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INCY - Q1 2019 Incyte Corp Earnings Call

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OVERVIEW:

Co. reported 1Q19 total revenue of $498m and non-GAAP operating income of $127m.

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PRESENTATION

Operator

Greetings, and welcome to the Incyte First Quarter 2019 Financial Results Conference Call. (Operator Instructions) As a reminder, this conference is being recorded. It is now my pleasure to introduce your host Mike Booth, Vice President of Investor Relations for Incyte. Please go ahead, Mike.

Michael Booth - *Incyte Corporation - VP of IR*

Thank you, Kevin. Good morning, and welcome to Incyte's First Quarter 2019 Earnings Conference Call and Webcast. The slides used today are available for download on the Investors section of incyte.com. I'm joined on the call today by Hervé, Barry, Steven and Christiana, who will deliver our prepared remarks, and by Dash, who will join us for the Q&A session.

Before we begin, however, I'd like to remind you that some of the statements made during the call today are forward-looking statements, including statements regarding our expectations for 2019 guidance, the commercialization of our products and the development plans for the compounds in our pipeline as well as the development plans of our collaboration partners. These forward-looking statements are subject to a number of risks and uncertainties that may cause our actual results to differ materially, including those described in our 10-K for the year ended December 31, 2018, and from time to time in our other SEC documents.

We'll now begin the call with Hervé.

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

Thank you, Mike, and good morning, everyone. So we have made excellent progress in the first quarter of 2019. Net product revenues of Jakafi continued to be strong, delivering 20% growth over the first quarter of last year. And last week, Novartis reported strong sales of Jakavi, ex-U. S., also at 20% on a constant currency basis with continued double-digit growth across all regions.

Including Jakavi and Olumiant priorities, sales of Iclusig and the milestone from Innovent, we reported total revenue of $498 million, up 30% compared to Q1 last year.

On the right side of Slide 4, you will see some of the important progress from across our development portfolio. Our GVHD development work is on track, and we have recently completed recruitment into the GRAVITAS-301 trial of itacitinib in patients with treatment-naive acute GVHD. And we plan to announce top line results from this trial before the end of 2019.

We're also on track to submit the NDA seeking approval of pemigatinib in cholangiocarcinoma in the second half of 2019, and we expect that the data supporting the NDA would be presented at the medical meeting in the second half of the year.

This morning, we announced the successful completion of the Phase II trial of ruxolitinib cream in vitiligo patients, which represents a robust proof-of-concept in a second indication beyond atopic dermatitis where we are already in Phase III. Based on the Phase II results for ruxolitinib cream in vitiligo, we are also moving forward with Phase III development in this indication, and we look forward to sharing this data with you at the Medical Meeting in the coming weeks.

Novartis continues to plan for the NDA submission for capmatinib in the second half of the year, and updated data from the GEOMETRY trial have been accepted for oral presentation at this year's ASCO in June.

Exciting data from 2 of our early-stage projects were presented at AACR earlier in April. The presentations of our oral PD-L1 inhibitor program as well as the PD-L1 x CD137 bispecific were developed -- we are developing in collaboration with Merus were very well received, and I believe are emblematic of the importance of discovery science for long-term value creation.

Today, we also announced that we will no longer participate in co-funding baricitinib development with Lilly. We intend to make a reallocation of this capital to late-stage development programs during 2019 and 2020 as we now believe that certain projects such as the acceleration and expansion of ruxolitinib cream development and the acceleration of other opportunities in our later-stage portfolio warrant increased funding.

We continue to believe that baricitinib has an important place in the treatment of rheumatoid arthritis and potentially in other autoimmune and inflammatory conditions. But with our cumulative investment already earning us a substantial royalty rate, we believe that now is the right time to opt-out and to reallocate capital to support exciting project to help us reach our strategic goals of diversification and growth.

With that, I'll turn the call over to Barry for an update on the U.S. business.

Barry P. Flannelly - *Incyte Corporation - Executive VP & General Manager of U.S.*

Thank you, Hervé, and good morning, everyone.

Jakafi continues to perform well, and Q1 performance was in line with our expectations and with full year 2019 guidance for net sales of $1.58 billion to $1.65 billion. Jakafi sales increased by 20% over Q1 of last year driven by demand in both approved indications. We saw total MF and total PV patients grow by 8% and 18%, respectively, in the first quarter versus the same period in 2018.

