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INCY.OQ - Q1 2022 Incyte Corp Earnings Call

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OVERVIEW:

Co. reported 1Q22 total product and royalty revenue of $728m.

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PRESENTATION

Operator

Hello, and welcome to the Incyte First Quarter 2022 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 Christine Chiou, Head of Investor Relations. Please go ahead.

Christine Chiou - *Incyte Corporation - Head of IR*

Thank you, Kevin. Good morning, and welcome to Incyte's First Quarter 2022 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. Incyte's strong momentum in 2021 continued into the first quarter with product and royalty revenues up 20%. Jakafi grew 17% year-over-year with patient demand driving growth in MF and PV as well as in GVHD following the successful launch in the chronic indication. Our hematology and oncology portfolio grew 24% year-over-year, driven by our new product uptake consisting

of multiple new launches, including Pemazyre in Europe and Japan and Minjuvi in Europe. The Opzelura launch continued to be very successful with strong uptake by dermatologists, high satisfaction reported by both patients and physicians and significant advancements with payers, which Barry will address in his remarks.

We made progress across all stages of our pipeline with important updates that include positive 52-week data for ruxolitinib cream in vitiligo, the prioritization of 280 and 318 in our oral PD-L1 program and the start of our CDK2 clinical program.

Our royalty revenue remained strong, growing 23% year-over-year, contributing to our growth profile.

Turning to Slide 5. As you can see on the left, we are still in the early phase of launch for many of these products, including Opzelura in atopic dermatitis, Pemazyre in cholangiocarcinoma, where we are expanding geographically; and Minjuvi, which is just starting to launch in Europe and Jakafi where we have recently launched in chronic GVHD in the U.S. There is ample room for growth with each of these new launches. On top of that, we have new potential indication that we'll be providing additional growth opportunities with Opzelura in vitiligo and with our partner product where we have new indication being planned over the next few months for Olumiant, Tabrecta and Jakavi.

In addition to these launches, there are a number of programs in our mid- and late-stage pipeline, as shown on the right that could have a meaningful impact on our revenue.

Before handing the call to Barry, I would like to provide an update on Opzelura manufacturing. We have recently received FDA approval and have implemented the new manufacturing process to improve the dissolution of API for Opzelura. In addition, consistent with best practices, we have received FDA approval for a second manufacturer of Opzelura to support our successful launch. We are also preparing to reintroduce samples in the U.S.

Now to share more details on product performance and outlook, I will turn the call over to Barry.

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

Thank you, Hervé, and good morning, everyone. The launch of Opzelura in the U.S. is off to an excellent start with over 68,000 total prescriptions written through the end of the first quarter. More than 38,000 new patients were treated in the first quarter bringing the total number of new patients treated with Opzelura to over 57,000 since launch. We attribute the robust uptake and the very high satisfaction of both patients and physicians which is fueling the positive feedback loop and driving demand. Patients are requesting refills, which accounted for roughly 23% of prescriptions in the last week of Q1, another good indicator of long-term growth potential for Opzelura. On the payer front, we have added coverage of over 75 million additional lives since the end of January. This brings the total number of covered lives to 146 million, highlighting the progress we have and continue to make in the early months of launch.

Turning to Slide 8. Multiple leading indicators are supporting the long-term potential of Opzelura, including market share gains for new patients and positive feedback on patient experience. In just 6 months since launch, our 12% new patient share now exceeds that of Eucrisa and Dupixent, highlighting the unmet need for more efficacious treatments for atopic dermatitis patients. Over 7,500 physicians have now prescribed Opzelura. We continue to increase our prescriber depth week-over-week, gaining an average of 200 to 300 new writers each week. Our high decile prescribers, those who see the highest volume of AD patients each week and who have written the scripts for Opzelura have initiated an average of 18 new patients of Opzelura since launch.

This repeat prescribing shows the positive experience and confidence that physicians are having with Opzelura and is supported by recent market research from the field. We are receiving very favorable feedback from the physicians about the efficacy of Opzelura, resulting in a high rate of satisfaction among both patients and physicians. In a recent survey, over half of physicians indicated they expect to increase prescribing of Opzelura in the next 3 months with over 60% of our top dermatologists indicating (technical difficulty) use of Opzelura will more than double in the coming months.

Moving on to our progress with payers on -- (technical difficulty) Since our last update -- Q4 earnings call, we were able to get NDC blocks removed with one national PBM, one large national health plan and multiple key regional plans, adding approximately 53 million commercial lives, which are now covered, including our progress with Medicaid and government channels, our total number of lives covered has increased by 75 million to reach 146 million, which is outstanding progress in the short amount of time. As a final note on Opzelura, we are also preparing to reintroduce samples in the United States.

