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INCY.OQ - Q1 2023 Incyte Corp Earnings Call

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OVERVIEW:

INCY reported 1Q23 total product revenues of $693m.

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PRESENTATION

Operator

Hello, and welcome to the Incyte First Quarter 2023 Earnings Call and Webcast. (Operator Instructions) As a reminder, this conference is being recorded. It's now my pleasure to turn the call over to Christine Chiou, Head of Investor Relations. Please go ahead, Christine.

Christine Chiou - *Incyte Corporation - Head of IR*

Thank you, Kevin. Good morning, and welcome to Incyte's First Quarter 2023 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 Herve, 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 Herve.

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

Thank you, Christine, and good morning, everyone. So we'll be moving to Slide 4. And -- so in the first quarter, product revenue grew 14% year-over-year. The growth for the quarter does not fully reflect the strength of the underlying patient demand for Jakafi and Opzelura, which I will discuss in the next slide.

In hematology and oncology, the ongoing launches of Pemazyre and Minjuvi ex-U.S. drove the 17% year-over-year of growth. We also received additional approvals, including our first indication for Zynyz in Merkel cell carcinoma in the U.S. and more importantly, the approval of Opzelura for vitiligo in Europe with an excellent level.

Zynyz is available commercially in the U.S. and Opzelura will be launched in Europe in the next few months, starting with Germany.

Moving to Slide 5. Taking a closer look at the Q1 dynamics that affected net sales in the quarter for Jakafi and Opzelura. Jakafi patient demand was strong across all indications, growing 7% on a year-on-year basis. On gross to net, we have the typical Q1 negative effect with higher deductions due to an increase in Medicare coverage, gap rebates and patient deductibles.

We also had an increase in 340B purchases. Separately, channel inventory fell below normal level, resulting in an $11 million impact. Given the strong underlying patient demand, we are confident in our full year outlook and are raising the low end of our guidance to a new range of $2.55 billion to $2.63 billion for the full year.

Turning to Opzelura. There are 3 components to fully understand the dynamics of the first quarter. First, we saw a continuation of strong trends in weekly prescription growth in the quarter. 60,000 new patients were treated with Opzelura.

Second, as you can see in the TRx graph on the right, refills were being pulled forward in December, and this resulted in lower volume in the first 2 months of the year. And third, net price in the quarter was impacted by an increase in commercial co-pay and a higher Medicaid utilization.

So the outlook is strong for both Jakafi and Opzelura as we expect to drive further growth throughout the year.

Moving to Slide 6. With our R&D pipeline growing and advancing, we have recently decided to concentrate our resources behind the project with the highest potential to drive our revenue growth in the next few years. These eight programs of first or best-in-class candidates have large potential with multiple indications, such as Opzelura, Povorcitinib and oral PD-1 -- or PD-L1 or alternatively, they address a significant unmet need in an existing franchise like the LIMBER program with ALK2, BET, Axatilimab, mCALR.

We are discontinuing 6 programs, including Parsaclisib in MF and warm autoimmune hemolytic anemia, AXL/MER to adenosine program and GITR. This concentration of our internal and external resources will increase speed and efficiency for the 8 high potential programs and allow us to further accelerate our promising early clinical programs like CDK2, TGFβR2xPD1, bispecific and Auremolimab.

With that, I would like to pass the call to Barry.

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

Thank you, Herve, and good morning, everyone. Turning with Jakafi on Slide 8. Patient demand for Jakafi was strong across all indications. New patient starts, which are a strong leading indicator for growth in future quarters grew 8% year-on-year to reach an all-time high.

Unit demand, as shown by the chart on the bottom left shows good growth in Q1 versus the past 2 years.

Turning to Opzelura. Net sales in the quarter were $57 million. On the right, our total prescriptions as reported by IQVIA. Launch trends continue to be strong with robust growth seen in both March and April. As we continue to drive further awareness and adoption of the brand, the number of dermatologists gaining experience with Opzelura continues to increase.

Turning to Slide 10. I want to take a step back and recognize the significant achievements we have been able to accomplish with the launch of Opzelura. When reflecting on the first 18 months of launch, Opzelura outperformed other brands prescribed by dermatologists on a launch-aligned basis. The rapid adoption of Opzelura highlights its compelling product profile and its ability to address significant unmet needs. In addition, we were able to secure payer access far quicker than any other recent launches in dermatology.

Looking at Slide 11. The momentum with Opzelura is strong, and we are continuing to see very positive trends in terms of uptake, awareness and reception for the brand in Vitiligo. We launched our first TV direct-to-consumer campaign for vitiligo on February 12 this year, and early data supports the success we've had in just a few weeks.

Based on a survey conducted of approximately 100 dermatologists, NPs and PAs, they indicated that nearly 20% of their vitiligo patients requested Opzelura and that 85% of those patients request are filled. This level of brand awareness and patient activation is substantially higher than almost every other product in dermatology offices. And with our continued efforts, we believe we can reactivate a significant percentage of the diagnosed vitiligo patient population.

Turning to Slide 12. Opzelura uptake in atopic dermatitis is driven by its efficacy and in particular, by the impact on itch. This is the clear differentiator for the brand, and Opzelura is the only topical therapy with itch reduction in its label.

