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INCY.OQ - Q4 2021 Incyte Corp Earnings Call

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OVERVIEW:

Co. reported full year 2021 total product and royalty revenue of $2.9b and 4Q21 total product and royalty revenue of $813m.

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PRESENTATION

Operator

Hello, and welcome to the Incyte Fourth Quarter and Full Year Earnings Call. (Operator Instructions)

It's now my pleasure to turn the call over to Christine Chiou, Head of Investor Relations. Please go ahead.

Christine Chiou - *Incyte Corporation - Head of IR*

Thank you, Kevin. Good morning, and welcome to Incyte's Fourth Quarter and Full Year 2021 Earnings Conference Call and Webcast. The slides presented today are available for download on the Investors section of our website. Joining me on the call today are Hervé, Barry, Steven and Christiana, who will deliver our prepared remarks, and Dash, who will join us for the Q&A.

Before we begin, I'd like to remind you that some of the statements made during the call today are forward-looking statements and are subject to a number of risks and uncertainties that may cause our actual results to differ materially, including those described in our reports filed with the SEC. We will now begin the call with Hervé.

Herve Hoppenot - *Incyte Corporation - Chairman, President & CEO*

Thank you, Christine, and good morning, everyone. Slide 4. So we had another year of strong commercial performance with product and royalty revenues growing 17% to reach $2.9 billion, representing a CAGR of 24% over the past 5 years. We have been able to maintain this level of growth

through continued commercial execution for Jakafi, launches of new products and new indications across the U.S., Europe and Japan, and a rapidly growing royalty revenue stream.

Jakafi grew 10% for the full year and was up 15% in the fourth quarter, driven by the launch in steroid-refractory chronic GVHD and robust new patient growth in MF and PV.

For the full year, our other hematology and oncology portfolio grew 40% year-over-year with contribution from new product launches, including $69 million from Pemazyre and $5 million from Minjuvi. And our royalty revenues grew 45% to $569 million for the full year. What's important to note is that this growth does not yet include meaningful contribution from recently approved products such as Minjuvi in Europe and Opzelura in the U.S.

On Slide 5, as we look ahead to 2022, we have multiple opportunities for growth across our portfolio with our recently launched product, Opzelura in atopic dermatitis, Pemazyre in cholangiocarcinoma, Monjuvi and Minjuvi in relapsed or refractory DLBCL, and Jakafi in chronic GVHD. Later this year, we expect regulatory decisions in the U.S. and in Europe for ruxolitinib cream in vitiligo, a disease that affects millions of patients and for whom there is no approved treatment for re-pigmentation.

For our partnered products with Novartis, ruxolitinib is under review in Europe and Japan for GVHD and capmatinib is under review in Europe for non-small cell lung cancer. Regulatory applications were also submitted by Lilly for baricitinib in the U.S., Europe and Japan for alopecia areata. 2022 is a year full of important milestone where we will develop and expand our pipeline, deliver new data in key clinical program and continued driving uptake of our newly launched products and new indications.

Before handing the call over to Barry, I want to say a few words on the launch of Opzelura and our expanding footprint in dermatology. A few years ago, we expanded our development capabilities into dermatology with an intention to bring ruxolitinib cream to market. We were able to implement a robust and successful development program for ruxolitinib cream in atopic dermatitis and vitiligo. And Opzelura became the first topical JAK inhibitor approved in atopic dermatitis in the U.S. and has the potential to be the first FDA-approved product for re-pigmentation in vitiligo.

As you can see on the right, we have since expanded our dermatologic clinical development pipeline to include multiple products and indications. We also established a dedicated commercial organization in the U.S. to support the launch of Opzelura and these efforts have been translating into a very successful launch thus far.

We expect our dermatology franchise to become an important growth driver for Incyte starting with Opzelura, which we believe can reach $1.5 billion in peak sales in atopic dermatitis in the U.S. alone.

And to share more details on Opzelura and Jakafi's performance and outlook, I'll now turn the call over to Barry.

Barry P. Flannelly - *Incyte Corporation - Executive VP & GM of North America*

Thank you, Hervé. Good morning, everyone. We are very pleased with the performance of Opzelura thus far, and we are making significant progress with the launch on multiple fronts. Starting with the uptake of Opzelura. On the left-hand side is 867 data, which is number of units of Opzelura 60-gram tubes that our wholesalers are shipping to pharmacies. These data tied closely to prescriptions dispensed given the low level of inventory retail pharmacies typically hold for specialty dermatology products.

In the fourth quarter, since launching on October 11, nearly 21,000 units have been shipped to pharmacies. And in the month of January, nearly 11,000 units have been shipped -- as you can see, the demand for Opzelura in recent weeks continues to climb and the trends are very encouraging. On the right-hand side is IQVIA data, showing new-to-brand share for Opzelura in our market basket, which includes Dupixent, Eucrisa, Protopic and Elidel and their generics.

In the 16th week since launch, as shown on the chart, Opzelura is capturing over 10% of all new-to-brand prescriptions after steroid failures. Not shown on this slide are the refills, which comprise 15% of the total Rxs as of the week ending January 28. The number of refills demonstrates the satisfaction that patients and physicians are experiencing and is a very positive indicator of the long-term potential of Opzelura.

On Slide 9. What further excites us about the launch is the very positive feedback we are receiving from physicians who are prescribing Opzelura, which is supported by the most recent survey conducted in the field. Prescribers were asked how many atopic dermatitis patients they prescribed Opzelura to for the first time in the past month.

They were also asked how many new patients they expect to treat with Opzelura in the next month. Results showed that there is an increased willingness to prescribe Opzelura and physicians are highlighting the efficacy, specifically the rapid itch relief and skin clearance as well as the safety in a topical formulation as the top reasons for prescribing.

