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OVERVIEW:

Company Summary

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PRESENTATION

Operator

Hello, and welcome to the Incyte Second Quarter Earnings Conference Call and webcast. (Operator Instructions) As a reminder, this conference is being recorded. It's now my pleasure to turn the call over to Greg Shertzer, Investor Relations for Incyte. Please go ahead, Greg.

Greg Shertzer

Thank you, Kevin. Good morning, and welcome to Incyte's Second 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, Pablo, Barry, Steven and Christiana, who will deliver our prepared remarks, and participate in 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 and 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 - CEO & Chairman*

Thank you, Greg, and good morning, everyone. So we had another quarter of strong performance with product revenues growing 25% year-over-year, driven by Jakafi, Opzelura and launches in Europe. Jakafi net product revenue grew 14% compared to the second quarter of 2022. For Opzelura, the growth trajectory continues with net product revenues in the second quarter of $80 million driven by new patient flow and growth in Refill.

Additionally, the launch in Europe is underway and Opzelura is now available to patients in Germany and Austria. Our other hematology and oncology net product revenues were $64 million for the quarter, up 30% year-over-year, driven by the growth of Pemazyre and Minjuvi in ex U.S. Markets.

Now turning to Slide 5. We continue to execute on our development efforts. Recently, we announced positive top line results from 2 of our high potential program. The TRuE-AD3 study evaluating Ruxolitinib cream in pediatric atopic dermatitis and the AGAVE-201 study evaluating axatilimab in chronic GVHD, met their respective primary endpoint.

Steven will discuss these results in more detail during his prepared remarks as well as provide updates on the important progress we made across many of our high potential programs as shown at the bottom of the slide. We also strengthened our research and development organization by appointing Pablo Cagnoni as President and Head of R&D; and in this position and as a member of the executive team, Pablo will lead Incyte's R&D activities. This new role aligns chemistry, biology and early and late-stage clinical development with the goal of maximizing speed and productivity in our research and development efforts. I will now turn the call over to Pablo for a few words.

Pablo J. Cagnoni - *Incyte Corporation - President and Head of Research & Development*

Thank you, Herve. I'm thrilled to join the team at Incyte. A company with such an impressive history of success and who has refined -- redefined as standard of care in myeloproliferative neoplasm, graft versus host disease and vitiligo. Since joining just a few weeks ago, I have spent time with our teams, and I'm even more enthusiastic about the capabilities of our organization and about the quality of our science.

We're prosecuting a broad range of biology with a diversity of modalities and I look forward to working with them to continue to deliver major advances across our portfolio in order to make a meaningful difference for patients. Herve?

Herve Hoppenot - *Incyte Corporation - CEO & Chairman*

Thank you, Pablo. And with that, I would like to pass the call to Barry for a commercial update.

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

Thank you, Herve. Good morning, everyone. Starting with Jakafi on Slide 7. Net product revenues for the quarter were $682 million, up 14% year-over-year driven by the continued growth in patient demand across all indications. Total patient demand grew 5% year-over-year while new patient starts, a good indicator for future growth, was up 9% year-over-year. Given the strong underlying demand for Jakafi, we are raising the bottom end of our full year 2023 revenue guidance to a new range of $2.58 billion to $2.63 billion.

Turning to Opzelura on Slide 8. The launch continues to be strong and is gaining positive momentum with both physicians and patients. The rapid adoption of Opzelura is driven by its compelling product profile and its ability to address significant unmet need in both atopic dermatitis and vitiligo. Opzelura net product revenues in the quarter were $80 million, up 42% compared to the prior quarter.

U.S. patient demand increased during the quarter with total prescriptions growing 16% compared to the last quarter and Refills growing by 23%. The monthly prescription trend, as shown on the right, demonstrates the continued growth of Opzelura, which is coming from both atopic dermatitis and vitiligo. In AD, growth was primarily due to new patient flow driven by Opzelura's efficacy and impact on inflammation and itch. In Vitiligo,

where Opzelura is the only approved treatment for repigmentation. Growth was driven largely by refills and our educational and awareness initiatives. We are very optimistic about the long-term potential of Opzelura as we continue to see the strong uptake and positive momentum.

On Slide 9, Monjuvi net product revenue in the U.S. for the quarter were $24 million, up 2% year-over-year and were driven by continued growth in community accounts. Minjuvi Net product revenues outside of the U.S. were $13 million, up 198% year-over-year and includes $6 million of previously deferred revenue related to the early access program in France, which ended in June. Pemazyre net product revenue grew to $22 million, a 14% increase year-over-year with $5 million coming from outside the U.S. where the launches 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. Starting on Slide 11. As Herve mentioned, we have 2 exciting program updates we want to highlight from this quarter. First, for ruxolitinib cream. The primary endpoint was met in the Phase III TRuE-AD3 trial in pediatric atopic dermatitis patients aged 2 to 12. The top line results showed that significantly more patients achieved Investigator Global Assessment treatment Score, or IGA-TS with ruxolitinib cream .75% and 1.5% than with the vehicle control.

