of time and that does affect most companies. Last year was exacerbated by an impact to government patients that was external. It affected the whole HAE space. That came down significantly this year as patient out-of-pockets declined. So we saw about half the impact that we saw last year. And next year that should stabilize completely I think with patient out-of-pockets coming down to around US$2,000. So I think you can say by the time we get to next year, it's steady state. So yeah perhaps we should expect a decline as we always have year-on-year, but I don't

expect what's happened last year and this year to continue. That's the result of a very specific event affecting government patients.

Hartaj Singh: Yeah, no Stephen, that makes sense and we heard that from other companies also. I think the IRA, Inflation Reduction Act, has exacerbated these first quarter fluctuations. The other question I would just have is on OpEx. You know, really like all the color there; but let me put the – there's a question asked previously. Let me put it another way which is that, you know, if you're expecting, you know, your guidance suggests a pretty significant increase in revenue this year, is opex expected to grow at the same rate? Or can we hope for some operating leverage, which would mean OpEx going at a slower rate than revenues? And I've got one last question after that.

Sijmen de Vries: Yeah, sure. I think Jeroen already commented on that Hartaj, you know, about the still to be expected slight increase in the operating expenses for the coming quarters. Having said that, you know, it's not the spectacular increase anymore before because, you know, we did the US launch of course. That is very capital-intensive. On the other hand, you know, we continue to invest in all those things in the US market. And of course, we're preparing, as Jeroen was already alluding to, for the preparations for launch of Joenja® outside of the US. And in addition to that you also see that, gradually R&D costs will, not spectacularly, but will continue to go up as well because of the fact that we are starting clinical trial programs for leniolisib in the subsequent indications. So all in all, we're not at this point in time of course aiming for profitability per se in this year because it's still a launch here. And it takes time. And you already heard that for instance, you know, the leverage. I think the real leverage if you look at the patient growth in APDS you heard Stephen say there that conclusive VUS MAVE experiment that Anurag was talking about will or should be bringing a very significant bolus of patients in the US market towards becoming available for paid therapy next year. So, you know, this is typically, you know, when you have a new disease that is not fully described, it is typically, when you're dealing in ultra rare diseases that it takes time and it takes a lot of investment. But eventually, it will be a fairly of course profitable operation. I hope that answers your question a little bit, Hartaj.

Hartaj Singh: Yeah, no, absolutely. And in line with what you've said before also previously Sijmen, I just wanted to get more color around it. My last question is just on the Phase II design. Anurag, you might have mentioned this already but, can you just kind of walk us through, roughly how long would it take for you to sort of get all the sites open, recruiting? You know, when could we see, essentially what I'm trying to get to is, when could we see a sort of a read-out. You know, would that be a 2025 event or 2026? And thank you for all the questions.

Sijmen de Vries: Thank you Hartaj. Anurag, please?

Anurag Relan: Hi Hartaj. Yes, this next phase II dose-finding study is being conducted at a single center and that's at the NIH. So with that and the fact that we're anticipating 12 patients in the study, this is a center that's actually already identified which patients they anticipate being able to enroll. We believe that they'll be able to enroll the study in relatively rapid fashion once we get going. And we expect to be able to read out the results probably in the course of 2025.

Hartaj Singh: Great, thank you all.

Sijmen de Vries: Thank you Hartaj.

Operator: Thank you. We will now take the next question from the line of Alistair Campbell from Royal Bank of Canada. Please go ahead.

Alistair Campbell (RBC): Thanks very much for taking the questions. I've got three if that's okay. Just first of all looking at Joenja®, I mean, obviously we've seen more diagnoses through Q1, but we haven't seen progression in terms of patients on therapy. So I just want to ask, you know, get a sense of that. I mean, just check we're not seeing an underlying dynamic here or perhaps what you've done in the first instance is kind of hoovered up the most severe patients and maybe now we're moving into patients who are diagnosed but don't have quite so severe disease and are potentially harder to pick up. So maybe some commentary on that in terms of what's happening with severity in patients on drug. And then if I do some quick mathematics, I'm assuming you had about 80 patients on paid therapy through the quarter, that would sort of point me to a US number based on the WAC a chunk higher than the quarterly sales. And would sort of indicate something like a 25% gap in the system. Is that a good proxy for how much kind of discounting there might be from the WAC price in the system?