To understand how quickly Opzelura can work in some patients, this past weekend, at the revolutionizing atopic dermatitis meeting, we presented data from our scratch AD study. Results showed that patients were able to attain substantial itch reduction as early as 15 minutes after the first application of Opzelura and peak reduction after 4 hours.

We continue to focus our efforts on driving refills and have implemented several new initiatives to further grow the brand. Some of these programs include patient relationship and support programs as well as partnering with pharmacies to help with the education and to drive patient adherence.

And lastly, on Monjuvi, Minjuvi and Pemazyre on Slide 13. Monjuvi sales in the quarter were $21 million, up 11% year-over-year with community accounts making up the majority of the volume. Minjuvi sales were $7 million, and the product is now reimbursed in 6 key launch markets in Europe. Pemazyre grew to $21 million in net sales in Q1 with $5 million coming from outside the U.S., where the launch is now ongoing in 10 key markets in Europe.

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

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

Thank you, Barry. On Slide 15 is a snapshot of a few of our programs, including our high potential programs as depicted in the red and blue boxes, segmented by estimated launch timing. Over the next 6 to 18 months, many of these programs will be expanding into new indications, new combination studies and into pivotal trials.

By focusing resources on these assets, it could allow for an acceleration of certain timelines and increased efficiency as we bring these innovative therapies to patients. We are well positioned for growth and diversification with multiple launches expected in the near to midterm.

Moving to Slide 16. We made significant progress across our high-potential dermatology programs. Opzelura was approved for vitiligo in Europe, and we presented new data for both Opzelura and Povorcitinib at 2 major dermatology conferences. We also progressed into new indications, including prurigo nodularis with Opzelura and asthma and chronic spontaneous urticaria with povorcitinib.

Now to highlight our dermatology portfolio in more detail, starting with Opzelura and the recent European approval on Slide 17. The label was very favorable with regards to both efficacy and safety. The full indication is for the treatment of nonsegmental vitiligo with facial involvement in adults and adolescents from 12 years of age upwards.

This encompasses the majority of vitiligo patients in Europe, where roughly 85% of all vitiligo patients have nonsegmental disease and where around 60% to 80% of facial involvement. Regarding safety, the most common adverse reaction was application site acne. No black triangle was placed on the label and the regulatory agency determined that the class effect identified for the oral class were not considered relevant for Opzelura.

And as such, the label does not include any special warnings or precautions as seen with the oral JAK inhibitors.

Turning to Slide 18. We recently initiated 2 Phase III studies evaluating Opzelura in prurigo nodularis, a disease driven by inflammation and characterized by hard modules and an intense itch. TRuE-PNI and PN2 are 52-week studies where patients will receive ruxolitinib cream or vehicle for 12 weeks, followed by a 40-week open-label extension.

The primary endpoint is WI-NRS, which is defined as a 4-point or greater improvement in worst-itch numerical rating scale score from baseline to week 12. There is a strong rationale for Opzelura in prurigo nodularis where we have seen promising early data and where there is already a regulatory precedent for approval with clearly defined endpoints.

With no topical or oral therapies approved, we have a significant opportunity to help a large population of patients who are suffering from this disease.

Turning to Slide 19. We continue to expand the development of Opzelura into new indications, which has the potential to provide significant value as either the first approved therapy or first topical therapy for patients living with these dermatologic conditions.

Moving to Povorcitinib on Slide 20. We recently presented positive Phase II results at the American Academy of Dermatology Annual meeting, highlighting the effect of Povorcitinib on repigmentation in patients with extensive vitiligo. Substantial repigmentation was seen with Povorcitinib treatment and continue to improve with longer duration of therapy with up to 36% of Povorcitinib-treated patients achieving a facial VASI75 by week 36.

Based on these positive Phase II results, we plan to move into Phase III development. Being able to provide patients with an effective oral therapy to treat their vitiligo is part of our strategy to strengthen our leadership in vitiligo and to be able to provide multiple treatment options for patients across the entire disease spectrum.

On Slide 21, at the European Hidradenitis Suppurativa Foundation Conference, we presented Phase II data showing that 52% to 56% of patients treated with Povorcitinib achieved a HiSCR50 at week 16. Perhaps even more impressive was that up to 29% of patients on Povorcitinib reached HiSCR100 at week 52, which is a 100% reduction in abscess and nodule count, with no increase in abscess or draining tunnels relative to the baseline.

This is a very high clinical bar of efficacy. We were the first to ever present the achievement of HiSCR100 in HS. Based on the Phase II results, we initiated 2 Phase III trials: STOP-HS1 and STOP-HS2.

Similar to ruxolitinib cream, we are building a portfolio for Povorcitinib around the science all while leveraging our extensive dermatology capabilities. As mentioned earlier, we are initiating 2 phase trials in moderate to severe asthma and chronic spontaneous urticaria. Given what is known about the involvement of the JAK pathway in the regulation of cytokines and Th2 cells, initiating a study in asthma is a logical next step for the development of Povorcitinib.

Likewise, we know JAK inhibition can modulate mast cell activation, including degranulation and cytokine production, both of which are drivers of chronic spontaneous urticaria.

Moving to our hematology and oncology portfolio on Slide 23. Looking at our high-potential oncology programs, we continue to make progress in myeloproliferative neoplasms, or MPNs, with our ALK2 and BET program and axatilimab in chronic graft-versus-host disease.