No new safety signals were observed, and the overall safety profile is consistent with previously reported data. The long-term safety portion of the trial is ongoing and data will be submitted for presentation at an upcoming scientific meeting. We also plan to discuss these data with regulatory agencies, and we anticipate a submission in the first quarter of 2024. We are excited about the potential relief ruxolitinib cream can bring to the roughly 2 million pediatric atopic dermatitis patients in the United States.

Moving to Slide 12. In partnership with Syndax, the AGAVE-201 study, a global pivotal trial evaluating axatilimab in patients with chronic graft versus host disease after 2 or more prior therapies, met its primary endpoint of overall response rate across all 3 treatment cohorts, with the 0.3 milligram per kilogram every 2-week dose achieving a 74% overall response rate. In the 0.3 milligram per kilogram cohort, 60% of responders maintained their response at 1 year and 55% of patients achieved at least a 7-point decrease in the modified Lee Symptom Scale indicating that responses were both durable and with symptom improvements. Axatilimab was well tolerated, and the most common adverse events were consistent with on-target effects.

The full data set is planned for presentation at a scientific meeting later this year with a potential BLA submission by year-end 2023. We are excited about the potential of axatilamab in chronic graft versus host disease and in this heavily pretreated and severe patient population. A Phase I/II trial of axatilimab in combination with ruxolitinib is also being planned.

Moving to Slide 13. An updates on our broader dermatology pipeline. For Opzelura, in addition to the positive top line pediatric AD data, 3 Phase II studies for lichen planus, lichen sclerosus and hidradenitis suppurativa have completed enrollment. For povorcitinib, the Phase II study in prurigo nodularis has completed enrollment, and we expect to have data in this indication later this year. Additionally, we previously announced the expansion of povorcitinib development into inflammatory and autoimmune diseases beyond dermatology and now have initiated 2 Phase II trials in asthma and chronic spontaneous urticaria, CSU.

On Slide 14, I want to provide a little more detail on our studies in asthma and chronic spontaneous urticaria. Asthma is a chronic inflammatory disease with 2 endotypes. Type 2 eosinophilic asthma, the most common type is primarily driven by Th2 cytokines, whereas non-type 2 asthma is characterized by a neutrophilic response. Many asthma patients have disease progression despite therapy with inhalers.

Povorcitinib appears to have efficacy in both type 2 and non-type 2 endotypes. In preclinical data, povorcitinib results in a reduction of eosinophil activation and may potentially reduce neutrophil activation as well. The Phase II study is being evaluated in moderate to severe uncontrolled type 2 and non-type 2 asthmatic patients. Unlike monoclonal antibodies that target a single cytokine, povorcitinib inhibits the actions of multiple cytokines, potentially providing superior efficacy in both endotypes.

CSU is a mast-cell driven disease, presenting with hives and severe chronic itch. Overactivation of dermal mast cells and basophils results in increased serum levels of Th1, Th2 and Th17-related cytokines. We know JAK inhibition can modulate mast cell activation, including degranulation and cytokine production, both of which are drivers of chronic spontaneous urticaria.

The Phase II study has been evaluated in patients who are inadequately controlled or progress on second-generation antihistamines. Moving to hematology and oncology. We achieved multiple clinical milestones across our high potential portfolio during the second quarter. We continue to make progress in myeloproliferative neoplasms or MPNs where we presented updated clinical data at ASCO for our ALK2 and BET program. We also initiated the Phase I study of INCA33989, our mutant CALR antibody. And as previously discussed, axatilimab met the primary endpoint in chronic graft versus host disease.

For oncology, both of the Phase III studies evaluating tafasitamab in first-line diffuse large B-cell lymphoma and in relapsed or refractory follicular and marginal zone lymphoma are fully enrolled, and the small molecule Oral PD-L1 program continues to advance with multiple new studies initiated.

Turning to Slide 16 and an update on our small molecule oral PD-L1 program. Immune checkpoint inhibitors have transformed cancer treatment for patients. Despite the remarkable clinical benefits, intravenous formulations have disadvantages, and there is ample opportunity for innovation and improved outcomes in this space. As the first company to demonstrate clinical activity with an orally available PD-L1 targeted agent, we have a unique opportunity for differentiation. As an oral small molecule, INCB99280 has a short half-life, which can reduce the burden of managing immune-related toxicities and provides a switch-off option if needed, which may offer improved overall safety, especially when combined with other agents.

Additionally, the convenience of an at-home oral administration is often preferred by patients and they offer the potential for an improved quality of life. On the right, you can see the current studies of INCB99280. We've initiated Monotherapy Phase II studies in both checkpoint inhibitor naive patients and in cutaneous squamous cell carcinoma. We also initiated 2 Phase I/II combination studies with axitinib and ipilimumab, a third Phase I/II study in combination with adagrasib is in preparation. We also announced last night that in partnership with Replimune, we are starting a neoadjuvant study to evaluate 280 In combination with RP1, a tumor-derived oncolytic immunotherapy in patients with cutaneous squamous cell carcinoma.