Turning to Slide 10 and Jakafi performance. Jakafi net sales in the first quarter grew 17% year-over-year to $544 million. Total patient demand grew across all indications and the growth in new patient starts of 12% and versus the first quarter of 2021 remains above pre-pandemic levels. New patient starts in GVHD grew 25% year-over-year, with strength coming from the launch in the chronic indication. With the strong demand for Jakafi, we are raising the bottom end of our Jakafi full year net product revenue guidance from $2.3 billion to a new range of $2.33 billion to $2.4 billion.

Turning to Slide 11. Monjuvi net product sales in the U.S. grew 21% year-over-year to $19 million in the first quarter, and we are continuing to see uptake in new and existing accounts, more second-line use and a gradual improvement in duration of therapy. Minjuvi net sales were $5 million, with the launch ongoing in Germany, and we continue to seek reimbursement in other countries. Pemazyre grew 34% to $18 million with the duration of therapy continuing to drive its performance.

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

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

Thanks, Barry, and good morning, everyone. Starting with ruxolitinib cream on Slide 13. Last month, we presented updated 52-week data for ruxolitinib cream in vitiligo at the American Academy of Dermatology Annual Meeting. As a reminder, during the 24-week double-blind period, patients were randomized 2:1 to receive ruxolitinib cream 1.5% b.i.d. or vehicle. After the 24-week visit, all patients crossed over to active therapy.

At 52 weeks, approximately 50% of the patients initially randomized to ruxolitinib cream experienced at least a 75% improvement in their VASI score from baseline, and nearly 1/3 of patients experienced at least a 90% improvement in facial VASI. No new safety signals were seen and ruxolitinib cream was well tolerated with no serious treatment-related adverse events reported. These data demonstrate the potential for substantial improvement in repigmentation with a longer duration of treatment with ruxolitinib cream.

Also at AAD, we presented data from our population-based VALIANT study, which aim to better understand quality-of-life burden faced (technical difficulty). In studies, anxiety and depression were reported in up to 68% and 62% of patients with vitiligo, respectively.

The psychological impairment that may result from vitiligo can be similar to that of other skin diseases such as psoriasis or eczema and can impact patients of all types, indiscriminative skin color, percentage body surface area involvement or the area affected. Many patients of vitiligo have stopped seeking treatment due to a lack of approved therapies. We are excited with the potential to bring the first FDA-approved therapy for repigmentation to people with vitiligo and to be able to offer them a new choice of therapy. Ruxolitinib cream is under review both in the United States and in Europe with the PDUFA date in the United States of July 18.

Moving to Slide 15. We are initiating a study in vitiligo to evaluate the benefit of adding phototherapy to ruxolitinib cream treatment. This is a 48-week trial where patients will receive 1.5% ruxolitinib cream twice daily for 12 weeks followed by ruxolitinib cream plus or minus phototherapy.

Rounding up dermatology, INCB54707, is in Phase II studies for vitiligo, hidradenitis suppurativa and prurigo nodularis where there continues to be high unmet medical need and the lack of effective therapies or in some cases, no approved therapies at all. We expect to present data for vitiligo and hidradenitis suppurativa in the second half of this year.

Turning to Slide 17 and our Oral PD-L1 program. Last year at SITC, we presented data on the 3 compounds in our oral PD-L1 program, where we demonstrated the first clinical activity with an oral PD-L1 inhibitor. We saw evidence of tumor shrinkage with all 3 compounds. And in the case of 86550, an increased rate of peripheral neuropathy. Based on clinical data from ongoing studies and positive therapeutic ratios seen for 280 and 318, we have opted to move forward with these 2 compounds. Enrollment is progressing well in both studies with 280 and 318. We continue to

observe tumor shrinkage with both compounds and to date, no evidence of peripheral neuropathy has been seen. There are several benefits to an oral PD-L1 including the potential for better management of immune-related adverse events due to a shorter half-life, the opportunity of developing oral-oral combinations and the ease of dosing with an oral agent. We expect to provide a data update from our oral PD-L1 program in the second half of this year.

Moving to early development on Slide 18. We are initiating a Phase I dose escalation and dose expansion study in advanced solid tumors with our novel, potent and selective oral small molecule CDK2 inhibitor, iNCB123667. 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 amplified tumor models. -- Cyclin E is an amplified oncogene in multiple aggressive cancer types, including ovarian and endometrial cancer.