Our small molecule oral PD-L1 program is advancing into multiple Phase II studies in combination with adagrasib, ipilimumab and axitinib. For our early-stage assets, we recently presented data at the American Association for Cancer Research Annual Meeting for CDK2 and our newly disclosed bispecific TGFβR2 x PD1 antibody.

And lastly, we recently announced the approval of Zynyz for Merkel cell carcinoma, which is currently in Phase III trials in squamous cell anal carcinoma and non-small cell lung cancer.

Turning to Slide 24. We have several programs progressing in MPNs in graft-versus-host disease. Zilurgisertib is in dose escalation. We are currently at doses of 400 milligrams once daily in combination with ruxolitinib, and we were adding a treatment arm for newly diagnosed patients. We continue to see signs of clinical activity, including decreased levels of hepcidin as well as hemoglobin responses with no dose limiting toxicities to date.

For our BET inhibitor, dose escalation is ongoing, where we are currently at doses of 6 milligrams once daily in combination with ruxolitinib. In monotherapy and in combination therapy, we have seen reductions in spleen length and volume as well as improvements in both symptoms and hemoglobin, suggesting 57643 is an active compound.

INCA33989, our mutant CALR antibody is on track to enter the clinic later this year. And the study evaluating Cellenkos' CK0804 in combination with ruxolitinib continues to progress.

Lastly, we expect results from the AGAVE-201 study later this year. Before moving on to the next slide, I did want to speak briefly on the CRL for ruxolitinib XR. The FDA determined that while bioequivalence was achieved in the area under the curve or AUC they had questions around Cmin and its correlation with efficacy. We will work with the FDA to determine the appropriate next steps and we will provide an update at that time.

Turning to Slide 25. Preclinical data from our CDK2 and TGFβR2 x PD1 bispecific. INCB123667, a selective oral small molecule CDK2 inhibitor, is in a Phase I dose ranging study in advanced solid tumors. CDK2 in complex with Cyclin E is a cell cycle regulator, which, when inhibited, has been shown to suppress tumor growth, mainly in Cyclin E high tumor models in vivo.

On the right is INCB33890, a TGFβR2 x PD1 bispecific, which has been engineered to avoid the known toxicity of broad TGF-beta pathway blockade. 33890 has a tenfold higher affinity for PD-1 and TGFβR2 and blocks TGFBeta signaling in cells co-expressing PD-1, thus potentially protecting normal tissue. Preclinical in vivo data presented at AACR showed that 33890 has a greater antitumor effect and individual benchmark antibodies or a simple combination of these.

Turning to Slide 26. For the remainder of the year, we expect numerous data readouts and important strategic decisions for many of our high potential programs, and we look forward to updating you throughout the year.

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 first quarter results reflect continued strong revenue growth with total product revenues of $693 million, representing an increase of 14% over the first quarter of 2022.

Total product revenues are comprised of Jakafi, other hematology/oncology products, which include Iclusig, Pemazyre, Minjuvi and Opzelura. Jakafi net product revenues for the first quarter were $580 million, which reflects continued growth in patient demand across all indications, partially offset by higher gross to net deductions as a result of both contributions to close the Medicare gap and commercial copay assistance in line with prior year's first quarter as well as an increase in 340B.

The quarter was also negatively impacted by lower than normal channel inventory at quarter end due to the timing of certain customer purchases. Other hematology/oncology net product revenues were $57 million, representing a 17% increase compared to the first quarter of 2022 driven by

patient demand, partially offset by unfavorable changes in FX rates. On a constant currency basis, the other hematology/oncology net product revenues grew by 22% over the prior year period.

Finally, Opzelura net product revenues for the quarter were $57 million, representing a 4.5-fold increase year-over-year driven by increased patient demand and expanded coverage. This year-over-year growth was partially offset by an acceleration of refills at the end of last year and by higher gross to net deductions as a result of higher Medicaid utilization and higher commercial copay assistance, which is a typical Q1 dynamic.

Turning to royalty revenues. Total royalty revenues for the quarter were $115 million and are comprised of royalties from Novartis of $77 million for Jakavi and $4 million for Tabrecta and royalties from Lilly of $34 million for Olumiant.

Jakavi and Olumiant royalties for the quarter were negatively impacted by FX headwinds, while Olumiant royalties were also impacted by a decrease in net product sales of Olumiant for use as a treatment for COVID-19. Excluding the impact of COVID-19-related sales and currency fluctuations, Olumiant royalties increased 37% compared to the prior year period.

Moving on to Slide 30, our operating expenses on a GAAP basis. Ongoing R&D and total R&D expenses were $404 million and $407 million respectively, for the first quarter. Total R&D expenses increased 15% year-over-year, driven primarily by the progression of our pipeline including the expansion of the clinical development program evaluating ruxolitinib cream in additional indications and the progression of Povorcitinib into pivotal studies, and were partially offset by lower upfront and milestone expenses in 2023.

Total SG&A expenses were $316 million for the first quarter. SG&A year-over-year growth was driven primarily by promotional activities launched at the beginning of the year to support Opzelura in AD and in vitiligo and the timing of certain other expenses.

Moving on to our guidance for 2023. As a result of Jakafi's strong demand growth, we are raising the bottom end of our full year Jakafi guidance range of $2.53 billion to $2.63 billion to a new range of $2.55 billion to $2.63 billion. We are reaffirming our other hematology/oncology revenues COGS, R&D and SG&A guidance for the year.