Slide 7 shows the sales bridge for Q1 2018 to Q1 2019. The growth of Jakafi was mostly driven by volume, and you can see that amounted to an increase of $42 million compared to Q1 of last year. You will remember that the negative effect on gross-to-net is highest in Q1. It is also important to note that drug manufacturers are now required to contribute 70% of the coverage gap or donut hole as compared to 50% in previous years.

I'll finish by reminding you of the May 24 PDUFA date on our sNDA for ruxolitinib in steroid-refractory acute GVHD and that we are ready to launch immediately should the FDA approve ruxolitinib in this indication. Our field force has already been sized and structured to support the launch.

Our REACH development program also continues as planned. The results from both REACH2 and REACH3, the global Phase III trials of ruxolitinib, which we're running in collaboration with Novartis, in steroid-refractory acute and chronic GVHD are expected by the end of this year.

I'll now turn the call over to Steven for the clinical update.

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

Thanks, Barry, and good morning, everyone.

Incyte is currently running 6 key late-stage development programs as summarized on Slide 10. These have the potential to treat a significant number of patients across numerous indications. More broadly speaking, these programs aim to transform Incyte into a company with multiple approved products in the United States, Europe and Japan over the next several years.

Today, we are focusing our attention on 4 of them as these are the projects that we expect to generate important updates during 2019. Barry has already highlighted our ruxolitinib program in steroid-refractory graft-versus-host disease, and I will touch on the remaining 3 in my remarks.

We were pleased to announce today that the Phase II trial of ruxolitinib cream in patients with vitiligo successfully reached its primary endpoint and that the plans for Phase III development are now underway. This was a randomized dose-ranging and vehicle-control Phase II trial in more than 150 adults with vitiligo, and we look forward to sharing the data with you at a medical meeting soon.

Vitiligo is an inflammatory disease of the skin, which results in patches of depigmentation and the potential for significant impact on patients' lives. It is estimated that there are 2 million to 3 million patients in the United States with this disorder, and there are no currently approved FDA treatments. Many patients try steroids or phototherapy, but these options have not shown significant or long-lasting repigmentation of the skin. We expect to initiate Phase III development by the end of this year, and we are hopeful that ruxolitinib cream will be the first therapy approved by the FDA and will provide these patients with a meaningful improvement in their disease.

We believe that there are significant opportunities within our pemigatinib program. We expect to file the NDA for second-line FGFR2 translocated cholangiocarcinoma in the second half of this year. And we are also planning to share the data that supports the proposed NDA at a medical meeting in the second half of 2019.

The second indication we are pursuing for pemigatinib is FGFR3 mutated bladder cancer, and we are currently recruiting the continuous dosing cohort of the pivotal Phase II trial. We expect that this cohort will reach full recruitment by the end of this year, and we are hopeful that the sNDA for this indication could be submitted in 2020.

The first-line Phase III trial in cholangiocarcinoma is now open for recruitment, and plans for first-line bladder cancer study are also in preparation. We are also opening a registration-directed Phase II study in the tumor-agnostic setting, which could further expand the number of patients eligible for the therapy, and therefore, the potential of the molecule.

Moving back to our development efforts in graft-versus-host versus disease, and the GRAVITAS program, which is investigating itacitinib in first-line treatment. GRAVITAS-301, the Phase III trial in treatment-naive acute graft-versus-host disease, has now completed recruitment, and we expect results to be available before the end of this year.

In January, we launched GRAVITAS-309, which will evaluate itacitinib in patients with treatment-naive chronic graft-versus-host disease. It is important to note that in major markets globally, approximately 15,000 new graft-versus-host patients are diagnosed each year. The unmet needs here is clear, and we are encouraged by the potential of JAK inhibition to treat this often deadly disease.

I'll end my update by mentioning 2 very exciting opportunities in our early-stage portfolio, both of which were recently highlighted at AACR. We have discovered a series of novel orally-available PD-L1 inhibitors, and the first molecule, 86550, is now in the clinic. Its mechanism of action, which binds, dimerizes and internalizes PD-L1 is novel and could result in a differentiated clinical profile versus injectable monoclonal antibodies. We are in the early innings, but we look forward to sharing clinical data for this program next year.

Through our collaboration with Merus, MCLA-145, a PD-L1 x CD137 bispecific antibody, is ready to enter clinical development, and we expect to have the first patient dosed with MCLA-145 this quarter. This is also a very exciting mechanism where the bispecific directs CD137 agonist activity to the tumor microenvironment by its selectivity for PD-L1. This may limit systemic CD137 agonist activation while targeting 2 important immunomodulatory pathways.

With that, I'd like to turn the call over to Christiana for a financial update.