RP1 is Replimune's lead oncolytic immunotherapy product and is based on a proprietary new strain of herpes simplex virus engineered for robust tumor selective replication and is genetically armed with a fusogenic protein and GM-CSF.

RP1 has already demonstrated substantial activity in cutaneous squamous cell carcinoma. At ASCO, we presented data for zilurgisertib, our ALK2 inhibitor in patients with myelofibrosis. Initial data from 36 patients demonstrated early signs of clinical activity through hepcidin reduction and anemia response in monotherapy and in combination with ruxolitinib. Zilurgisertib was well tolerated with a favorable safety profile, allowing for continued dose escalation.

We have added an additional treatment group in first-line JAK-naive myelofibrosis patients with anemia and we plan to have updated data later this year. Additional data presented at ASCO for our BET inhibitor, INCB57643 demonstrated improvements in spleen volume and symptoms in both the monotherapy arm and in combination with ruxolitinib. It was generally well tolerated with 2 dose-limiting toxicities observed in the higher 12-milligram once-daily monotherapy arm. We believe we have an active compound with encouraging early data. Dose finding work is ongoing with 10 milligrams once-daily as monotherapy as well as continued dose escalation in the combination arm.

Turning to Slide 19. We continue to make progress in other development programs. During the quarter, INCA33890, a TGF-betaR2 by PD1 bispecific antibody entered the clinic and a Phase I study was initiated. Additionally, Auremolimab, our anti-IL-15 receptor beta antibody received IND clearance and we plan for it to enter the clinic later this year. Retifanlimab, which was recently approved in Merkel cell carcinoma has completed enrollment in the Phase III non-small cell lung cancer study and in the squamous-cell anal carcinoma study.

Finally, on Slide 20, we have a number of upcoming data readouts and other exciting milestones expected, and we look forward to sharing additional details throughout the remainder of this year. With that, I'd 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. Q2 was a very strong quarter with total product revenues increasing 25% year-over-year to $827 million, driven by the strong performance of Jakafi and Opzelura. Jakafi net product revenues for the second quarter were $682 million, representing a 14% year-over-year increase driven primarily by continued growth in patient demand across all indications and an increase in channel inventory.

At the end of Q2, channel inventory had recovered from the depressed Q1 levels and was towards the high end of the normal range. The increase in inventory represented around $35 million in net product revenues. Opzelura net product revenues for the second quarter were $80 million, representing a 384% increase year-over-year, driven by increased patient demand and expanded coverage.

Finally, other hematology oncology net product revenues were $64 million, representing a 30% increase compared to the second quarter of 2022 driven by patient demand and the recognition of $6 million of previously deferred Minjuvi revenue related to the early access program in France, which ended in June.

Turning to royalty revenues. Total royalty revenues for the quarter were $128 million and are primarily comprised of royalties from Novartis of $90 million for Jakavi and $5 million for Tabrecta and royalties from Lilly of $32 million for Olumiant. Jakavi and Olumiant royalties for the quarter were negatively impacted by FX headwinds.

Turning now to Slide 24 and the performance of Opzelura. The launch of Opzelura has been very stronger with 2023 year-to-date net sales of $137 million. Since the launch of Vitiligo, Opzelura net product revenues have grown at an average quarterly rate of 28%. Net product revenues grew 42% compared to last quarter, primarily driven by demand and the normalization of the typical Q1 dynamics.

Moving on to Slide 25 and our operating expenses on a GAAP basis. Total R&D expenses were $401 million for the second quarter, representing a 15% year-over-year growth, 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. The SG&A expenses were $284 million for the second quarter, representing a 12% year-over-year growth, driven primarily by promotional activities launched at the beginning of the year to support Opzelura and 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 again the bottom end of our full year Jakafi guidance to a new range of $2.58 billion to $2.63 billion. We are reaffirming our other hematology oncology revenue, COGS, R&D and the SG&A guidance for the year.

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

QUESTIONS AND ANSWERS

Operator

(Operator Instructions) First question today is coming from Brian Abrahams from RBC Capital Markets.

Leonid Timashev - *RBC Capital Markets, Research Division - Biotechnology Analyst*

This is Leonid on for Brian. I guess I had 1 maybe on MF development in the limber program. Given the high bar that Jakafi sets and the challenges on TSS50 exemplified by difficulties, one of the competitor drugs recently had in hitting on the symptom score. I guess how is this shaping your thinking about going to the front line or the second line of the BET inhibitor and just positioning of these molecules going forward?

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

It's Steven. Yes, and for acknowledging ruxolitinab's incredible activity in terms of both spleen responses, but especially symptom improvement, and as you point out, it's a very high bar to beat. In terms of our own thinking, one has to be obviously careful in study design, in adequate powering in terms of end points and also making sure that you maintain adequate JAK inhibitor dose intensity going forward.

And so both -- just to point out in terms of our combination programs, we talk about ALK2 first. You can see where it's heading. Clearly, we have an increase in Hepcidin reduction with increase in doses, and we're starting to see very encouraging hemoglobin responses. So the thinking along those lines would be potentially looking at in the first-line study and an ability to prevent anemia development and thus maintain very importantly, rux dose intensity and get the maximum benefits in terms of JAK inhibition in spleen and symptoms. And so that's where that's heading.