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

QUESTIONS AND ANSWERS

Operator

(Operator Instructions) Our first question is coming from Salveen Richter from Goldman Sachs.

Salveen Jaswal Richter - *Goldman Sachs Group, Inc., Research Division - VP*

Two questions here for me. One is, given the first quarter headwinds for Opzelura, where you saw an increase in commercial co-pay and higher Medicaid utilization, which led to the higher gross to net. How should we think about the gross to net for the rest of 2023?

And maybe you could discuss the disconnect with IQVIA scripts and whether this is driven purely by higher Medicaid utilization? And then secondly, with regard to the CRL for QD Jakafi, what is your view on the base case on the path forward here? And how does this impact the combo program with BET and ALK2 in terms of your registrational path? Would you run a Phase III combo with BID Jakafi and then do bridging studies? Or is there -- or does the path you have ongoing kind of still stand and afford?

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

Salveen, it's Christiana. Let me take the first 2 questions on gross to net and IQVIA, and then I will turn it to Steven. First of all, regarding Opzelura gross net, there were 2 main factors that impacted gross to net in Q1. First one is the higher copay and deductibles at the beginning of the plan year and this is typical. We see it every -- for every product. In the first quarter, those deductibles and co-pays are higher and we are paying them down, which are impacting gross to net.

The second is an increase in Medicaid utilization and that was driven by the very rapid uptake that we saw for Opzelura across all 50 states. That increase in Medicaid utilization had 2 components that impacted Q1. The first one was the utilization that we saw for Medicaid in Q1. And the second one is related to the actual claims for Q3 and Q4 received during Q1 which were higher than we were expecting. And therefore, there are certain true-ups related to those claims for Q3 and Q4 that are reflected in Q1.

So the average gross to net for the quarter was 60%, but as we look at the average for the year, we continue to expect this to be at around 50%. The first factor, the higher co-pays and deductibles that we saw in Q1 are expected to come down through the course of the year. And in terms of the Medicaid, even though the utilization will be higher, the true-ups that we saw in this quarter are not expected to continue at the same level in subsequent quarters.

So that's in terms of the gross to net. Regarding IQVIA, as we have discussed in the past, the IQVIA data is not fully reflective or accurate relative to our actual numbers. So it's good to look at it directionally, but there are a couple of things that are happening with the IQVIA data. One is it includes free drug. And as we have discussed in this past, I expect that, that is at around 20% of the total scripts that you are seeing.

The second is that there is an overestimation. We were expecting this to be at around 5% to 10%, which is typical for newly launched products, but we see some variation in the level of estimation during the quarter, and that can be as high as 20%. So it's better to look at the IQVIA data more in terms of the trend.

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

But the trend -- Herve here. The trend is sort of reflecting the demand that we are observing ourselves. It's just that IQVIA is, in fact, overestimating a little bit by 10% to 20% depending on the region.

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

And then, Salveen, in terms of your question on the CRL for ruxolitinib XR, as I said in my prepared remarks and the FDA was clear that we had met the area under the curve criteria for RUX XR versus IR, but had concerns on the lower (inaudible) theoretical concerns that it may potentially impact efficacy.

In terms of the base case, it's hard to say right now how long it will take, but we're absolutely marching forward for the intent to get RUX XR approved, and we'll work with the FDA on the various options, which may include modeling or some other work that needs to be done, we'll update you as soon as we know. It does not impact either the BET or the ALK2 program that continue to march forward, again, as I said in my prepared remarks.

And in terms of moving into pivotal studies, you are correct, we will proceed with the RUX IR with the intent to do bridging work on the back end to an FDC. Just to mention that the fixed-dose combination work is not impacted by anything to date, and that continues to move forward for both BET and ALK2 as well. Thanks.

Operator

Your next question is coming from Eva Privitera from TD Cowen.

Eva Xia Privitera - *TD Cowen, Research Division - Associate*

My first is also on the gross to net and more specifically on the shift towards Medicaid. Do you expect this to continue into Q2 and for the rest of the year? Is this likely permanent?

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

It's Christiana. The Medicaid utilization or the uptake was faster than we were expecting. So now we have Opzelura available under Medicaid in all 50 states. So the increase is not expected to be at that same level, but we would expect to continue to see those levels of Medicaid utilization. So it go to the levels that -- we're expecting eventually, but the uptake was faster than what we were expecting.

Eva Xia Privitera - *TD Cowen, Research Division - Associate*

Great. And to follow up on the full year expectation for gross to net to be roughly around 50%. So given that Q1 was 60%, is the assumption correct that the rest of the year, the average should be around in the high 40s?

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

You would expect the gross to net to gradually come down through the course of the year.

Operator

The next question is coming from Vikram Purohit from Morgan Stanley.

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

So we also had a question on Opzelura. I just wanted to get your updated thoughts on when in the coming quarters, you might feel comfortable providing a breakout of sales and/or scripts between vitiligo and AD? And is guidance for the product, either total guidance or indication-specific guidance something you would consider for this year? And then we had a follow-up.

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

Let me start, and then I will turn it to Barry. In terms of the guidance for Opzelura, we want to see more quarters of the uptake before we can provide guidance for -- annual guidance for Opzelura. We are still early in the launch for vitiligo. We still want to see how fast patients will be activated and have more information on the refills before we are comfortable to provide guidance. So let me turn it to Barry for the script question.