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

Thanks, Steven, and good morning, everyone. The financial update this morning will include GAAP and non-GAAP numbers. Before moving to our results for the quarter, I would like to discuss a change in our methodology for non-GAAP reconciliation. After reviewing our non-GAAP reconciliation and at the request of the SEC, beginning with the first quarter of 2019, we'll no longer be adjusting our revenues or research and development expense for upfront consideration and milestones that are part of our collaboration agreements with new or existing partners. This new methodology is reflected in the GAAP to non-GAAP reconciliation on Slides 25 and 26 in the backup section of the deck and in the press release that we issued this morning.

In addition, I'd like to further discuss our decision to end additional co-funding of baricitinib development with Lilly. As you know, under our agreement with Lilly, we have the right to a base, tiered royalty of 11% to 20% on global net sales of Olumiant. We also have the right to receive a 9% incremental royalty if we co-fund 30% of the post-POC development cost per baricitinib indication.

Based on the cumulative investment made to date, we have already earned a substantial incremental royalty rate, especially in rheumatoid arthritis, and have now reached a point, given the acceleration and potential of certain key internal projects, where we believe that the best decision is to add additional co-funding of baricitinib development and reallocate capital over the balance of 2019 and in 2020 to other projects.

Through 2018, we were entitled to receive the full 9% incremental royalty in addition to the 11% to 20% base-tiered royalty. With our decision to end our co-funding effective at the end of 2018, we expect the incremental royalty rate for rheumatoid arthritis to come down over time. The timing and the rate of decline in the incremental royalty rate will be based on Lilly's additional development costs in this indication and the pace at which those costs are incurred.

The base royalty rate is unaffected by levels of development spend, and as it is a tiered royalty structure, it is expected to grow over time as global net sales of Olumiant continue to grow.

Moving on to our financial results. For the first quarter, we recorded $458 million of total product-related revenues, an increase of 20% over the first quarter of 2019. This is comprised of $376 million in Jakafi and $21 million in Iclusig net product revenues, $46 million in Jakavi royalty from Novartis and $16 million in Olumiant royalties from Lilly. We also recognized $40 million in contract revenues from the upfront payment received under our collaboration agreement with Innovent, resulting in total revenues for the quarter of $498 million.

R&D expense for the quarter was $243 million on a non-GAAP basis driven by the progress across our development programs as Steven has outlined. And in this quarter versus last year, this expense was partially offset by the impact of our decision to stop co-funding baricitinib development and lower costs related to the epacadostat program.

The net effect was a 9% decrease in ongoing R&D expense for the quarter compared to the prior year period. SG&A expense for the quarter was $111 million on a non-GAAP basis, relatively flat in comparison with the prior year.

The increase in total revenues and decline in non-GAAP costs and expenses has resulted in operating income for the quarter of $127 million on a non-GAAP basis as compared to an operating loss of $19 million in the prior year period.

Moving now to our guidance for 2019. We are reiterating our revenue guidance for the full year as well as our SG&A guidance. We have received our GAAP -- we have revised our GAAP R&D guidance from a range of $1.185 billion to $1.255 billion to a range of $1.145 billion to $1.195 billion, which largely reflects our decision to discontinue co-funding baricitinib development and the timing of resource reallocation. Please note that this guidance does not include any additional potential future strategic transactions beyond agreements previously announced.

I will now turn the call back to Hervé.

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

Thank you, Christiana.

Our next slide outlines the key news flow events we expect during 2019, including news from our partners. With this list of exciting late-stage program, we are taking important steps toward our strategic goals of diversifying and accelerating revenue growth. We look forward to keeping you updated on our program.

And for now, we are happy to take your questions. 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 is coming from Marc Frahm from Cowen and Company.

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

Maybe first, just kind of housekeeping one for Barry. Can you disclose the gross-to-net in the quarter, just how it worked out with the new rules around the donut hole? And do you still think the full year's going to be about 15%?

Barry P. Flannelly - *Incyte Corporation - Executive VP & General Manager of U.S.*

Yes. The full year gross-to-net is going to be about 15%. The gross-to-net, as you know, is highest in the first quarter. The additional 20%, so going from 50% of the donut hole is 70% of the donut hole, amounted to about $5 million, we estimate.

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

Okay. And then maybe just turning to the topical ruxolitinib, so for Steven. One, so there's a new maximal use trial that's on clinicaltrials.gov. Is there anything else that needs to be done other than reading out that and reading out absolute Phase III data in atopic dermatitis for a filing? And then maybe initial thoughts on the design for a Phase III trial in vitiligo? Does it need to be as large as atopic dermatitis? Or can you leverage a lot of the safety data?