There are millions of AD patients living with uncontrolled disease in the U.S., and there is enthusiasm from both physicians and patients to try a new nonsteroidal topical treatment with a novel mechanism of action, with the expectation that patients will be able to find relief of their AD symptoms.

On the payer front, I'm happy to report that contract negotiations have been progressing well. We now have base rebate agreements signed with 2 of the 3 largest GPOs. These agreements establish utilization management criteria and discount rates for approximately 55% of commercial lives covered under these 2 PBMs.

For this non-NDC block business, PBMs and associated plans are now establishing policies to provide access to Opzelura. For the other 45% of covered lives under these 2 PBMs, we are in active contract negotiations to remove the new-to-market or NDC blocks. For the third PBM negotiations continue to advance. These are important steps towards gaining full coverage for Opzelura for the millions of patients whose prescription services are managed by these PBMs.

Turning to Slide 11. In the fourth quarter, our patient support program covered the vast majority of prescriptions, where we covered the full cost of Opzelura for many patients. As the coverage for Opzelura improves, the utilization of this specific program will decrease and will lead to an improvement in gross to net. Our co-pay mitigation program will continue and allow patients to lower their out-of-pocket cost to as little as $10.

In summary, the strong launch of Opzelura has been driven by several factors. The product has a unique profile unmatched by any other topical therapy for atopic dermatitis and we are launching into a market where there are millions of patients living with uncontrolled disease. Patients and physicians are reporting positive experience and are requesting refills, and this cycle is fueling much of the momentum behind the launch of Opzelura, which is on track to be a significant growth driver for Incyte.

Now turning to Jakafi. In the fourth quarter, Jakafi grew 15% year-over-year to $592 million. Patient demand continues to drive the uptake of Jakafi with robust new patient growth across all indications. In GVHD, patient growth was up 28% for the full year and up 39% in the fourth quarter, benefiting from the launch in the chronic setting and the transition of GVHD patients from our expanded access program to commercial product.

We expect growth of new patients to continue into 2022 and for the full year net product revenues to be between $2.3 billion and $2.4 billion. This guidance range takes into account the newly launched indication in chronic GVHD and the continued recovery of new patient starts.

And lastly, on Monjuvi, Minjuvi and Pemazyre. Monjuvi sales in Q4 were $24 million. We continue to make progress with penetration into key accounts and increasing uptake of Monjuvi in the second-line setting. Full year guidance for 2022 of $110 million to $135 million for net product sales as recorded by MorphoSys takes into consideration a continuation of the momentum in Q4, new account penetration and impact from COVID.

Minjuvi, which was approved in Europe in August of last year and was launched in Germany, net sales in the fourth quarter were $4 million. While it is still very early, we are encouraged by the initial uptake and expect Minjuvi to become a meaningful growth contributor as we continue to gain reimbursement in other European countries.

Pemazyre grew to $69 million in net sales in 2021, with $10 million coming from outside the U.S. In the U.S., new patient starts continue to grow with duration of therapy likely to drive performance.

With that, I'll turn the call over to Steven.

Steven H. Stein - *Incyte Corporation - Executive VP & Chief Medical Officer*

Thank you, Barry, and good morning, everyone. In 2021, we made significant progress across our development pipeline with multiple clinical and regulatory achievements. We announced 4 product approvals that include Jakafi in the United States for chronic graft-versus-host disease. Monjuvi in Europe for diffuse large B-cell lymphoma, Pemazyre in Europe and Japan for cholangiocarcinoma, and most recently, Opzelura in the United States for atopic dermatitis.

Further on the regulatory side, ruxolitinib cream is under review at both the FDA and EMA for vitiligo. Throughout the year, we delivered key clinical highlights as listed on the right, which include positive Phase III data for ruxolitinib cream in vitiligo and the initiation of a Phase III study evaluating parsaclisib in autoimmune hemolytic anemia following positive Phase II results.

We also signed a collaborative agreement with Syndax for axatilimab in chronic graft-versus-host disease which granted us the right to develop axatilimab as a monotherapy following treatment with Jakafi or in combination with the JAK inhibitor earlier in the treatment paradigm. And we shared data from our oral PD-L1 program, where we've demonstrated for the first time ever clinical activity with an oral PD-L1 inhibitor.

Moving to Slide 16. As I mentioned, the sNDA for ruxolitinib cream in vitiligo was accepted for priority review by the U.S. FDA with a PDUFA action date of April 18. Vitiligo represents another significant opportunity for our growing dermatology franchise. In the United States, there are currently 1.5 million people living with vitiligo and only 150,000 to 200,000 patients currently seek treatment due to a lack of effective treatment options.

The quality of life for some patients with vitiligo can be poor, with 1 in 4 patients reporting depression and 1 in 7 reporting anxiety due to their disease. Many vitiligo patients experience psychological, social and the physical impacts of vitiligo and represent the true unmet need where they may benefit from a new approved agent, like ruxolitinib cream.

Now to look more broadly at our dermatology franchise on Slide 17. Within our expanding dermatology portfolio, we are pursuing multiple additional indications with ruxolitinib cream, including pediatric atopic dermatitis and chronic hand eczema.

INCB54707, our JAK1 specific inhibitor, is being evaluated in vitiligo in patients with larger body surface area of involvement greater than or equal to 8%, and is also in Phase II studies for hidradenitis suppurativa and in prurigo nodularis. We expect results from the vitiligo and HS trials in the second half of this year. There is significant potential with each of these indications where there are limited treatment options, or in some cases, no FDA-approved treatments.

Slide 18 shows the opportunity for growth across our portfolio in MPNs and graft versus host disease. We expect an NDA submission in the first half of this year for once-daily ruxolitinib.