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

So just vitiligo as far as we can tell at this point, as we estimated, it seems to be about 30% of the total Rxs are related to vitiligo. Vitiligo growth is continuing, and we'll have to have more time to figure out exactly how many vitiligo refills will have for patients. But as we said in the past, we fully believe that on average, over time, vitiligo patients should be receiving about 10 tubes.

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

Understood. That's helpful. And then for a follow-up. We had a question on the LIMBER ALK2 combination data expected in the second half of this year. Could you just help us kind of characterize how many patients, what level of follow-up we could see and what you would consider to be a good outcome here?

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

Yes, Vikram, thank you for the question. So just to separate each program and deal with it separately, as I said in my prepared remarks, and I'll deal with BET first. It's really encouraging to see that both with monotherapy, we see in spleen volume reduction, symptom improvement and hemoglobin response and in combination with ruxolitinib as well. So we aim at an appropriate meeting in the second half of the year to show as much data as we can.

It's hard to quantitate that for you right now, because different meetings have different cutoffs. But you can get a sense of where we are in terms of the combination dosing thus far. And then we'll proceed with registrational intent decisions by the end of the year sort of time frame.

For ALK2, we've seen both, again, in monotherapy good hepcidin suppression and some evidence of early hemoglobin responses and then in combination as well. But it looks like we're going to have to go to higher doses than we initially projected there. And also, we have no dose-limiting toxicity. So that's good as well.

And the same sort of thing, hard to quantitate for you exactly how many patients will be presenting at the appropriate meeting, the second half of the year because of cutoffs, but it's appreciable numbers, and we're able to enroll both studies well. And the same intent to declare registrational intent programs in that time frame as well because both are proceeding well.

Operator

Next question is coming from Srikripa Devarakonda from Truist.

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

So I have a couple of big-picture questions. When I look at the pipeline mix right now, it seems like maybe this time of the time frame, but there seems to be a gradual switch towards inflammatory diseases, maybe it'll shift away from oncology. And even within oncology, the earlier stage programs seem to be more focused on biologics with at least a few of the small molecule programs being discontinued. Is this just a dynamic shift or is it intentional?

And then a question on the proposed EU legislation. I would just love to get your thoughts on it. And if you think that it could potentially impact Incyte or if Incyte could be immune from it because of the market you target?

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

Let me take some of that, and maybe Steven can speak and Dash on the pipeline. Starting on the EU legislation, frankly, you -- I mean, what we have seen is a proposed draft. It's not yet even close to be the final one. It has impact on exclusivity, which is obviously the key for the entire biotech industry.

So we live with patents and patent rights. And that will be the subject of our efforts in Europe to make it work for us. I mean Incyte is a company investing in R&D. And the only way we can be valuable in the long term is with enough patent and exclusivity after that.

So that's the big picture. I frankly -- I'm not yet ready to speak about the specifics of it, because it's a lot of work on our side to identify where we will specifically be impacted or not by the new legislation, which, by the way, will take time to be implemented. I mean it's not a very short-term thing.

On the portfolio, it is clear that we have been moving resources into inflammation and dermatology, but not just dermatology, I mean you heard the scope of the program we have for Povorcitinib, we have auremolimab coming also very soon. We have RUX cream, which is in dermatology. And they are all 3 very important program.

We are not moving away from oncology, but we are certainly consolidating our portfolio in immunology. And I think it's an important move for Incyte over the past few years of sort of becoming now a company that has 2 different franchises that are fueling the growth and the derm or immunology and oncology are coexisting.

Remember, we have a lot of synergies in research because a lot of the work we are doing there can be leading to products that can be used in cancer and could also be used in non-oncology indication. So regarding the biologics, frankly, we have, bispecific, we have antibodies and we have small molecules. We treat them equally.

So there is no strategic goal of moving away from small molecule, for example, like you have heard from some other companies. In our case, we are totally committed to each of them. It just happened that some of the targets we are pursuing and you saw that with CALR, for example, are well suited for an antibody or biologic type of approach, and that's what's driving the mix between biologic and small molecules for that.

Operator

Next question today is coming from Jessica Fye from JPMorgan.

Jessica Macomber Fye - *JPMorgan Chase & Co, Research Division - Analyst*

A couple on Jakafi. First, where does duration of therapy with Jakafi and MF stand historically? And have you seen that evolving at all? Is there any change in duration of therapy baked into the 2023 guidance? And then I think you mentioned the change in inventory year-over-year. Was there a sequential change in inventory relative to the fourth quarter?

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

Sure. So Jessica, this is Barry. So in terms of duration of therapy for MF, it's about 21 months as far as we can tell, but many patients are on drug. They've been on drug since the Phase II study. So we haven't seen any change at all, particularly if there's a couple of drugs that might be used in the second-line setting, we haven't seen it. In fact, the growth for MF for this quarter is the highest that we've seen year-over-year, quarter-over-quarter. And we'll let the inventory go question -- go over to Christiana.

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

So Jessica, regarding the inventory, we ended Q1 with channel inventory levels that were slightly below the low end of the normal range and the normal range that we see is 2.5 to 3 weeks of hand of channel inventory. And that had to do with the timing of certain customer orders.