And hopefully, as we've said repeatedly, by next year, we'll complete the dose escalation and be able to declare where we want to go. It's incredibly safe in terms of tolerability. So we're able to continue to dose escalate at the moment. In terms of the BET program, it's a little bit of a different thing in terms of tolerability. There's no on-target toxicity in terms of thrombocytopenia in terms of going in higher doses. So in monotherapy at the 12 milligram, we saw dose-limiting toxicity there and we back at the 10-milligram dose in terms of monotherapy. We've seen, again, extremely encouraging spleen response, symptom response and also occasionally hemoglobin improvement. But to your point, we have to think carefully about where to go in terms of first-line or suboptimal study.

And obviously, also there's a competitor reporting our BET data later this year, which we're going to watch carefully. And again, to be repetitive, power in terms of symptoms, you have to be very careful in the first-line setting because ruxolitinib is so good.

So that program as well, we'd like to declare by the end of year time frame next year, earlier part of the year where we go in terms of registration directed efforts. And then also just to remind you, completely different efforts, the CALR antibody is in the clinic now, potentially disease-modifying DASH even curative in the 30% of CALR patients that are in the MF population and in the ET population. And that could be a completely different way of thinking, if you can eliminate the clone and change the disease trajectory completely, and you wouldn't even be thinking then in terms of spleen and symptom response, it would be eliminating the clone. So that's where we are with the program at the moment. Thanks.

Operator

Next question today is coming from Srikripa Devarakonda from Truist Securities.

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

I have a question about the axatilimab data from the Phase II trial you reported recently. The big question we've been getting is around the unusual dose response. So we've heard that this could be because of potential impact of SAEs and response rates. I know it's not been too many days since you reported the data, but it's been a few days since you've had to digest the data. I wonder if you have a sense of what it might take to understand what's going on there. And more importantly, how this might affect regulatory review and then for Minjuvi, as you continue to work through reimbursement in EU, are you seeing a difference in how it's being used in U.S. versus EU?

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

It's Steven. I'll start off with your axatilimab question. So the AGAVE-201 study had 3 doses and a schedule difference as well. So the first 2 are 0.3 milligram per kilogram Q2, 1 milligram per kilogram Q2 and the third dose level was 3-milligram per kilogram Q4. And you're right, we had a pleasant surprise in having excellent activity across all the dose levels in patients who had actually a median of 4 prior therapies and included in prior ROCK inhibition, you're getting that with the 0.3, a 74% best overall response. The 1 milligram per kilogram is not really different, just to be clear.

When you're up at 67% on best overall response. And then if you look across it, some other ways of looking at responses in the very similar territory. So we don't think there's a difference in response rate, but there is a difference in terms of tolerability, in terms of on-target effects likely on liver Kupffer cells in transaminitis, that gets worse with increasing dose. And certainly, at the 3-milligram per kilogram there's clearly more transaminitis and that is likely not the regulatory dose. So it will be the discussion with the regulators on the 0.3 versus the 1 both showing excellent activity in terms of overall response rate and tolerability, and we're still in the early days of working that out with regulators. But we'd like to get that submission in the BLA in by the end of this calendar year 2023. I'll turn it over to Barry for your second question.

Herve Hoppenot - *Incyte Corporation - CEO & Chairman*

I will take it on Minjuvi in Europe. So there are 2 ways to look at it. I mean, the overall profile of patients that we are seeing using Minjuvi in Europe is not dissimilar to what we have in the U.S, and that you have basically a group of patients who are not eligible to CAR-T obviously not eligible to transplant. And in many cases, would be patients who are frail and are attracted by the very good safety profile that we have with Minjuvi Len.

And obviously, a very good efficacy that you can get there. Now the extent to which CAR-T is used in different European countries is different from the U.S. So I would say it's a little bit maybe earlier on the curve. And what we see is that the volume, there's a group of patients that end up being eligible for Minjuvi is, in fact, larger in Europe and we see that from the uptake that we are seeing. Now we have reimbursement in Germany, Italy, Spain and a few other countries, and we continue to work, as you heard in France and the rest of Europe to have full access. But the curve, the adoption curve for Minjuvi in Europe is, in fact, faster than what we saw in the U.S. in terms of volume.

Operator

Your next question today is coming from Allison Bratzel from Piper Sandler.

Allison Marie Bratzel - *Piper Sandler & Co., Research Division - VP and Senior Research Analyst*

First, just on Opzelura. Could you help us understand gross to net trends during the quarter and also just the mix you're seeing between atopic derm and vitiligo. I think it was 30% of scrips were thought to be for Vitiligo last quarter. Is that consistent now that we're into the second half of the year and I guess what are you seeing in terms of persistence and refill rates in vitiligo?

And then secondly, just a question on the pipeline. Just on the Replimune agreement announced yesterday, could you talk about the rationale for entering that agreement now? What aspects of RP1's clinical data in CSCC or other derm oncology indications give you confidence in evaluating the 99280 combo in neoadjuvant CSCC. And just help us understand that the scope of that trial expected to start early next year. Is that going to have registrational intent?