Within myelofibrosis, we have multiple strategies focusing on improving upon the standard of care by either addressing efficacy or safety. In patients who have an inadequate response to a single agent JAK inhibitor, combination therapy has the potential to improve efficacy, which we are pursuing through the addition of parsaclisib or a BET inhibitor. Our Phase III program evaluating ruxolitinib plus parsaclisib in inadequate responders and in the first-line setting for myelofibrosis is ongoing, and we expect results in 2023 for the suboptimal study.

For patients who are on sub-therapeutic doses due to anemia, these patients may benefit from the addition of an ALK2 inhibitor. We know that Jakafi has been a life-changing therapy for many patients with MF and PV. And we believe we can use our expertise in this area to provide additional options to patients. We continue to work towards addressing the unmet need in patients with graft-versus-host disease with Jakafi and other therapies including itacitinib, a JAK1 selective inhibitor, being evaluated in treatment-naive patients with chronic graft versus host disease. And as previously mentioned, axatilamab as monotherapy and potentially in combination with the JAK inhibitor.

Turning to Slide 19. A number of updates are expected this year for some of our earlier stage pipeline. We expect updated data from our oral PD-L1 program later this year, which could allow us to make decisions on indication and a lead program selection. Additionally, we expect data from the adenosine program for both our small molecule A2A/A2B antagonist and our CD73 monoclonal antibody later this year. As you can see on Slide 20, we're expecting multiple regulatory and clinical catalysts this year, and we look forward to another very exciting year ahead.

With that, I would like to turn the call over to Christiana for the financial update.

Christiana Stamoulis - *Incyte Corporation - Executive VP & CFO*

Thank you, Steven, and good morning, everyone. Our fourth quarter results reflect continued strong revenue growth with total product and royalty revenues of $813 million, representing an increase of 20% over the fourth quarter of 2020 and reflecting growth across products commercialized by Incyte and by our partners.

Total product and royalty revenues for the quarter are comprised of net product revenues of $592 million for Jakafi, $51 million for other hematology/oncology products and $5 million for Opzelura, royalties from Novartis of $96 million for Jakavi and $3 million for Tabrecta and royalties from Lilly of $66 million for Olumiant. This 15% year-over-year growth for Jakafi net product sales reflects higher patient demand across all indications.

The doubling of Olumiant royalties is driven primarily by the use of Olumiant for the treatment of COVID-19. As a reminder, for global net sales of Olumiant for the treatment of COVID-19, we are entitled to receive royalties equal to the base double-digit royalties applicable to all global net product sales, plus an additional 13% royalty. For the full year 2021, total product and royalty revenues were $2.9 billion and a 17% increase over 2020.

Focusing now on Opzelura for the fourth quarter, the launch and volume of prescriptions has been strong. While we are negotiating with PBMs and payers to get Opzelura on formularies and remove the NDC blocks, we have been utilizing patient support programs to cover the full cost of Opzelura so that patients have access to the product.

In the fourth quarter, Opzelura gross product sales of $58 million were reduced by 75% related to these patient support programs. In addition, other fees and discounts of 17% contributed to a total gross to net discount of 92% for the quarter. As a result of these reductions, net product sales for the quarter were $5 million.

Moving on to the -- our operating expenses on a GAAP basis. Ongoing R&D expenses of $345 million for the fourth quarter decreased 9% from the prior year period, primarily due to the ruxolitinib cream API-related costs incurred in the prior year quarter before Opzelura's regulatory approval. Ongoing R&D expense for the full year 2021 of $1.3 billion increased by 6% over 2020, primarily due to the progression of our pipeline.

Total R&D expense of $473 million for the quarter and $1.46 billion for the full year 2021 includes upfront consideration of $127 million for our collaborative agreement with Simdax. SG&A expense for the fourth quarter of $226 million increased 35% and from the prior year period, primarily due to our investments related to the establishment of our new dermatology commercial organization in the U.S. and the related activities to support the launch of Opzelura.

For the full year 2021, the 43% growth in SG&A expense was also primarily related to the commercialization of Opzelura. Our collaboration loss for the quarter was $8 million, representing our 50% share of the U.S. net commercialization loss for Monjuvi. For the full year 2021, the total collaboration loss was $37 million.

Finally, we ended the year with $2.3 billion in cash and marketable securities. Looking at the evolution of our P&L, you can see how over the past 3 years, the growth in our product and royalty revenues has exceeded the growth in our ongoing R&D and SG&A expenses, leading to increased operating leverage and reflecting our commitment to prudent management of our financial resources. As previously discussed, the uptick in expenses in 2021 reflects the build-out of our dermatology franchise and the Opzelura launch.

Moving on to 2022. I will now discuss the components of our guidance on a GAAP basis. For Jakafi, we expect net product revenues to be in the range of $2.3 billion to $2.4 billion, which at the midpoint represents an increase of approximately 10% over 2021 driven by continued growth across all indications.

We expect our gross to net adjustment for 2022 to be approximately 21%, reflecting expected continued growth in 340B volumes. As a reminder, the gross to net adjustments in the first quarter of the year is always higher relative to the previous quarter and subsequent quarters due to our share of the donut hole for Medicare Part D patients.

For other hematology/oncology products, which includes Pemazyre in the U.S., EU and Japan and Iclusig and Minjuvi in Europe, we are expecting total net product revenues to be in the range of $210 million to $240 million, which at midpoint represents approximately 23% growth over 2021.

Due to the early stage of its launch, we will not be providing guidance on Opzelura, but I will provide some additional color around Opzelura gross to net for 2022 in a moment. As in previous years, we are also not providing guidance for milestones or royalty revenues.

Turning to operating expenses on a GAAP basis, we expect COGS to range from 6% to 7% of product revenues. R&D expense is expected to be in the range of $1.55 billion to $1.59 billion, representing 18% growth at the midpoint versus 2021, excluding the impact of the Syndax upfront consideration in 2021. The growth rate primarily reflects expansion in our dermatology clinical development as well as investments in our LIMBER GVHD program, tafasitamab and our PD-L1 program.