To close, we expect multiple regulatory and key clinical data readout this year as shown on Slide 19. Specifically for LIMBER, the once-daily rux NDA will be submitted in this half of 2022. The BET and ALK2 combination with ruxolitinib are progressing well with data expected in the second half of 2022. The ruxolitinib cream, PDUFA, for vitiligo in the United States is July 18, and we expect an EMA decision in the second half of this year as well. For our partnered products, ruxolitinib in acute and chronic graft versus host disease and capmatinib in non-small cell lung cancer, both have received positive CHMP opinions.

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 products and royalty revenues of $728 million, representing an increase of 20% over the first quarter of 2021 and reflecting growth across products commercialized by Incyte and Incyte discovered products commercialized by our partners. Total product and royalty revenues for the quarter are comprised of net product revenues of $544 million for Jakafi, $49 million for other hematology/oncology products and $13 million for Opzelura. Royalties from Novartis of $71 million for Jakavi and $3 million for Tabrecta and royalties from Lilly of $48 million for Olumiant.

Turning to Opzelura, in the first quarter, the growth in prescriptions continued to be strong, leading to gross product sales of $90 million for the quarter. As payers add Opzelura to formularies, we are starting to see the improvement in the gross to net discount rate. The fully-loaded gross to net discount rate decreased from 92% in the fourth quarter of 2021 to 86% in the first quarter of 2022, leading to net product sales for the quarter of $13 million.

On our Q4 call earlier this year, we showed you our forecast of the evolution of the gross to net discount rate as depicted by the dotted blue line. The green line represents our actual gross to net discount. And as you can see, Q1 was very much on target. We expect the gross to net discount rate to continue to decline in Q2 and normalize at a fully loaded rate of 40% to 50% between Q3 and Q4, depending on the timing of the removal of the remaining NDC blocks by PBMs and the addition of Opzelura on formularies.

Moving on to our operating expenses on a GAAP basis. Ongoing R&D expense of $333 million for the first quarter decreased 13% from the prior year period primarily due to -- increased 13% from the prior year period, primarily due to the continued investment in our late-stage development assets. Total R&D expense of $353 million for the first quarter includes milestone consideration of $20 million for our collaborative agreements.

SG&A expense for the first quarter of $210 million increased 36% from the prior year period's total SG&A expense or 49%, excluding the $13 million onetime payment recorded in the first quarter of 2021. The growth was primarily due to our investments related to the new dermatology commercial organization in the U.S. and the related activities to support the launch of Opzelura. Our collaboration loss for the quarter was $5 million, which represents a 50% share of the U.S. net commercialization loss for Monjuvi.

Finally, our financial position continues to be strong as we ended the quarter with $2.5 billion in cash and marketable securities.

Moving on to our guidance for 2022, as a result of our strong first quarter performance as well as signs and expectations of sites reopening and providing us with increased access to physicians, we are tightening our Jakafi guidance range from $2.3 billion to $2.4 billion to a new range of $2.33 billion to $2.4 billion. We are also reaffirming our other hematology/oncology revenue, COGS, R&D and 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) Our first question today is coming from Vikram Purohit from Morgan Stanley.

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

So I had a few on Opzelura. First, could you speak a bit more about the manufacturing update you began the call with? Specifically, at this point, how many batches or what portion of the current commercial supply do you estimate has been impacted by some of the texture issues that you mentioned previously? And for the updated manufacturing process, what is the current thinking around the timeline for getting that up and running? And how long do you think it will be before the sampling program can be reinstated? And then I had a follow-up, but maybe I'll ask you those questions first.

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

Vikram, it's Steven. I'll take your question, and I'll just reaffirm some things we said on the actual prepared remarks. And just to reiterate, we know that the texture issue is due to a very small amount of active pharmaceutical ingredient that has come out of solution. And that has obviously been the focus of all our efforts. As Hervé said upfront, we have implemented a recent process change via a regulatory process called a CBE-30 that improved solubility. We've received FDA approval for this and that process is underway and is improving the dissolution of API. In addition, as Hervé said on his prepared remarks via a longer regulatory process called a prior approval supplement and as is best practice, we've initiated a second manufacturing site and that is coming on board as we speak to answer your question specifically. So those units from that second site will -- in the next couple of weeks will be out in the field and with patients.

We absolutely expect also within the next week or so, as Barry said in his remarks, to begin the sampling program as well, given that now we have a batch made for that. We don't give specific numbers on percentages, but as we have already said in the call, 68,000 prescriptions, with a very small amount of complaints, the rate is obviously coming down, and we expect it to do so now with these improvements as well going forward. .