And then finally just on the PID trials, is there any reason to think that PIDs need a different dose from APDS? I mean, do you maybe perhaps need stronger suppression or pathway? Just any sort of feedback on that would be interesting. Thank you.

Sijmen de Vries: Okay, thanks Alistair. Let's maybe start with the two questions for Anurag about the severity and the PID dosing. Anurag, would you like to comment on that?

Anurag Relan: Sure, so I think Alistair the first comment is correct that, you know, the patients that we initially were able to convert over to paid therapy, these were patients of course that were in the clinical trial program, in the extended access program, so there was of course a bolus of those patients. And many of those patients were quite severely ill. Now, APDS in general is a serious disease, so there aren't, you know, a large number of let's say asymptomatic patients that were floating around out there. All of these patients are sick, most of these patients are on IG replacement therapy for example. So this is a serious disease and a progressive disease. So I think it's just a matter of continue to reach out to these doctors and educate them, as well as patients about the condition and the potential effects of Joenja®.

On to the question about the dosing in this study as well as in a future study. And I think that it's really an open question. We're starting with a lower dose than we have approved for Joenja® currently. So we're starting at the 10mg dose which is the same dose that we used initially with APDS, and we'll progress these patients through. Based on everything that we know so far about the activation of the pathway in these patients, the measurements that have been done about that activation relative to APDS patients, we feel like we're in the right dosing range. So we don't believe that we're going to need a higher dose to so-called suppress the pathway, but really trying to normalize and sort of balance the pathway. I think that's probably a better way to think about it.

Sijmen de Vries: Okay, thanks. And then maybe Jeroen you want to comment on Alistair's question about the discounting or the absence of it in Joenja®?

Jeroen Wakkerman: Yeah, absolutely. So basically, it's not just discounting like in other drugs. It's mainly because of the mix with Medicaid/Medicare patients and mainly Medicare. And so we did have for that reason a discount of around 12%.

Sijmen de Vries: Does that answer your question, Alistair?

Jeroen Wakkerman: There's no other discounts than that Alistair.

Alistair Campbell: Yeah, that's good. Very clear. And is that broadly what we should be thinking about carrying on going forward or do you think the mix will change over time?

Sijmen de Vries: That's a good question.

Jeroen Wakkerman: Well, it really depends on the patient mix so it's very difficult to say. But other than that, it's been relatively stable so far.

Alistair Campbell: Great, thanks very much.

Sijmen de Vries: You should realize also it's a relatively young population that we're treating, right, here in this case.

Alistair Campbell: Very good, very clear, thank you.

Operator: Thank you. As a reminder, if you wish to ask a question please press star one and one on your telephone. That's star one and one to ask a question. There are no further questions at this time. I would like now to turn the conference back to Sijmen de Vries for closing remarks.

Sijmen de Vries: Thank you, Sandra. Yes, thank you very much. Yes, so you heard, our total revenue guidance continues to be between US$280 and US$295 million. You heard about the progress of finding the additional APDS patients in the US. And outside of the US, of course, and then bringing also a relevant part of the revenues for Joenja®. You heard about the expectations towards the big effort that's ongoing during the remainder of the year to clarify the full description of the disease by means of the MAVE experiment, so which will we expect deliver a significant new bolus of patients next year becoming available for therapy. Obviously, the clinical trials are ongoing and especially here the pediatric label expansion trial progresses very well. And that trial with 4-11-year olds has the majority or the vast majority of the pediatric patients in it. And no doubt of course we'll be delivering a significant bolus of patients in addition to that. You heard about the regulatory actions that are ongoing in the various territories outside the US and where we expect to see some progress there continuing. And then of course last but not least, we're very excited about the start of our Phase II clinical trial, proof of concept trial in PID with immune dysregulation that will very significantly expand long-term commercial opportunity of leniolisib. And very lastly, you know, we continue to look for in-licensing opportunities of clinical stage rare disease opportunities to be either in-license preferably or acquired.

So with that I would like to all thank you for being present at our conference and we look forward to updating you on our next call which will be our half-year results in the beginning of August. Thank you very much and goodbye.

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

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