We expect SG&A expense for the year to be in the range of $950 million to $1 billion, primarily reflecting continued support for the Opzelura launch. Excluding the impact of Opzelura-related cost, we expect SG&A expense to grow at a rate of less than 5%. With respect to our profit share for Monjuvi in the U.S., in 2022, we expect to be around breakeven.

As I previously mentioned, while we are not providing guidance for Opzelura due to the early stage of the launch, I would like to discuss what you could expect related to our gross to net adjustment in 2022. As we finalize coverage with payers, we expect gross to net for Opzelura to be relatively flat in Q1 compared to Q4 2021, begin to decline in Q2 and normalize at a fully loaded gross to net rate of 40% to 50% between Q3 and Q4, depending on the timing of the removal of NDC blocks by PBMs and the discontinuation of certain patient support programs.

Operator, that concludes our prepared remarks. Please give your instructions and open the call for Q&A.

QUESTIONS AND ANSWERS

Operator

(Operator Instructions) Our first question today is coming from Vikram Purohit from Morgan Stanley.

Vikram Purohit - *Morgan Stanley, Research Division - Equity Analyst*

Great. So I had 2 on Opzelura. The first on reimbursement progress. I wanted to see if the 40% to 50% gross to net that you just guided to for late '22 is expected to be the long-term gross to net you expect for the product. And secondly, while it's understandably early, I wanted to see what you might have learned on duration of use so far in terms of which areas of the body of patients find most suitable for the product and the speed at which patients who have received refills have been working through tubes.

Barry P. Flannelly - *Incyte Corporation - Executive VP & GM of North America*

Vikram, it's Barry. I can answer your first question. The 40% to 50% is what we say for this second half of the year. When things stabilize and we hope that continues into the future, I can't really predict what the future is going to bring after that. But certainly, we know that the value of the

product to patients, to physicians is high, and therefore, I think that we can continue to manage and work with the payers to make sure that we have a reasonable gross to net for the product.

The second question is just hard to predict. I mean patients are using the product everywhere. They're using it on their hands, their face. Obviously, a nonsteroidal product like Opzelura is good to use on sensitive areas, including the face and other sensitive areas. So I don't know. The refills are coming in. They're increasing each every month.

Obviously, as more and more patients come on, most of them have gotten one tube so far, and then perhaps 15% of them have gotten a refill and those refills will continue. We'll obviously have more data for you in the future, particularly about refills, and that's a very important component of our continued growth.

But as far as the areas of body they're using the drug on, I'm sure it's going to be all areas where they have continued problems with eczema and with atopic dermatitis.

Operator

Our next question today is coming from Brian Abrahams from RBC Capital Markets.

Brian Corey Abrahams - *RBC Capital Markets, Research Division - Senior Biotechnology Analyst*

Congrats on all the progress. Another question on Opzelura. Can you clarify how the patient journey and potential barriers to uptake and reimbursement might evolve as gross to net equilibrates by the back half of this year and you shift from the current patient support programs to the co-pay assistance? I guess I'm sort of wondering if we should expect any additional hurdles to adoption once we're through this initial launch period?

And then secondarily, maybe just asking the prior question a little bit differently, I guess I'm curious how the 15% refill rate aligns initially with your expectations for the number of tubes patients would use per year granted, obviously, early days.

Barry P. Flannelly - *Incyte Corporation - Executive VP & GM of North America*

As far as patient journey goes, I mean, obviously, there's millions of patients that have eczema, atopic dermatitis. Today throughout the United States, they've been cycling through low potency steroids, high-potency steroids and then TCIs. And so there, we don't really anticipate any future barriers whatsoever. We anticipate increased demand for the product, both from physicians and from patients because the more experience that they continue to have with the drug, the more happy they are with the drug. So while we -- I mean, this is common, in fact, for new products launching in areas like atopic dermatitis or psoriasis, to have a period of time where you're covering until coverage.

Sort of one of the things we like to say is that we're going to make sure that if a prescription is written by a dermatologist, by a dermatology office it's going to be -- the patient is going to be able to get it. And they're going to be able to get it now in the early periods of time with our help. But as coverage comes online, which is coming online every single day we expect that the gross to net will improve and that the barriers, if there is any barriers, will be removed.

As far as the refill volume, it's very early, and we actually think that this will continue. Patients are coming back all the time, and I think you'll see the refill percentage continue to increase with the new prescription volume. And obviously, as we move into vitiligo, things will even get better. We'll have even new Rxs going up and then those patients will be coming back for refills as well.

Operator

Our next question today is coming from Tazeen Ahmad from Bank of America.

Tazeen Ahmad - *BofA Securities, Research Division - MD in Equity Research & Research Analyst*

A couple from me on Opzelura as well. Can you give us any kind of color on where the use is coming from in the early days? Are these patients naive to any treatment before? Or are you seeing switches? And if you are seeing switches, where is that coming from? And then second question, as we think about when your gross to net will normalize towards the end of the year, how much do you think, at max, a patient will have to pay out of pocket beyond treatment? What kind of view do you have on elasticity of demand as it relates to what this co-pay should be? And can you give us an idea of what that range is?

Barry P. Flannelly - *Incyte Corporation - Executive VP & GM of North America*

Sure. So Barry, again. So the switches -- the vast majority of patients are coming off of steroids. They have been prior treated with steroids, but it's everything. In fact, patients who have been treated with Dupixent, with Eucrisa with TCIs, they're all coming off therapy or have been prior treated with those drugs and maybe they're not getting relief and now they're getting relief with switching to Opzelura.

So it's really mostly steroids, and that's what we expected because we think this is the perfect product for patients with atopic dermatitis from the beginning, from steroids all the way up to injectable biologics, and there's millions of patients right there that we can help with this drug.