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

That's helpful. And then as a follow-up for Vitiligo, assuming FDA approval in July, would you anticipate providing U.S. sales guidance for Vitiligo, the way you have for AD? And more generally, as you've evaluated the opportunity in Vitiligo over recent months, how do you think the commercial opportunity compares to what you're seeing now evolve in AD?

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

So Vikram, it's Christiana. In terms of the vitiligo peak sales potential, I think it's a little bit of a different situation than AD. In the AD, AD is an established market where it was easier to have a sense of not only the size of patients that are affected by AD, but the number of patients that are actively seeking treatment today and how this market looks like and how it may evolve.

In the case of vitiligo, we have discussed in the past, there are no effective therapies now. And as a result, the patients -- the majority of patients are not currently seeking treatment. So its a little bit harder to have right from the beginning a sense of how quickly that will change. And therefore, we may not be in a position from the beginning to give you the peak sales estimates that we did for AD. Actually, if you look at Vitiligo, and you run the numbers, even for the current number of patients that seek treatment you can see that you can very quickly get to very big numbers like in the billion-plus type of numbers. So we want to see a bit more of how this evolves before we come out with the peak sales potential for vitiligo.

Operator

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

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

I was wondering now that you're reinstating the sample program, would this continue if and when Opzelura is approved for vitiligo especially given that you might need to use it for a slightly longer period of time versus atopic dermatitis in order to see efficacy? And for Opzelura and atopic dermatitis, is that as the drug is being adopted and we moved through the launch, do you have a better sense now of duration of therapy? And is there any gap between refills? Or you're seeing people refilling at pretty good compliance rate?

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

So Kripa, this is Barry. So yes, when we initiate, reinitiate the samples for AD, we anticipate we'll still have samples and continued samples throughout the launch of vitiligo. As far as duration of therapy, it's too early in the launch. I mean we've launched for 6 months now. We see new patient growth continuing to accelerate. We see the refills at 23%. We think that's pretty good for right now. And so -- as far as the duration of therapies, we don't know. As far as gaps between tubes, for example, we also don't know. We'd have to go back to the clinical trial to see exactly what those patients did, but it may not be the same in the real world for duration of therapy. What we've said in the past, of course, is that once we stabilize over a period of time, as we get into launch, we anticipate that patients will generally get 3 to 4 tubes of Opzelura per year for atopic dermatitis.

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

Great. And if I can ask a quick follow-up question. One of the KOLs we spoke to said that consensus about Opzelura is broadly really good, but the black box label may be affecting uptake in community settings. Is that what you're seeing? Or is the use of the drug impacting how community doctors are looking at it?

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

No, I can't say that community doctors are any different than academic doctors. In fact, in dermatology, there's very -- there's very big practices that treat many, many patients [in their] uptake of Opzelura. So our highest decile prescribers, for example, continue to use it. They'll tell us sometimes that individual patients might have more questions about the black box, but they're very used to explaining black box or side effects or potential side effects that any drugs they use may have. So they're comfortable walking patients through that, but we really haven't seen it as a barrier.

Operator

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

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

First, on the PODIUM-304 study, following the recent FDA AdCom, even though this trial does have a couple of U.S. sites, it's not really comparing retifanlimab to the current standard of care in the U.S. So wondering if you've got FDA sign-off on that trial design? Or if you'll have to make changes based on kind of the FDA's pushback of Lilly sintilimab approach? And then second, at the time of the Monjuvi deal, you had mentioned longer-term upside was really from the potential of Monjuvi plus parsaclisib. So I assume given the recent FDA ODAC on PI3 kinases and the decision to withdraw the parsaclisib NDA, that option might be kind of gone now, but just wondering what it means for the top line study. And does the secondary OS endpoint in the myelofibrosis combination studies become really important after that ODAC -- or does it maybe not impact myelofibrosis as much?

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

Matt, it's Steven. Thank you for your question. So just for everybody else, PODIUM-304 is our IV checkpoint retifanlimab in non-small cell lung cancer. It's a replication, if you will, of the initial pembro approval in that indication, and that its combination with chemotherapy versus checkpoint inhibitor alone. And as you point out, it's a global study with sites all over the world, including in the United States. So we think that is the central difference from the Lilly issue they had with their checkpoint inhibitor where it was China-only data. So we have representation across Western Europe, Eastern Europe, Asia and a small amount of U.S. sites. So we think from a diversity of subject point of view, we're well covered with that.