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

It's Christiana. Let me take the first part of your Opzelura question, and then I will turn it to Barry to discuss the mix. In terms of the gross to net, in Q2, the average gross to net discount was 55%. So that was down from 60% in Q1. As we were expecting, Q1 has the highest gross to net, given the higher co-pays and deductibles at the beginning of this year that we have to pay down and that then comes down through the year.

So we are at 55% average gross to net in Q2. In terms of dynamics, one thing that we saw in Q1 and we continue to see in Q2 was an increase in Medicaid utilization. And that has continued in Q2 with Medicaid increasing as a percent of the total payer mix.

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

So Allison, it's Barry. So as far as your other questions, Vitiligo now represents about 35% of total prescriptions. In terms of refills, so for atopic dermatitis, I think we've said before that we expect 2 to 3 refills -- 2 to 3 tubes per patients, and that's where we are now with AD, we're over 2 tubes

per patient. For vitiligo, we don't have enough time yet. Most of the vitiligo patients coming on, as you can imagine, are new patients, and we need more time to reach the average number of refills. As we've said in the past, we expect the average to be around 10 tubes per year, and we think we're progressing towards that. I'll turn it over to Steven for a Replimune question.

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

Thanks, Barry. So Allison, in terms of cutaneous squamous cell carcinoma, it's an entity that's not very well captured by the groups that capture cancer statistics just because of the way it's treated, variability, often with surgery alone, et cetera, but it could be common enough that there may be upwards of 1 million cases across the board of cutaneous squamous cell carcinoma in the United States and actually north of 10,000 deaths. So it's clearly a medical problem with a lot of morbidity.

For 280 itself, we have now, as we've outlined for you, cutaneous cell squamous carcinoma study, ongoing up on clinicaltrials.gov, they're doing some dose ranging work with 280 and then we'll expand with a declared dose going forward and could potentially serve on its own as a registration effort, but that's down the pipe and to be determined.

Why Replimune, why RP1? It's a tumor oncolytic virus with actually outstanding efficacy already demonstrated in cutaneous squamous cell carcinoma that's advanced with checkpoint inhibitors, activity in terms of response rates in the 70% range, complete responses in a 47% range. So really, outstanding activity with checkpoints are already demonstrated, but with intravenous given on how this is administered with intratumoral injections, it really lends itself to combining with an oral agent like 280 and we view this as an exciting potential going forward. This is a proof-of-concept study though in the neoadjuvant setting, and then we'll determine if there's a registration path afterwards. So thank you for the question.

Operator

Next question today is coming from Vikram Purohit from Morgan Stanley.

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

So we had 2, both on Jakafi. So first, could you comment on whether there were any outsized or large inventory purchases that contributed to Jakafi's 2Q sales base? And then secondly, could you remind us where your dialogue stands with the FDA on QD RUX and just what the next steps are for moving this program forward.

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

It's Christiana. So first of all, in terms of your inventory question, as you may recall, Inventory at the end of Q1 was below the low end of the normal range. And that was because of the timing of an order. What we saw in Q2 was an increase in inventory to that brought inventory back within the normal range. And I would say it's towards the higher end of the range, but that variability, you see it from quarter-to-quarter within that normal range. So we are back at the normal range. And as I commented during my remarks, the inventory increase during Q2 represented $35 million in net sales. Let me turn it to Barry for the second part of the question.

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

Thank you, Christiana. So Vikram, in terms of RUX XR, just to remind you, the CRL from the FDA was a concern around [C-min] at steady state, not area under the curve and not Cmax and then resulting in a potential theoretic concern in terms of efficacy and that there was a 24% lower c-min when you compare it to the IR.

So in terms of the go forward, there is a potential approach that's quicker and involves modeling work that we're doing at the moment, and we need to discuss with regulatory agency and we can't give you timing yet on that. And then a potentially longer effort that may take a little longer.

And but clearly, for both we'll have them ready and be able to submit way before the loss of expiration for RUX itself. So it's too early to give you regulatory timing, but both efforts are underway.

Operator

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

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

You will share more combo data on the Jakafi out in that combo in the second half. But in the context of where key stands and the overall combination strategy here, can you just help us understand what your thinking is on how this could play out from a life cycle management standpoint.

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

It's Steven. Both, as I alluded to in my prepared remarks, both BET and ALK2 are progressing well. BET clearly activity with monotherapy and in combination. And now it's just about declaring the dose and then the registration intent for that and then also watching the competitive space. ALK2 very well tolerated. It can keep escalating and hopefully continue to see improved efficacy and then that may be potentially a first-line effort because of its tolerability and the ability to both treat the anemia and maintain RUX dose intensity and then I just outlined the QD effort on its own in terms of formulation development.