The second part of your question was, oh, out of pocket. Well, I think what I said is that no patients will have to pay more than $10 out of pocket. What we expect, of course, is that more and more of the plans, their insurance, will pick up the cost of the drug. Some of them obviously have high deductibles, some of them have low deductibles, some of them just have a $10 co-pay when they're covered by commercial insurance. But patients will have to pay no more than $10, and that's what we guarantee. And to be quite honest, that's what many other drug companies do. They keep the out-of-pocket cost to patients low.

Now patients on different tiers tend to have a different co-pay and it could average at Tier 1 that they have a $10 co-pay or no co-pay, and then the average is somewhere between $60 to $70 if it's Tier 2 or Tier 3. It's the rare patient that really has a big, gigantic co-pay that we have to pick up.

Tazeen Ahmad - *BofA Securities, Research Division - MD in Equity Research & Research Analyst*

Okay. I'm asking just because as I think about your future gross to net, to the question that was asked earlier, could this be a potential driver of your desire to make sure that the out of pocket is no more than $10? Did that play a role potentially in making your gross to net in the future a bit more variable than what you expect it to be?

Christiana Stamoulis - *Incyte Corporation - Executive VP & CFO*

So Tazeen, the co-pay assistance is reflected in the 40% to 50% range at steady state that we have indicated.

Operator

Next question today is coming from Jay Olson from Oppenheimer.

Jay Olson - *Oppenheimer & Co. Inc., Research Division - Executive Director & Senior Analyst*

Maybe a big picture question. Since Incyte has made a lot of progress diversifying the product portfolio beyond Jakafi. I was wondering how much of a priority do you place on geographic revenue diversification, especially since you're expecting a lot of revenue growth from your dermatology business, which seems like mostly a U.S.-focused opportunity? Are there growth opportunities that you expect to expand your revenues beyond the U.S.?

Herve Hoppenot - *Incyte Corporation - Chairman, President & CEO*

Yes we do. Hervé here. If you remember a few years ago, we made that decision to go and build our own organization in Japan and Europe. And you can see the result of that is starting to emerge. So we have had Iclusig for a number of years, now we have Minjuvi and Pemazyre launching in Europe, so that will contribute to that diversification, and we launched Pemazyre in Japan, which is a small number to this day, but we have a development organization also in Japan.

As you know, we have partnerships in China that are very important and doing very well. And around, for the rest of the world, we are, in fact, as we speak, signing distribution agreements that will give us another layer of diversification.

So the map today for Incyte is a map that includes for every project, Japan, Europe and U.S. And we think it's very important from the development standpoint, because we know these studies are always applicable -- most of the time applicable across the world. And we intend to keep that for the next few years.

As the footprint for Incyte with a big question of China, where we have a number of products that are already partnered and we are looking at what we could do with some of the new pipeline products that we are developing for the future. So that's the picture we have.

And I think it's an important aspect of the risk of our portfolio is that it's not all based on the U.S. sales. Even if today, it's still a big majority of our business.

Operator

Your next question today is coming from Marc Frahm from Cowen and Company.

Marc Alan Frahm - *Cowen and Company, LLC, Research Division - Director*

Maybe just probe on the gross-to-net question a little bit more. Does that guidance some kind of the trajectory through the year contemplate the vitiligo indication? Or is that already kind of being baked into some of these contracts, the ability to launch that more rapidly in terms of your reimbursement and things? Or should we expect a lot of free drug to come in and maybe have to adjust that guidance begin once that label is issued ?

Barry P. Flannelly - *Incyte Corporation - Executive VP & GM of North America*

Sure, Marc, it's Barry. No, the guidance is included of vitiligo launch. Now when vitiligo is approved, of course, so we don't have to go back and do new contracts with the GPO/PBMs again for Opzelura. But each of the plans, because now you have hundreds of downstream plans, obviously, write their own utilization criteria and add the drug to formulary and that takes a little bit of time.

But other than that, the drug is available. It will be available to vitiligo patients that can prescribe it and it just has to take a little bit of time for the various plans to add it to their formulary or update their utilization criteria.

Marc Alan Frahm - *Cowen and Company, LLC, Research Division - Director*

Okay. Great. That's helpful. And then maybe just as a follow-up in terms of some of the marketing activities, you initially launched with samples, which -- I don't know if there's an update that you can provide on kind of the texture issue and the ability to relaunch those samples, and kind of the importance you see of getting those out there, Barry, and related to the marketing. On the guidance on the SG&A side, Christiana, before -- in previous -- prior conversations, you and Barry have talked about possible need for DTC ads here, is that already contemplated in the guidance or no?

Christiana Stamoulis - *Incyte Corporation - Executive VP & CFO*

So let me start with the last question, and then I'll turn it to Steven to give you an update on the texture issue. In terms of the SG&A guidance, it does reflect all costs associated with commercializing and marketing and supporting the Opzelura launch, so including DTC. Also one thing that I think is worth noting, as you look at the guidance that we have provided for SG&A and R&D, it covers costs associated with both Heme/Onc as well as dermatology.

So the SG&A guidance fully reflects costs associated with Opzelura. However, when you look at the revenue guidance that we have provided, there, we have provided guidance on just the Heme/Onc part of the business, including MPNs. So you have part of the picture, you don't have the other part in terms of the Opzelura as well as royalties and milestones.

Steven H. Stein - *Incyte Corporation - Executive VP & Chief Medical Officer*

Marc, it's Steven. On your texture issue. So as you heard, we're in the midst of a very successful launch, and we've been able to maintain a healthy commercial supply for that. Additionally, as we said, for vitiligo, the PDUFA date is April 18. And obviously, we want to have a very healthy commercial supply for that as well. Given that, at the current time, the manufacturing of samples will have to wait a little bit later on. We want to get it done as soon as possible, but we're focusing on the commercial supply.