In terms of the impact, when you look at this relative to Q1 of last year, the impact is at around $11 million. Q4, both this past year and the year before ended up being at the higher end of the range, but within normal levels. And again, this quarter, we fell slightly below the low end of the range.

Operator

Next question is coming from Brian Abrahams from RBC.

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

On Opzelura, can you talk about what you're observing with regards to refills in the past few months? Are you seeing refills normalized in March and April? What's your latest thinking on the average number of tubes per year patients will be getting there.

And then with regards to Jakafi, I'm curious what you're seeing that prompted the raise in the lower end of the guidance range? Any differences in demand versus your expectations, changes in your expected -- expectations for competitive dynamics in the back half of the year or something else?

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

Sure. This is Barry. So Opzelura and Jakafi. So Opzelura, just in terms of -- yes, in March and April, refills have normalized. So we've said in the past and it seems to be holding up that refills account for at least 30% of the TRxs, so that will continue.

In terms of the number of tubes for patient, it differs, obviously, between AD and vitiligo. In AD, when we can follow a cohort of patients for at least 12 months, we can see that they average currently about 2 tubes per patient or a little above 2 tubes per patient.

For vitiligo, we fully anticipate that patients will, in fact, be using many more tubes. We've projected or forecasted about 10 tubes per patient over time. We haven't been able to follow a cohort of patients for vitiligo patients to see exactly what the refills are, but we know they'll continue to increase.

And as far as Jakafi goes, the dynamics are there. I mean, in fact, we're growing at a good rate in terms of demand in the first quarter and going forward. I think as we said before, in terms of new patient growth, it's been the best that we've seen since the launch of the brand. So we're very encouraged by that, and that generally carries through to the rest of the year. So we're growing total patients and total demand in MF, PV and GVHD. So that's what led to the tightening of the guidance.

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

Yes. Brian, on the refill, I think it is a key question for Opzelura. To put it in perspective, we had -- when we launched this calibration of saying it would be 2 to 3 tubes for atopic derm, it could be up to 10 for vitiligo. What we are observing is that we are now north of 2 for atopic derm. So that's the good thing. And it's evolving. It's a number that is increasing.

And frankly, for vitiligo, we don't have enough patients treated over a 12 months period to know where it is. But it is when you do the modeling, it is the one thing that is giving the curve a very different shape.

So a lot of the commercial effort we do today is obviously bringing new patients to their dermatologist asking for Opzelura. But the other side is refills and getting the refills done for vitiligo because that's what's going to impact the revenue for the next year.

Operator

Next question is coming from Tazeen Ahmad from Bank of America.

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

I have 2. Just to go back for a minute to gross to net. Is it still your expectation to exit the year at 50% gross to net? I know that you're expecting GTN to improve as the year progresses. But given where you started off with the 1Q results, how are you thinking about that guidance for the rest of the year?

And then secondly, as it relates to the LIMBER program, just with the retirement of your pursuit of parsa, how should we be thinking about LIMBER going forward? And can you highlight some of the potential catalysts for that program in the nearer term?

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

It's Christiana. I'll take the first part of the question on gross to net. As I indicated, we do expect the gross to net to improve through the course of the year to come down from the 60% level that we saw in Q1 and to average for the year around that 50% level that we had indicated in the past.

Again, some of the drivers that contributed to the higher gross to net in Q1 are expected to improve through the year, and that's both related to the higher deductibles and co-pays assistant that we typically see in the first quarter of the year as well as the higher Medicaid utilization and especially the true-ups related to actual claims for prior quarters received in this quarter.

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

And Tazeen, in terms of LIMBER program. So as I said earlier, both BET and ALK2 will deliver a recommended Phase II, Phase III doses in combination with RUX by the end of this year and then we'll declare registration intent programs for both very important programs with different intents, just BET both in terms of spleen reduction and symptom response and then ALK2 to the additive hemoglobin response from that.

CALR will enter the clinic in the middle of the year and will declare itself in terms of safety and efficacy relatively quickly given its mechanism of action and we can follow CALR allele burden reduction.

And then in graft-versus-host disease, axatilimab, the AGAVE-201 results will come in as well and will hopefully be a filing opportunity in third-line graft-versus-host disease. We'll continue the RUX XR work and work with the FDA on the path forward and continue the FDC work. So still a very active program underway with LIMBER. Thanks.

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

Can you clarify what would be good data for the BET study?

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

Yes. No, I think the idea is to get to the right therapeutic ratio in terms of BET. So we know that the on-target toxicity is thrombocytopenia and in combination with RUX to declare what the right dose is to use in combination. You may see a dosing paradigm evolve that is platelet count directed and different doses being used depending on patients' platelet counts maybe the right way forward for a best combination. Stay tuned on that.

Operator

Next question is coming from Ren Benjamin from JMP Securities.

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

Can you give us an idea as to the split between Medicare, commercial and the 340B hospitals? And ultimately, call it by the end of the year, what that split might be? And what's, frankly, the ideal split for you guys? And then I have a follow-up.

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

For Jakafi, you asked?

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

Yes, he means for Jakafi. So -- this is Barry. So for Medicare, we are a heavy Medicare drug just because of the age of the patients and diseases that we're treating. So it's about 50% that is Medicare, about 16% or so of our volume currently is going to 340B institutions and mostly the rest is commercial, but it's a variety of things. And remember that, included in the 340B is some commercial patients as well.