We also are working on fixed dose combinations for both BET and ALK2 and those aren't impacted by the CRL in any way but it is likely that when we go to pivotal studies with BET and ALK2, that those will be done with the IR in combination with BET and ALK2 and then should we want to use FDCs, we pivot to that with bioavailability bioequivalence work at that time. All of those efforts are underway aggressively. And again, we very much want to complete and should complete them before the loss of expiration of RUX itself.

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

Just a follow-up here. So then how does CALR and CK0804 kind of fall into this strategy as well?

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

So mutant CALR is on its own an entity that, as I said earlier, about 30% of myelofibrosis and in fact, 25% to 30% of essential thrombocythemia and is the oncogenic driver on its own. It's mutually exclusive, doesn't overlap with MPL Or V617F or anything else. And so should this work the way it looks preclinically and be well tolerated. It's an entity on its own and would be a different treatment paradigm in terms of thinking because the idea would be to eliminate the malignant clone and potentially cure you of the conditions. So you'd no longer have a clone that causes the disease and the disease symptoms and that is why it got a plenary at ASH and is potentially so exciting.

And should that pan out all the way to the end, then about 1/3 of each of those entities would be taken care of on their own with the antibody and would be no need for JAK inhibition, BET inhibition, ALK2 inhibition, et cetera. The [Cellenkos-0804] effort is a different effort entirely, it's umbilical cord T Reg cells that are enriched to home to the bone marrow and have already shown in small single case studies to change the natural history of myelofibrosis and potentially also improve fibrosis there as well and to be safe. So it's early days with that, and we want to again show data on that later this year. And it's too hard to comment on where that will go from a strategic point of view. But the idea there again is to be disease-modifying given the therapeutic modality.

Operator

Your next question today is coming from Evan Siegerman from BMO Capital Markets.

Conor MacKay

This is Conor MacKay on for Evan. Congrats on the quarter. Congrats on the quarter. So you noted in your press release this morning, increased demand for Opzelura. And I'm just wondering now that we're a bit further into the launch in vitiligo, could you just comment on if you're seeing any previously inactive patients or patients who have stopped seeking treatment previously starting to come on to Opzelura.

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

Conor, it's Barry. So we obviously have patients that have been seeking treatment all along for their vitiligo and then new patients that learned about Opzelura and go in to see their dermatologists. I can't give you any numbers at all, about the number of patients who were, in fact, inactive but we do want to -- part of our entire effort for any direct-to-consumer activity is really just to let those patients who want to have their vitiligo treated to know that there is a treatment available for the very first time that can actually help them to repigment their skin. So that's what we'll continue to do to drive the patients back to the office.

Operator

Your next question is coming from Jay Olson from Oppenheimer.

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

Congrats on the quarter, can you talk about the pace of Opzelura uptake in Europe versus the U.S. And any comments you could share on the momentum of Opzelura growth and when you might provide specific revenue guidance on Opzelura.

Herve Hoppenot - *Incyte Corporation - CEO & Chairman*

I can take the European -- I'll do the European part of this today. So the approval and the launch in Germany and Austria took place at the end of the end of the quarter. It was in the last days of June. So we are in the process. Now we have 1.5 months, we see a good uptake. In fact, we see adoption in Germany, where it's obviously the most important market, and it will continue to be the most important for the year because we anticipate the next reimbursement to take almost that long to become effective in other countries in Europe.

So what you can anticipate there is another 10 months where Germany and Austria would be the only or the main countries where Opzelura is being used. And what we see I mean, there was in Europe, when the approval was done first, the label in Europe is excellent. It's different from the label in the U.S. in terms of the entire safety profile.

In fact, it has no equivalent of whether Black Box in Europe. So all of this issue of systemic exposure to JAK has been looked at by the European authorities very differently from than what the FDA has done in the U.S. And the media impact of the approval has been very visible on TVs and everywhere across Europe, we had number of patients and physicians speaking about the importance of treating and repigmenting vitiligo. So the awareness of Opzelura is already very high. We have a lot of demand, we have programs we are trying to put in place to help patients where we can. And we are fairly optimistic that it will be a good product for Incyte, and it will have a reasonable potential. And the second part of your question is about guidance for Opzelura. I think you can...

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

So in terms of the guidance, we still want to see a few more quarters of uptake. It's still early. We want to be able to see -- to the earlier discussion, how vitiligo patients especially that have been active come into therapy and also more information on refills before we are in a position to provide guidance.

Operator

Thank your next question today is coming from Mara Goldstein from Mizuho Securities.

Unidentified Analyst

This is Jerry on from Mara Goldstein. Starting first with Opzelura with the free drug program and the IQVIA projection, are you seeing a difference between AD and vitiligo? And can you comment on the moving forward rates for the rest of 2023? And then looking towards axatilimab, could you share how Incyte and Syndax are planning to share responsibilities for the upcoming BLA filing and maybe potential commercialization as well?

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

So Jerry, for Opzelura for free drug. We don't really see any difference whatsoever between (inaudible) for free drug for atopic dermatitis and vitiligo. Obviously, I said before that there's more AD patients that are on Opzelura and a growing number of patients with the legos that are on Opzelura but the free drug difference, we don't know.