We knew early on in terms of the texture that this was due to an extremely small amount of crystal formation that we know is ruxolitinib. It's API that has come out of solution, and we've been focusing on process improvements that will improve solubility and avoid this issue.

Some of these changes are feasible within the NDA specifications and it can be implemented immediately, and some require regulatory back and forth and submissions and wait for the FDA approval to implement. But at the present time, we've been able to maintain a very healthy commercial supply and we'll continue to, with the focus on both AD and the upcoming vitiligo, and then as soon as possible thereafter, manufacture samples as well.

Operator

Our next question today is coming from Cory Kasimov from JPMorgan.

Unidentified Analyst

This is Tiffany on for Cory. Just one other one on Opzelura. How confident is Incyte in reversing the NDC block for the second major payer plan? And in case that, that block isn't removed, can you speak to the potential future impact on sales that you might anticipate?

Barry P. Flannelly - *Incyte Corporation - Executive VP & GM of North America*

Well, we're very confident. This is Barry again. So we're very confident in removing the NDC blocks. We're in active advanced negotiations with them. The first part is signing the base agreements. So to get all of the contract specifications locked up. So we know how to proceed going forward,

knowing what the base rebates are, what the rebates would be for, for example, if there is 1 step, 2 steps, that sort of thing, it's a sort of a menu approach.

So the team is actively negotiating right now. We're very confident. There's a great demand for this drug. There's a great push from the downstream plans. As you know, all these PBMs aren't just working for one insurance company, they're working for many insurance companies. They're getting contracts for many insurance companies.

And many of those have already established and put Opzelura on formulary and establish utilization criteria. And of course, they're not getting any rebate now they're paying at WAC. So they're pushing to get all of the NDC blocks removed.

And even when patients have an NDC block, you can still overcome that NDC block with a prior approval and a medical exception. So other companies live with NDC blocks forever because they might not be able to negotiate with 1 or 2 particular PBMs, we're very confident that we're going to be able to do this because of the value proposition offers both to patients and physicians, but also to the payers themselves because this is an effective therapy that most patients who are treated, 88% of them, are clear -- become clear over time, and therefore, they don't need any other therapy. So it's really the value proposition that will make them want to have this product on formulary under contract and to be able to get their rebate and fees that they desire.

Operator

Your next question is coming from Michael Schmidt from Guggenheim Securities.

Kelsey Beatrice Goodwin - *Guggenheim Securities, LLC, Research Division - Associate*

This is Kelsey on for Michael. Another one on Opzelura. I guess, clarifying on a prior question, what did you say was the anticipated contracting process for the label expansion into vitiligo? And then regarding the sales force, I guess, what's being done there to kind of prepare for the launch?

Barry P. Flannelly - *Incyte Corporation - Executive VP & GM of North America*

The contracting -- well, what I explained before is we don't need to go back to the PBMs that we already have contracts with and the PBMs that were -- and GPOs that we're currently contracting with for the full NDC block as vitiligo will be included in that process. But the whole step process is that then the downstream plans across the country just have to add it to their formulary. So that's just a P&T committee decision.

Our market access team works with all of those plans across the country to get that on formulary and have utilization criteria in place as soon as possible after launch. In fact, they can work with them now, talk about the TRuE-V1 data for the vitiligo indication, and hopefully, very soon after launch, all of them will have the drug on the formulary. So we don't have to go back to the PBMs, GPOs again for vitiligo.

As far as the sales force is getting ready, it is tricky. I have to admit. We're concentrating on accelerating the AD launch. It's going very well. Everybody is very excited about it. But of course, we have a dedicated team working on the vitiligo launch. To be honest, we work with our advocacy groups, our patient groups that are very interested in getting a drug approved for vitiligo.

There's been a great deal of interest, both from payers, dermatologists. What really helped was the patient-focused drug development meeting that the FDA held on vitiligo and emphasized the great need for a treatment like Opzelura for vitiligo because these patients are really suffering. And this is the first true drug that can re-pigment the skin and hopefully improve the quality of life for them.

And it's the same sales -- and if you're what you're asking is the size of the sales force. It's the same sales force, it's the same number of people going to see the same dermatologist. So there's no expansion there. Of course, there's some investments in advertising and promotion, but that's already figured in the SG&A that we laid out for this year.

Operator

Your next call is coming from Ren Benjamin from JMP Securities.

Reni John Benjamin - *JMP Securities LLC, Research Division - MD & Equity Research Analyst*

An outstanding quarter and congratulations on the guidance going forward. A couple of questions for us. If we think about once-daily rux in the NDA submission, can you just remind us, do you think it's just a 12-month review? And then maybe more importantly, does it find its way to the market right away? Or is this something strategically you might wait until the twice-daily patent expiration nears? So just a strategy update there.

And then the second question, as we think about Minjuvi's launch in Europe, so Germany is on board, can you talk about how the rest of the rollout might occur throughout Europe? And I noticed with peak revenues, you kind of don't have any from Minjuvi in Europe, I'd love to get a sense as to why that is or how you're thinking about peak revenues.

Steven H. Stein - *Incyte Corporation - Executive VP & Chief Medical Officer*

Ren, it's Steven. I'll start on your first question related to the regulatory review of once-daily Rux. So just to remind you, we completed bioavailability and bioequivalence work. We're within the FDA specifications for that and then the different strengths have put down in stability. As soon as that completes, we will file the first half of this year. We expect a 10-month review, a standard review. So it's likely to be right at the end of this year, early next year that we get a regulatory action related to that, just to clarify that time. As for the launch dynamics there are.