The modeling of the study is exactly from a statistical point of view, in keeping with what we're seeing in the initial pembro approval in that indication, that was discussed with regulators and feedback was given and aligned with them. So we feel we are in a completely different position to what was the central complaint against the Lilly submission with their checkpoint inhibitor in non-small cell lung cancer, given the diversity of our population across the world, the size of the study, replication of the statistics to achieve the same end points, which, again, wasn't exactly the case with the ODAC reference.

For tafasitamab in combination with parsaclisib -- we remain interested despite some of the negative halo on PI3 delta inhibitors for a number of reasons. Firstly, because, we know this is a tremendously active doublet from work that MorphoSys have done before with tafasitamab with idelalisib -- and that having upwards of 100% response rates. So we are absolutely continuing to look at our data in top-MIND, which is ongoing across different disease segments, including lymphoma, including chronic lymphocytic leukemia.

But you are right. I mean, there is a large increase in the safety of delta inhibitors, and it's something we will have to consider very carefully before going forward with any bigger study there. We hope in the second half of this year to have decent data sets for the different subgroups of diffuse large B-cell lymphoma, low-grade lymphomas, chronic lymphocytic leukemia with that doublet and then we'll have to make decisions in keeping with the context you alluded to.

I'm glad you also brought up the myelofibrosis program because, again, it's rux in combination with parsaclisib in 2 different settings. So there's a first line study, which is enrolling very well. It's a goal enrollment of around 440 patients, and it's a very clean study in that its rux plus parsaclisib versus rux alone in that indication with the SVR 35% decrease primary endpoint. So the differences, again, given the [milieu] you talk about the PI3 delta inhibitors is that this is a randomized study at a different dose of a delta inhibitor. There's no induction therapy, it's a standard constant dose. It's a defined treatment period. The studies were agreed to and signed off with regulatory authorities and thus has, as you point out, also the ability to capture overall survival. So we think we're well covered in that indication.

The suboptimal study there is in about 220 patients also enrolling very well, should complete next year, different endpoints, again, a randomized study and in capture primary endpoints as well as secondary endpoints that will include safety. So again, a different dose, and we think we're well covered there as well. But we're not immune to the fact that the road for delta inhibitors will be extremely safety focused as [they] should be.

Operator

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

Unidentified Analyst

This is Leonid on for Brian. So thanks for providing all the gross to net color. I was just wondering if I could ask a little bit more on that. I guess, in previous calls, you mentioned that you have levers to adjust gross to net on your end. So I'm curious if the improvements in gross to net are largely from better insurance coverage or if also you're adjusting any of the patient assistance programs? And I guess for how long and to what degree do you expect these patient co-pay systems to last? And then if I can just squeeze in one more. Have you had any sense that there might be patient and doc perceptions that because insurance isn't covering Opzelura that's actually limiting willingness to write scripts. And so I guess when you see better coverage? Are you expecting that there might be a script inflection as well for Opzelura?

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

So it's Barry. So on the gross to net, so as we said, as we continue to get better coverage as the NDC blocks are removed, our gross to net, as Christiana said, is going to improve in the second quarter, in the third quarter and in the fourth quarter. So we have 146 million lives that are covered now, so they have access to the drug and our -- as far as our full buy-down program goes, we knew from the very beginning when we launched this drug that we wanted to have a generous program -- patient assistance program, where if a dermatologist wrote the prescription, the patient would be able to get it regardless of NDC blocks. As those NDC blocks are removed and utilization criteria are written, then we take down those full buy-down programs and that actually does improve our gross to net over time because it's just unnecessary now, insurance companies are going to pay for it.

As far as coverage goes, I mean, just as I said, the prescribing is not impacted. We did not want it to be impacted because we had a generous patient assistance program in place and there really hasn't been any barriers. As prior approvals, of course, come into place, dermatologists and their offices are very familiar with going through the prior approval process. Every prescription for psoriasis, every prescription for atopic dermatitis for branded drugs, all have to go through prior approvals. So there really isn't the barriers. And we tried to remove those barriers as much as we could so people could get great experience with Opzelura, and we know that they're really having great experience with Opzelura. Physicians, dermatologists are telling us they're having great experience with Opzelura. So we think the uptake that we're experiencing now is going to continue throughout the end of the year and beyond.

Operator

Our next question is coming from Cory Kasimov from JPMorgan.