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

Jerry, it's Steven. In terms of the BLA, obviously, both companies have worked really well together. The study was executed well, brought in well, high quality, et cetera. But Incyte will be leading the filing activities, with Syndax appropriately helping along the way. On the commercialization question, I'll ask Herve to address it.

Herve Hoppenot - *Incyte Corporation - CEO & Chairman*

The commercialization of AXA will be different in the U.S. and Europe and rest of the world. So in the U.S., it's co-commercialization led by Incyte, where we would be booking the revenue and where there is an option for Syndax to field up to 30% of FTEs in the field force if they choose to. And so that would be for them to decide if they want to do that. And at the end, we will do a 50-50 profit split of the commercial activities in the U.S. Outside of the U.S., it's a license where we will be paying a royalty to Syndax, and we will be prosecuting all activities related to regulatory and commercial for axatilimab.

Operator

Next question is coming from Eva Privitera from TD Cowen.

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

A few questions from us. Can you help set expectations for povorcitinib in prurigo nodularis? What would be considered a good profile in that disease? And what's the efficacy bar for moving into Phase III.

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

Yes, Steven. Yes, the povorcitinib prurigo nodularis Phase II enrolled really well. It's complete, we'll have data later this year. The central problem for those patients is a very intense and severe itch and then obviously, the actual skin lesions. But what the patients really want is the itch-relief and that's why we feel an oral JAK inhibitor is appropriate in these patients with more severe prurigo nodularis.

There is already approved drug in terms of Dupixent in PN in general. So the regulatory path is pretty well established. This study, there is a Phase II proof-of-concept study. If we get the profile we want in terms of itch relief and the lesion resolution, then we'll advance to Phase III development, but we'll talk about that later this year. Thanks.

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

And another question on povorcitinib. Can you give a quick enrollment update for the Phase III and HS? You know that AbbVie has recently opened a Phase III for Rinvoq.

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

Yes. Thank you. So we don't give numbers as we progress. We have 2 Phase IIIs up and going. They're enrolling really well. We obviously started before them. I think across dermatology, in general, when you go back to rux cream, AD, vitiligo, et cetera, our operational execution has been excellent. So we've got really good at knowing the derm space and how to conduct these studies. But we don't provide patient-by-patient enrollment updates.

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. I just had 2 on axatilimab, maybe could you just remind us how it might be positioned competitively versus Sanofi's Rezurock in the third-line setting based on the previously announced top line data? And then, I guess, could you just tell us how you're tracking with the planned Jakafi combo study in the frontline setting? And maybe what you might need to see in order to advance that into a Phase III trial, any specific efficacy outcomes.

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

Kelsey, it's Steven. So the axa-data I won't go through again. I had them in my prepared remarks, but the eligibility criteria was for 2 or more prior therapies. The median on the patients is actually 4. So we'll have to be discussing with regulatory agencies as to what line of therapy that will be given in terms of a label. It's likely to be at least in the United States somewhere in the third-line territory given the data set.

But as I said in my prepared remarks, that efficacy of 74% were seen across the board, including in post-rezurock patients. And obviously, those were predominantly in the United States given that's where that drug is approved. But it's premature to comment on the exact line we're getting labeling until we have those discussions.

In terms of the combo work, I assume you're talking about graft versus host disease again. And in combination with ruxolitinib, there's theoretically a huge appeal because, one, you have a small molecule with a large molecule and no theoretic concern in terms of drug-drug interactions, nonoverlapping MOA, a JAK inhibitor with a macrophage monocyte targeted drug, so we don't expect to run into tox. And then we want 2 very

now very active drugs in graft versus host disease, it's really appealing. Can you move up the treatment paradigm. So we're going to start that combination as soon as possible with Rux and axa, tested likely in the first, second line setting and then we'll work out, see that activity and see where we want to go. There is appeal to go first line because steroids are dominantly used there are active but have a lot of long-term toxicity but there's also appeal in second line as well. So we'll see where the data leads us with an exciting time for that combination.

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

Congrats on the quarter.

Operator

Our next question is coming from David Lebowitz from Citi.

David Neil Lebowitz - *Citigroup Inc., Research Division - Research Analyst*

Could you provide more detail on the number of tubes per patient on Opzelura, just curious as to where to the extent that overall growth in the quarter was driven by new patients coming to therapy or increase in the tubes per patient?

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

Sure. So David, it's Barry. So basically, I mean, where they're driven from is we said that the total RXs grew by 16%. So that's across AD and vitiligo and refills grew by 23%. So we expect refills to continue to grow and be more than 50%, in fact, going up much higher than that, over time. As far as the growth from AD and vitiligo, both are growing, new patient starts in both vitiligo and AD continue in the right direction in terms of refills for each.

I discussed it before, that we expect, in fact, that 2 to 3 tubes for the AD patients, and we hope to get to an average of 10 tubes per patient for vitiligo. We think we're headed in that direction now, and we'll continue to reinforce how to use the drug both with dermatologists and with patients, and we think we'll achieve at least that number.

Operator

Next question is coming from David -- I'm sorry, Derek Archila from Wells Fargo.