Herve Hoppenot - *Incyte Corporation - Chairman, President & CEO*

Yes, I can speak about that. I mean -- so as you have seen, I mean, the uptake in Germany specifically has been very good. So there is a sense that the launch is doing well when it's taking place. And as usual, in Europe, as you know, we have to go through reimbursement across a number of countries. So what you will see over the next months are new countries where we are launching coming on board. And hopefully, the same type of dynamic taking place there.

Now peak for Minjuvi, we never disclosed it. As you know, in Europe, prices or net prices are somewhat lower than what we have in the U.S., but volume tends to be higher because of universal access. And so we think at the end of the day, the potential for Minjuvi is meaningful, and it will be a key contributor for us. As you know, we are not booking revenue in the U.S., but we are in the rest of the world. So that would contribute to our net product revenue growth over the next year.

Reni John Benjamin - *JMP Securities LLC, Research Division - MD & Equity Research Analyst*

Got it. And just to clarify, regarding once-daily Rux, does that -- once you get -- plus hopefully an approval, does that hit the market right away? Or is that something that you hold back on until later?

Herve Hoppenot - *Incyte Corporation - Chairman, President & CEO*

I think -- as you know, the once daily Rux, the key aspect of it is the ability to combine with once-daily products that are also used in myelofibrosis, so that's the key strategic aspect. Tactically, will we launch it the day we get approval or will there be a delay, we frankly don't know yet. So I want to give you a precise information on that because we are looking at what it would -- what kind of impact it could have to the overall Jakafi business.

And obviously, we don't want that impact to be negative. So we are looking at it. But I think it could be something that would be available certainly in the years following the -- from today, but it may be at the time of approval or a little later, depending tactically on what's best for the franchise.

Operator

Your next question is coming from Matt Phipps from William Blair.

Matthew Christopher Phipps - *William Blair & Company L.L.C., Research Division - Senior Biotechnology Research Analyst*

I'll have another one on the LIMBER program, but the ALK2 combination, what are you really looking for with the update later this year? Is it primarily going to focus on change in hemoglobin levels? Or can we expect some conversion of patients to transfusion independent and maybe compare that to what we saw recently with the momelotinib their results?

Steven H. Stein - *Incyte Corporation - Executive VP & Chief Medical Officer*

It's Steven. I'll take your question. So just to remind, as part of LIMBER, there are multiple aspects. There's a formulation work we just spoke about with the once daily formulation. And then the different combinations, the most advanced of which is the parsaclisib in the suboptimal and first-line settings, which is in pivotal studies, and then our BET and ALK2 program.

For ALK2, we're tremendously excited by it because it's a specific potent inhibitor of ALK2 as opposed to momelotinib, which you mentioned, which is probably a weaker JAK inhibitor with this off-target ALK2 effect, but does seem to alleviate anemia there and that's why we're so excited for this program.

What we're in at the moment is the monotherapy safety and dose escalation. And already with that we've seen in iron kinetics and hepcidin that are favorable. So hepcidin is decreasing, so we know it's working through the mechanism of action we wanted to work. And the iron kinetics are going the way we want. Over time, that should translate to a hemoglobin increase, and that's what we'll be trying to demonstrate this year.

With that, we'll have proof of concept and we'd go very quickly to a Rux combo. We'll be doing Rux/ALK safety anyway. And that combination's promise is twofold or maybe even threefold.

So one, it will address potentially the underlying anemia for myelofibrosis itself -- and then we know for ruxolitinib, while an incredibly effective drug, about 20%, 25% of patients tend to have anemia with the drug and sometimes discontinue or can't tolerate high doses because of that.

So alleviating the anemia of the underlying disease, alleviating the anemia from Rux will allow you to maintain Rux dose intensity as well and translate also to a better efficacy. So we believe the promise of that combination is large, and we want to get a lot more both safety data this year plus iron, hepcidin and hemoglobin data as well. Thanks.

Operator

Our next question is coming from Salveen Richter from Goldman Sachs.

Matthew Michael Dellatorre - *Goldman Sachs Group, Inc., Research Division - Research Analyst*

This is Matt on for Salveen. Congrats on the quarter. I just had 2 quick questions on Opzelura. First, I just want to confirm that you expect agreements with the third PPM -- third PBM to be finalized this year? And do you have any expectations on the timing of that? And then secondly, could you discuss the chronic hand eczema opportunity? What kind of potential dosing would you expect there? And you're starting a Phase III this year, should we expect data before year-end?

Barry P. Flannelly - *Incyte Corporation - Executive VP & GM of North America*

Sure. So I'll answer the first part of the question, maybe Steven can jump in a little bit on chronic hand -- so yes, we expect all of the agreements that I discussed, the third PBM coming on board this year and then the NDC blocks removing for all of the PBMs this year. So that's what our expectation is. Chronic hand eczema, I think it is an opportunity for us. It's a severe disease. It's difficult to handle, and I think it will demonstrate the effectiveness that Opzelura really provides to these patients.

Steven H. Stein - *Incyte Corporation - Executive VP & Chief Medical Officer*

Yes. Just maybe a little more color on that. Thanks, Barry. Obviously, it's within label to treat any part of the body, as Barry said, upfront, although there's a very distinct clinical entity where patients can get severe involvement of their hands only and there's a contact aspect to that in terms of contact dermatitis in the hands. And you've seen it become quite prevalent during the pandemic, during COVID where people, and particularly physicians and other health care providers, wearing gloves, where you see a lot more hand eczema.

So the idea is that the separate opportunity gets addressed as a stand-alone indication that we generate robust clinical data. We expect the study to enroll through this calendar year 2022, and then have data for you in 2023. And that's the premise behind studying that condition.

Operator

Our next question is coming from Kripa Devarakonda from Truist Securities.