Gavin Scott - *JPMorgan Chase & Co, Research Division - Analyst*

This is Gavin on. There's been a lot of focus on Opzelura, so I'll stay away from that. But just on the pipeline, I guess, the adenosine program and CD73, this has been an increasingly competitive area of development. Perhaps you can just bring some expectations for us on the initial data we're expected to see later this year.

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

Gavin, it's Steven. Thanks for bringing it up. Yes, we have all 3 components of the program that's needed or in our pipeline. So we have a small molecule, potent and selective A2A, A2B inhibitor. We have a large molecule CD73 inhibitor. And then we have the combination availability with checkpoint inhibitors, either IV and retifanlimab or with our oral PD-L1 program. So that's somewhat of the uniqueness. Then in terms of the A2A, A2B and CD73, we are slightly behind the competition, but we have the ability to learn from them and see where they go. And you're right. There is a lot of interest in inhibiting adenosine in the tumor microenvironment either through a doublet or triplet, as I point out. The dose escalation and expansion phases for the A2A, A2B have gone very well and on track with data this year and CD73 is slightly behind, but also on track, and now we're doing the doublet. So we're progressing well with the program and expect to provide you some updates in the second half of 2022.

Operator

Your next question is coming from Mara Goldstein from Mizuho.

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

I just wanted to ask, I know you talked a lot about Opzelura. But I just wanted to get a little bit of clarification on the gross-to-net steady state at 40% to 50%. And is that also anticipated in a post vitiligo commercialization that, that would be sort of the long-term steady state? And then also, is there any update on the NDA filing for rux QD?

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

Sure. I'll take the first part of your question, Mara. So yes, so the gross to net that we say 40%, 50% includes the vitiligo launch. And going forward with AD and vitiligo, our gross to net will try to keep in that range as we possibly can, but we're very confident going through the year, as we said by the end of the year, second half of the year, 40% to 50% is our goal. I'll turn the other one about rux QD over to Steven.

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

Mara, it's Steven. So our rux-once-a-day file is going in now this half of 2022. The critical path was stability, which is complete. We expect a standard 10-month review period -- so it should be first quarter of 2023 that we'll be expecting that approval. The reason we expect it to be successful is that from a bioavailability, bioequivalence point of view, we met the criteria that's in the FDA guidance for area under the curve. So we're within that range that's required for the multiple dose strength. And now that stability has been complete, we have confidence in that submission and should have it actioned around the first quarter of 2023.

Operator

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

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

[Irrespective] to vitiligo's various combinations, Barry and maybe Steven, just for the label, what do you guys view as kind of the important elements to get in there from a commercial perspective, particularly to drive, as Christiana mentioned here that the increased patient flow into the clinic seeking treatment? And kind of what are the elements of the TRuE-V studies that probably aren't going to be in the label, but are going to be important to kind of stress to the community to drive that out?

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

I mean, I'll turn it over to Steven. I'll try to give you an answer to your question. I actually think the most important thing is just that this is the first and only drug approved for repigmentation of vitiligo. And it's -- there really should be no barriers really other than that if Steven has other viewpoints about what should be included or not included in the label, I'm not sure.

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

Yes. Marc, it's Steven. I think if you go back to the eligibility criteria from the two large Phase III studies, the age would be key, 12 and above; the body surface area involvement, up to 10%; and in the dosage and administration section we feel that it's likely to reflect the fact that it's different from AD and a continuous dosing is needed to achieve the benefits I spoke about in my prepared remarks, which are quite remarkable when you get over time, 20% absolute percentage improvement in facial VASI 75% between week 24 and week 52.

On the week 52-point, the initial submission was obviously on the primary endpoint on week 24. During the 4-month safety update, we were able to provide some of the 52-week data. But now with the 3-month extension on the PDUFA, we've been able to also supply more of that data. So that would be a good upside -- and obviously, it will depend on the FDA and the negotiations that are forthcoming to have the complete 52-week data set in, so reflect the entirety of both the efficacy and the safety data.

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

Okay. That's helpful. And then maybe, Steven, just for 707, the updates coming in the second half across some of the other dermatology indications. If -- what do you view as kind of meaningful responses in hidradenitis to move forward with this type of mechanism given kind of all of the labeling concerns around JAK? And then on the vitiligo side, is the long-term plan there with that to kind of have people on oral therapy chronically? Or is it more of just get them to a place where Opzelura becomes a better option for them and then they transition to Opzelura?