Unidentified Analyst

This is (inaudible) for Derek. Two quick ones for me. First, how are you thinking about M&A? And what would be your priority between [I&I] and oncology assets? And second, what are your thoughts on the HS opportunity for povorcitinib in light of recent competitor data?

Herve Hoppenot - *Incyte Corporation - CEO & Chairman*

You want to take the HS.

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

So I'll do the second question first. So the profile in HS for povorcitinib, which we presented earlier this year at a medical meeting is outstanding in terms of efficacy. In fact, we think as far as we can tell, it's the first time ever that a HiSCR 100 has been reported by a compound in this entity. And that -- by that, I mean, a complete response. So abscess, nodules, fistula is completely disappearing. And that's really encouraging for the profile going forward for povor.

The -- you're right. It's now an active space of research. There's many biologics, including IL-17 targeted drugs. And there's lots of unmet need. And so it's good that other people are trying to address that. I would just say when you compare studies, look carefully at patient populations look carefully at concomitant antibiotic administration, we didn't allow that on our studies. And then obviously, the placebo arm activity as well when comparing but the profile we saw in our Phase II is outstanding. And if we replicate that in Phase III, we'll have a potentially best-in-class compound there.

Herve Hoppenot - *Incyte Corporation - CEO & Chairman*

Maybe I can say a word about M&A. I mean, we are in a position where, as you can see, I mean, the growth of our existing business is very strong. The pipeline is very promising. We have a number of very good products that we are now developing at late stage, and we didn't speak very much about some of the early stage projects, but they are also very interesting. So we are looking at what could be the best use of the cash that we have, we have north of $3 billion now and how we could add to this diversification and growth that we are doing with our organic portfolio. It could be M&A or it could be licensing, business development. You see axatilimab was a license from Syndax and it's clearly helping us strategically with the portfolio and the limber program and also adding mechanisms that we can combine with Jakafi.

So this type of agreement could continue when we see them, when we find them or acquisitions that could be in dermatology or oncology, assuming that these products that we would be acquiring have the potential to contribute to the growth in the year '25, '26 and beyond because that's where really we need to add to the portfolio at that point. So that's really the criteria we are using. And we are sort of agnostic of onco versus derm, I think the question is the quality of the science, the quality of the product and the timing and the potential of products we would be adding to our portfolio.

Operator

Your next question today is coming from Ren Benjamin from JMP Securities.

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

Congratulations on a great quarter, can you talk a little bit about the opportunity in Prurigo nodularis, how big or small is this opportunity and how should we be thinking if these current studies are positive, how should we be thinking about pivotal studies and how big they might be going forward? And maybe a bigger picture question is, when we think about derm as a business, is this something that ultimately will be part of Incyte kind of going forward and taking up a significant part of the revenues, is something that might get spun off at some point, just given the size of the studies that you might need to conduct for these other indications? Any thoughts there would be helpful.

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

Yes, Ren, it's Steven. So prurigo nodularis is often not diagnosed or underdiagnosed. It's hard to be precise on the epidemiology, but there are probably around 200,000 or north of that patients in the United States with PN. And as I said earlier, their biggest morbidity is itch, and it's a massive impact on quality of life. So that's what we're looking for in terms of povorcitinib. The regulatory part has already been defined by the DUPIXENT approval and how it gets there. And it's premature to talk about sizing and powering until we see our Phase II proof-of-concept data there. Just by the way, ruxolitinib cream, Opzelura in more mild PN is also very active, and it's something we're obviously interested in studying and seeing the outcome of as well. In terms of the second question, I'll turn that over to Herve.

Herve Hoppenot - *Incyte Corporation - CEO & Chairman*

So yes, I mean, you can -- I mean, the question is really is dermatology business that we believe has the potential to continue to grow to be of a meaningful size, and the answer is yes and yes. And you can see it. You can see the program we are developing for rux cream. There are 4 or 5 new indications we are prosecuting on top of vitiligo and atopic derm, where we believe there is a clear medical need and where. In fact, the power of topical JAK is with the safety profile it has and with the efficacy it has, is really competitively well positioned.

We choose to develop povorcitinib in a number of indications where there is interest. And you can see that interest, in fact, now coming from the biologics and some other ways of approaching this biology, but we believe again that the JAK inhibitor is a very good way with the fact that we are ahead of the pack in that development process, is a very good way to help these patients and being first or best-in-class in that case is very feasible.

And then we have auremolimab, which is a new mechanism that needs to be proven, but could be also very promising. So we have this view of developing an IAI dermatology portfolio over time that will be contributing equally to the revenue or to at least to the growth of the corporation in the next few years. And we see a lot of complementarity in the research that we are doing in inflammation, in immunology and how it could apply for cancer on one hand and in some cases, how it can apply for autoimmune disease or inflammatory disease on the other hand. So all of that now is something that is well established. We have the team on the commercial side in the U.S. now fully fielded, and we are building it in Europe. So I think it's a picture of Incyte for the next 5 years will be both derm and onco in parallel.

Operator

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

Greg Shertzer

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.