Srikripa Devarakonda - *Truist Securities, Inc., Research Division - Associate*

Have a question about the guidance for Jakafi. The midpoint guidance implies year-over-year growth, but it's sort of flattish versus the 4Q run rate. Middle of 2021, you talked about how you were going to implement and you executed on a strong recovery in the second half of 2021. I was wondering if there are any metrics or any implementations that you did in the second half that you can expect to leverage in this year to provide additional growth with Jakafi. And also in that vein, can you maybe talk about your level of comfort in the long-term guidance you gave for Jakafi?

Christiana Stamoulis - *Incyte Corporation - Executive VP & CFO*

So let me start and Barry can add here. But when you look at the 2022 guidance range that we provided for Jakafi is $2.3 billion to $2.4 billion. So if you look at the high end of the range, implies a 12% year-over-year growth or in dollar terms, incremental revenues of $265 million relative to 2021.

So that level of incremental revenue growth is very much in line with the growth we've been seeing pre-pandemic. And that reflects and assumes continued growth across all indications and especially GVHD, where we have the most recent approval for chronic GVHD use. The low end of the range reflects the uncertainty around COVID-19 and how these may play out in the year, but that's how -- what is really reflected by the 2 ends of the range.

Barry P. Flannelly - *Incyte Corporation - Executive VP & GM of North America*

Yes. And just to add to it. I mean we are very happy with the new patient starts, actually, that recovered throughout 2021, especially in Q4. Obviously, the chronic GVHD launch is a big factor in that. And even the benefit for patients with chronic GVHD has sort of a halo effect over the rest of the indications. So as Christiana said, the low end of guidance is simply the uncertainty over COVID.

Last year, we thought things were getting better in the summer moving into fall, and then we had Omicron hit. And so -- we're fully expecting to have a good COVID-free, hopefully, year coming forward so that patients do not stay away and that our field force can have access to the offices, which oncology offices tend to close down.

But as far as what's happening with the rest of the indications for Jakafi, as I said, chronic GVHD, growing very well. Myelofibrosis patients, in fact, we believe that physicians are starting myelofibrosis patients earlier now just because of the survival benefit that Jakafi offers to MF patients, PV patients are staying -- the duration of therapy continues to increase. So we hope, we expect, that the MF, PV and GVHD growth will continue.

The high growth of GVHD in the fourth quarter, obviously, was a little affected by the expanded -- patients on our expanded access program that gets switched over to commercial. But nevertheless, we fully expect Jakafi to continue to be the standard of care in steroid, refractory, acute and chronic GVHD. And of course, it's life-saving potentially can extend life for myelofibrosis patients and provide a great quality of life, a better quality of life for patients with polycythemia vera.

Herve Hoppenot - *Incyte Corporation - Chairman, President & CEO*

Yes, for the long-term guidance, we are very much in line. I mean this is -- it's getting closer and closer. And if you remember, the long-term guidance applies to the franchise. So it would -- in the situation where we would have new products being launched in the next few years, it will be -- it's included in the $3 billion guidance we gave in the past.

Srikripa Devarakonda - *Truist Securities, Inc., Research Division - Associate*

Great. And if I can ask a pipeline question. I know you recently opted out of the CD137 PD-L1 bispecific, but we still see collaboration candidates, multiple I-O candidates listed as part of your pipeline. Is there an expectation to provide big picture strategy on how you plan to develop the I-O platform this year at some point?

Steven H. Stein - *Incyte Corporation - Executive VP & Chief Medical Officer*

Yes. Kripa, it's Steven. Whether we conduct an R&D day or not, we'll wait to tell you on that. I'm not sure we've decided. Just in terms of the IO platform, as we alluded to in the prepared remarks, the oral PD-L1 program is at a very exciting stage of development. We have 3 products in the clinic, all of whom have shown clinical activity. The 2 other products behind 550 have no peripheral neuropathy, and we want to make further decisions this year.

We also have an exciting adenosine program, both the small molecule A2A/A2B antagonist and a CD73 antibody, which is also going through the clinic this year. And then our LAG-3 program.

The field has been sort of reignited beyond checkpoint alone now with data on LAG, TIGIT and potentially TIM-3 as well, and there'll be some moving targets and we'll give more clinical plans when we're ready to share them. But we are -- we have a very healthy I-O pipeline. We're positioned in all those areas well and stay tuned on the oral PD-L1. I'll just leave it at that.

Operator

Our final question today is coming from Maneka Mirchandaney from Evercore ISI.

Maneka Mirchandaney - *Evercore ISI Institutional Equities, Research Division - Analyst*

Great. Just a follow-up on one of the prior Opzelura questions. In your discussions with payers so far, are you seeing requirements for step through more than just topical steroids? In some of the prior auths we found it looks like some plans are acquiring a second agent as well, but just curious

what you're seeing more broadly. And then just to clarify for the 17% in other deductions, what are those? And do you expect going forward in the coming quarters?

Barry P. Flannelly - *Incyte Corporation - Executive VP & GM of North America*

Sure. As far as step therapies go, they vary. Like I said, there's millions of patients that have been treated already with topical steroids, calcineurin inhibitors. They'll continue. Some will have 1 step, some will have 2 steps. Some will just be 2 topical therapies, which may be a low-potency steroid and a high-potency steroid. The other part of the question, you...

Christiana Stamoulis - *Incyte Corporation - Executive VP & CFO*

Yes, I can take the second part. In terms of the 70%, there you have other discounts and fees, distribution of fees and related discounts that we may be providing as well as the co-pay assistance for that bucket as well.

Operator

We have reached end of our question-and-answer session. I'd like to turn the floor back over to Christine for any further closing comments.

Christine Chiou - *Incyte Corporation - Head of IR*

Thank you all for participating in the call today and for your questions. Greg and I will be available for the rest of the day for follow-up. Thank you, and goodbye.

Operator

Thank you. That does conclude today's teleconference and webcast. You may disconnect your line at this time, and have a wonderful day. We thank you for your participation today.