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

Yes. Thanks, Marc, for both questions. So hidradenitis suppurativa, distressing condition for patients, a lot of unmet need, there is an approved TNF inhibitor, but not widely used in this indication, probably due to somewhat lack of efficacy with it. It's a condition that involves abscesses, nodules, and scarring in areas of the body like the armpits, axilla and groin, and it can be very distressing psychologically to patients as well. The established endpoint for the one approved drug is something called the HiSCR endpoint. It attempts to capture the improvement in abscess and nodule formation and seems to be the regulatory reprieved endpoint that's needed. But you're right, it's a tricky to measure. There's both object and subject of components to it. But the -- in our Phase II data, which we'll show you, we feel it's very encouraging for the effect of a JAK inhibitor in this unmet need area.

Just to address the safety part of what you said, we fully expect given that this is an oral JAK inhibitor in an inflammatory condition, clearly an inflammatory condition that it's likely that we'll be dealing with black box class labeling language. I mean that has been known to us for a while now. And so we feel the therapeutic ratio is important, right? So in settings of high unmet need with a lot of severity with the efficacy that we desire, you'll get to the desired therapeutic ratio that's needed to use the drug. So that's the HS component.

For vitiligo, here I just want to stress that it's different from the cream indication. So this is for people with more extensive body surface area involvement. The principal eligibility criteria here is 8% or above body surface area involvement. So it's a little confusing because the cream is 10% or below and this is 8% or above. So there's a little bit of overlap. But it gets to the therapeutic ratio question again that these are people with extensive vitiligo that there will be more acceptance to use an oral JAK inhibitor with a different therapeutic ratio. We know it's efficacious. I mean you know now from the cream data, from multiple reports with oral JAK inhibitors that you get repigmentation here, but you'll have to have suitable safety. And again, we're very likely to be dealing with the black box labeling down the pike when it gets there and that will factor into our decision making with that particular indication.

Operator

(Operator Instructions) Our next question today is coming from Jay Olson from Oppenheimer.

Unidentified Analyst

This is Chung on the line for Jay. I guess on the oral PD-L1 program, I am just curious, any learnings like dosing optimization or tumor selection that you can apply to the development of the [follow-on]; molecules you are prioritizing right now? And also between the 2 follow-on molecules, would you further prioritize one over the other? If so, when will that happen?

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

Yes. Chung, it's Steven. So in terms of dose, I don't know exactly what you're alluding to, but just to make broad comments and across all areas at the FDA, but particularly in oncology now, there's project Optimus. There's a refocus on getting the dose correct. It's likely that everybody in the space now will have to do a lot more dose work, a lot more exposure, efficacy analysis, a lot more exposure toxicity analysis and may even be down the pike an area where we'll be taking more than one dose into pivotal studies. And you cannot argue that getting the dose right is critically important, that this effort from the regulators will be a big deal, and we've already adapted like many other companies to have the right resources now to do these analysis and get it right.

For oral PD-1 specifically, we do have a pharmacodynamic marker. We can measure PD-1 inhibition in peripheral blood mononuclear cells. So we know that we get in the right degree of inhibition. And just to be clear, we want 90% of above inhibitory concentrations of that PD marker constantly when we dose our drug. So we're working that now with both 280 and 318.

Your question around what histologies are important, it somewhat remains to be seen. I mean, given that we now know these are all active compounds. We've seen activity in areas that are known to be I/O responsive. So the hotter tumors, if you will, microsatellite high tumors are also of particular interest here. So that's currently the main focus.

As I said in my prepared remarks, given that it's oral, that it may differentiate on safety with its quick off rate, you can do oral-oral combinations. People can go home and not need to come into a clinic set in for infusions. It could lend itself more also to adjuvant and maintenance settings. But we're not there yet in declaring what particular histologies and what area we're going to particularly go after. We hope, though, to be making those decisions towards the end of this calendar year, perhaps early next year on where we'll be going from a registration point of view.

Your last question as regards, will we take both forward or only one in terms of 280 and 318? I still think it's a little premature to answer. We have both in the clinic at the moment, both are enrolling well, both have shown tumor reduction in terms of shrinkage and no neuropathy with either agent yet, and we'll do more of what I was talking about in terms of dose optimization and modeling before declaring which particular one will take forward in oncology. But my own view at this juncture, there may be interest in non-oncology settings, for example, enhancing hepatitis B virus directed therapies, et cetera. So there may well be utility down the pike and having a second compound for non-oncology settings. So it's just a little early to declare which way we will go.

Operator

Next question today is coming from Leiyang Wang from Bank of America.