So it's really -- that's -- the rest is just a little bit of VA and other government ordering. And it will continue the same for the rest of the year. The 340B is, it grows and it's going to continue to grow for everybody, but it will grow at a reasonable rate, we just had a little bit of a bump this quarter, and that's why we pointed it out.

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

Got it. Okay. And then just switching gears to both Monjuvi and Pemazyre, I'm trying to get a sense as to -- sticking with Monjuvi, the upcoming sort of inflection points, when these trials might ultimately read out? And at what point you kind of look at, call it, the new indications and either kind of assess whether this will be a commercial success or it's something that you ultimately write off?

And we saw some great data, I thought, at Pemazyre at AACR, I'm kind of curious what your plans are in terms of either doubling down on Pemazyre and some other tumor indications? Or do you kind of feel the commercial opportunities maxed out?

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

I'll take the development side of those questions, Ren. Thank you. So for Monjuvi, both the follicular and the frontline diffuse large B cell studies have enrolled incredibly well. We expect data on -- in mind, the follicular marginal zone trial in the second half of next year and frontline the year after, very important studies in this arena to get data on, and I certainly feel will be important for patients there.

And thanks for also pointing out the Pemazyre, pemigatinib data at AACR. I think if you have tumors that are driven biologically by either FGFR1, 2 or 3 and that is the oncogenic driver, then perturbing that with a good inhibitor, which Pemazyre is you can see results. And so we have ongoing work in glioblastoma multiforme where we are seeing activity there, and we'll see whether that translates to a more fuller registration program down the line with massive unmet need there as well.

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

So just in terms of the commercial potential for Monjuvi, obviously, the first-line diffuse large B cell lymphoma is extremely important to us. We think we have a good chance of succeeding there. So those patients are in the curative setting. So it's extremely important to us. So the opportunity there is large. We're studying in a particularly high-risk population, which I think will benefit everyone in indolent lymphoma or follicular lymphoma.

Again, they're in combination with Rituxan and Revlimid compared to our drug Monjuvi and R squared. I think we have a good chance of succeeding there as well, and we have the opportunity to really take over that market share. As Steven said, for Pemazyre, it's a good product. There's a few cholangiocarcinoma patients.

Now we have an MLN indication. We don't really know how many MLN patients there are. It's a very rare tumor type. But in fact, as we have more physicians, clinicians testing for FGFR1 rearrangements, we'll find out exactly how many MLN patients are. And as Steven says, we have ongoing work with Pemazyre, and we have hope that we can bring some relief to patients with GBM.

Operator

Next question is coming from Evan Seigerman from BMO.

Unidentified Analyst

This is Conor MacKay on for Evan. Maybe just one on the Opzelura launch in the EU. Any nuances there versus the launch in the U.S. in terms of SG&A expenses or expectations for uptake?

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

Yes. So I mean, the EU, I mean, one of the news today is the quality of the label for Opzelura in Europe. It's a very good label. It's for vitiligo. So the sequence is very different from the U.S. where we started with AD followed by vitiligo. There, we are vitiligo first and then additional indication will come in the future.

We have a team in Germany for the next year or so, like 12 months, most of the activity in Europe will be in Germany because that would be the place where we have reimbursement. So it is, in fact, the coverage of the approval was excellent on multi -- on TVs and the newspaper, it was something and fairly noisy there and the team is getting prepared for a launch that could be happening in July.

So that's the timing. In terms of SG&A or resources, we have them in place. So you should not anticipate an increase in the next quarter that will be related to the launch of Opzelura in Europe.

Operator

Next question is coming from Jay Olson from Oppenheimer.

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

Congrats on the progress. We have a question about the LIMBER program. What are some of the lessons learned from the parsaclisib studies? And is ALK2 now the top priority in your LIMBER program? And then what kind of patient numbers and duration of follow-up should we expect at ASCO on the ALK2 program?

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

It's Steven. Thanks. I think in terms of the parsa studies, obviously, it's unfortunate that they did not meet the criteria to continue past their interim analysis in terms of futility. In lessons learned, I mean, we always learn from studies and from patients. We learned how to enroll efficiently around the world, find these patients and a lot of learnings on the operational side.

On the clinical side, we again had a good Phase II signal, which didn't pan out in Phase III. And that, as you know, happens about half the time in hematology/oncology. And the important thing is just to do things efficiently and focus on doing the right things for patients and their families in terms of the shutdown of the studies, which we're doing now and then pivot into the other programs.

Just to manage in terms of what you said, it will not be at ASCO in terms of updates BET and ALK2, they are in meetings in the second half of the year. And as I said earlier, it's hard to be precise on patient numbers that we'll be able to present, but both monotherapy and combination work has gone well.

And we're at doses with ALK2 around 400 milligrams in combo with RUX currently, no dose-limiting toxicities. We are seeing hemoglobin responses, but we can go higher. And that's what -- so we'll continue to dose escalate there, and I can't give you precision on numbers right now on a meeting yet. Thanks.

Operator

Next question today is coming from Michael Schmidt from Guggenheim Securities.

Michael Werner Schmidt - *Guggenheim Securities, LLC, Research Division - Senior Analyst & Senior MD*

Maybe just another follow-up on LIMBER. Steve, as you think about the ALK2 and the BET combinations. How do you think those could be positioned perhaps relative to the emerging competitive landscape in the MF space, where we have the Navitoclax combo going on as well and then potentially momelotinib coming in later this summer?