Leiyang Wang - *BofA Securities, Research Division - Research Analyst*

This is Leiyang Wang calling forward to (inaudible). I guess so one more question on Opzelura gross to net. You previously mentioned that one of the benefits of talking to payers relating to vitiligo is that when your current negotiations and when vitiligo is approved, you don't have to necessarily go back to payers to negotiate brand-new contracts. Now if that's the case and would you say some payers are waiting for the label of vitiligo to be approved before kind of finalizing the payer coverage negotiations. So I'm trying to understand the cadence of when you might see that next basically percent lives covered and improvement from that dynamic?

And my second question is, previously, you mentioned the gross to net range could normalize anywhere between the 30% to 50%. Today, you said expect that to be around 40% to 50% by the end of 2022. But just as a clarification, going forward beyond 2022 do you see, I guess, potentially gross net discounting to be somewhere lower, perhaps in the 30% to 40% range?

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

So Leiyang, it's Barry. So as far as negotiation goes for vitiligo, no, we don't have to go back. So there's a couple of different things. One is that you're talking about contracts with PBMs for the large part, so that's one part. So those contracts are at least one is fully completed. And remember, those are divided in 2 parts. So the 3 big PBMs really cover about 80% of the commercial lives in the country. But think about that as variable and nonvariable. About 50% of patients are, let's call them variable where, in fact, the plans, the insurance plans themselves, like you and I have, they, in fact, can make their own decisions and in fact write their own utilization criteria about how the drug is being used. So we don't have to go back and -- and then the other half, sorry, are the ones that you might say are a preferred formulary where they have [true] NDC block. So we have one the big PBMs that are fully NDC block removed and the rest of the variable plans have written their utilization criteria.

And then we -- and then in fact, when we launch vitiligo, we don't have to go back and negotiate with the PBMs for new contracts. But utilization criteria once the vitiligo is launched, will be written by the plans, and it will take weeks to months for those utilization criteria to be written for each of the various insurance plans, of which there are many throughout the country.

Before launch, no, they're not going to have utilization criteria before approval, they're not going to have utilization criteria written for vitiligo. In fact, even though they know about the Phase III data for Opzelura in vitiligo. They're not going to write a plan until it's approved because they just don't want to take time to do that. But we're educating, of course, payers that this is, in fact, coming and they know it's coming, and we know that they're going to write utilization criteria for it because most of them have utilization criteria already for other products, not all of them, but some of them do for things like light therapy and so forth. So we know that the utilization criteria will be written for vitiligo.

As far as the gross to net is concerned, at least for over this year, last couple of quarters, we've always said 40% to 50% gross to net is our goal, and that's what we're shooting for, particularly as we continue to negotiate with the various payers.

Operator

Our next question today is coming from Andrew Berens from SVB.

Unidentified Analyst

This is Chris on for Andrew Berens. I was just wondering if we could get a little bit more color on the prescriber details for Opzelura. How many dermatologists and how many general practitioners are in the mix for Opzelura? And are those docs primarily those that you've detailed to from the sales force? Or are you seeing more of a halo effect? And then just as a quick follow-up question. Wondering if the new product manufacturing method for Opzelura is going to change anything fundamental about the drug, the PK or the pH or anything like that? And if so, is that going to concern any of the regulatory agencies in terms of the safety and efficacy?

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

So Chris, I'll take the first part and then hand the second part over to Steven. But as far as -- there's about 8,000 dermatologists in the United States or so, and general practitioners, no, we don't really see any -- I mean they could obviously write for Opzelura, but we really don't see any. All of our detailing, all of our educational work goes towards dermatologists and their offices. But remember, especially in dermatology, nurse practitioners and physicians assistance are very important to their prescribers. There's tens of thousands of them. So when we call on dermatologist offices, we of course, call on the nurse practitioners and the physician's assistants are very important. In fact, the medical assistants as well, that are very important, particularly when it comes to reimbursement. So it's all direct education and we're working very well and have reached all of our top prescribers and we'll continue to educate all of the dermatologists, nurse practitioners, PAs in the offices as we move forward. For the product manufacturing changes, I'll turn over to Steven.

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

Yes, Chris, thanks for your question. I mean the top line, clear answer is there's nothing fundamental change on the drug currently as PK or pH. The CBE-30 change by the regulations, is a mild-to-moderate change that specifically doesn't do that. And the prior approval supplement change was bringing a new manufacturer on board using the same process. In fact, you specifically do not want to do what you alluded to because that would require you to redo all your clinical studies. So you have to be very careful to not make changes that affect those in any substantial way, either PK or pH.

Operator

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

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.