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

So Michael, I'll start and some of my colleagues may add things after it. I think there is still unmet need there despite RUX being a fantastically successful drug and great for patients in terms of spleen symptoms and overall survival.

Just to talk individually about the programs, BET addresses both spleen reduction and associated symptom improvement and it's clearly an active compound both with a competitor and with ours as well, as I just alluded to in my prepared remarks.

So we'll continue to progress, get to a recommended dose and address those needs. ALK2 Is a difference. Here, it's about addressing the anemia component of the disease, both the underlying disease of myelofibrosis and potentially the drug-induced anemia from RUX as well. And again, as I said in my remarks, we've seen the directionally hemoglobin responses that we want, but we can keep going in terms of dose increases.

I think just because you mentioned it in terms of momelotinib, the study -- MOMENTUM study is after RUX against danazol and it probably works through ALK inhibition as well as far as we can tell. But it is not as good a JAK inhibitors as RUX as we saw from the early SIMPLIFY study where there were non-noninferior to RUX. So we expect, and we'll see what the FDA does that they'll have a label post RUX there, and it's a different need for patients there in terms of that. I don't know if anybody else wants to add anything?

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

Maybe I can say a word on -- the picture is really JAK inhibitors are the backbone of all the combinations. So -- and there, you see ruxolitinib is obviously the most important JAK to combine with because it has all these benefits and survival. So there, ALK2 and BET, the question is where do you start introducing a combination versus a single-agent JAK inhibitor. That's what we looked at with our suboptimal responder studies we were doing with parsaclisib.

And you can imagine that with the BET inhibitor, you could do the same type of positioning of just letting patients start on Jakafi alone and then go to the combination. With ALK2, there is another dimension, which is that it could be a very good combination partner in the first line by definition, because it's not adding to the safety profile or the toxicity profile, and it could help, in fact, in terms of anemia.

So BET and ALK are not really exactly at the same stage of disease progression in MF, and ALK2 could be used earlier than BET in many of the patients. Now we'll see -- we'll do the experiments, we'll do the clinical trial. But at the end of the day, that's what we are looking at. And then there is a question of can you treat patients with MF who are refractory to Jakafi with a non-JAK based type of treatment, and that's also something that for a BET inhibitor, we could test in the late-stage setting.

Operator

Next question is coming from Mara Goldstein from Mizuho.

Mara Goldstein - *Mizuho Securities USA LLC, Research Division - MD of Equity Research Department*

I just had 2 questions. And the first, I'm curious about your thoughts on any potential change from a clinical, either enrollment or trial process in the HS arena, given the pending approval for Cosentyx, at least in the U.S., I know it was just approved outside the U.S.?

And I'm curious about the planned study for Povorcitinib in asthma. And can you speak to where you think the potential opportunity is from a clinical context there?

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

Sure. Thanks for the question. We saw this Povorcitinib data that, again, I alluded to in my prepared remarks at a meeting earlier this year, which was incredibly well received. And as I said, with the first time ever reported HiSCR100 responses in terms of complete disappearance of abscess and nodules and no new fistulas. And I think that data is driving enrollment in the Phase III program in STOP-HS1 and 2 incredibly well. I mean so a lot of interest there.

I don't see any impact, quite frankly, from the approvals of biologics there and a lot of excitement for the agents, and we expect to get those studies done very, very efficiently. Asthma, the pathophysiology here is, again, relevant JAK stat biology in terms of the cytokines that it affects beyond IL-4 and 5, IL-13 as well.

T helper 2 biology. It's targeting the moderate severe plus asthmatics. So people who are on moderate plus doses of inhaled corticosteroids and long-acting bronchodilators and are still having exacerbations on a yearly basis, plus still have a subnormal forced expiratory volume. So it's for the more severe patients who still having exacerbations and that's a population will be targeting to get to proof-of-concept with Povorcitinib in asthma. Thanks.

Operator

Our final question today is coming from Gavin Clarke-Gartner from Evercore ISI.

Gavin Clark-Gartner - *Evercore ISI Institutional Equities, Research Division - Analyst*

So for Jakafi and myelofibrosis specifically, roughly what percent of patients are on the lower 5-milligram dose? And just wondering if you think these patients could be at higher risk from other JAK competition?

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

All I can say is that -- so I don't know exactly for how many myelofibrosis patients are on 5 milligram. What we do know is that maybe about 25% of the bottles that we dispense are 5-milligram tablets. But as you can imagine, most of those are actually PV and GVHD patients.

Now what's at risk in myelofibrosis as well. We continue to grow strong in myofibrosis. We continue to go up in the treatment paradigm, meaning that newly diagnosed patients more often are coming on Jakafi, and therefore, they're better -- they're less anemic and they're better able to gain a spleen response and a survival advantage in that particular setting. So regardless of whether patients were anemic or not to survival benefit, spleen benefit and symptom benefit remains the same as patients who were not anemic.

So that's what's most important. We're not -- we think that any competitors that are coming will mostly be moved to the second-line setting. We've seen that with fedratinib and pacritinib, and we think that will continue just because of the advantages that Jakafi has for all patients regardless of dose.

Operator

We've 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. The IR team 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.