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

Yes, Marc. It's Steven. Thanks for your question. So for atopic dermatitis for the entirety of the filing package, there will be nothing additional that needs to be done other than obviously completing both Phase IIIs and the maximal use study that's done for the guidance for dermatological products and that -- we have high confidence in our atopic dermatitis database on our very strong proof-of-concept with the cream.

In terms of vitiligo, obviously we've just delivered the proof-of-concept data. We're very, very encouraged by it. It'll be presented at a medical meeting soon. Obviously, we've been thinking about the Phase III designs all along and have relatively well-developed concepts, which we'll now, at an end of Phase II meeting with the FDA, discuss with them and come to decisions on the end point and the size. And as we said, our intent is to start those before the end of the year.

In terms of what I think you're alluding to, will the safety package be able to leveraged from atopic dermatitis for vitiligo, we expect that would be the case. But there will be a discussion point to the regulatory authorities. Having said that, the vitiligo space will still have to be appreciable in size. It's a different area from oncology, and you require larger studies. But we expect that the safety package from atopic dermatitis will be very helpful for the vitiligo file.

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

Okay. Great. And then maybe a bigger picture for Hervé. In the past, with these mid-stage dermatology projects, you mentioned that you'd have a decision to make ultimately about whether it's right for Incyte to market them and build a whole commercial infrastructure in that space versus ultimately partnering these out. Now that you kind of have randomized data in-house at least in two indications? Are you ready to make that decision? Do you have an answer on that?

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

Yes. So obviously, the -- I mean, you know our approach was -- in terms of commercialization was driven by cancer portfolio. And we decided to commercialize ourself in North America, Europe and Japan. That was like 2 years or 3 years ago, 4 years ago. We have built that infrastructure now. So we have a new question here is does this apply to dermatology? And the answer is it's very different that in term of size of the opportunities by -- for each of the regions. So we're looking at it on a regional basis. And from that first review, what we see is that there is a lot of attractiveness to doing it ourself in the U.S. There is certainly less of that for Japan where it's a complicated and different market from what we see in cancer. And we are basically reviewing also for Europe what would be the best approach, and it could be either to commercialize along fully or to find a core commercialization partner and book the revenue or to out-license completely and book milestones and royalties.

And frankly, we are looking at each of the 3 opportunities and what will make the most sense from the Incyte standpoint financially and in term of investment and risk. So it's completely open. We have time because the Phase III results from atopic dermatitis are anticipated at the beginning of -- in 2020. So we are planning to use the next 6 months to have an in-depth analysis of what makes sense with our Board, and we will probably be ready by the time we get the Phase III data. And after the Phase III, there will be another year before the commercialization is starting. So we are basically on a good track to be able to make that decision based on very rational financial analysis.

Operator

Next question is coming from Michael Schmidt from Guggenheim.

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

I had a couple on pemigatinib, specifically regarding bladder cancer. Can you just help us frame the opportunity here in context of some news recently around approval of erdafitinib from J&J and the Seattle Genetics top line data as well? How do you think about the opportunity here? And help us understand if there will be any updates from your Phase II study in bladder cancer this year.

And then the other question was regarding Jakafi. I guess what was the gross-to-net in the first quarter? How should we think about that in the second half of the year?

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

Thanks for your question. It's Steven, and Barry will answer your gross-to-net question.

So as I said in my prepared remarks, this is the second indication we're pursuing. Obviously, a very important indication and quantitatively bigger than FGFR2 translocated cholangiocarcinoma. This is the FGFR3 mutated or fusion patients with bladder cancer, and the opportunity is larger in the 15,000 to 20,000 patient range.

We view the J&J erdafitinib approval very positively. It's -- it gives us proof-of-concept that the pathway is important, that hitting this driver mutation is effective. We're always ahead, although we have caught up substantially. We're doing our continuous dosing now. We expect to complete that continuous dosing cohort in or around the third quarter of this year, but you're only likely to see data from us next year in 2020. And in addition, that's where we'll be filing as well should the data be supportive of filing.

The Seattle conjugated monoclonal is a different target, probably in some respects, mutually exclusive and potentially important drug in bladder cancer as well. So it doesn't affect anything in terms of our program at all.

And then obviously, we have the ongoing MPN 8p11 FGFR1-driven study that's actually accruing very well after our ASH update. And then very importantly, the tumor-agnostic program, which substantially expands the potential population in areas like endometrial cancer, glioblastoma, et cetera, this could be upwards of another 15,000 patients if we deliver efficacy in all these populations. So as you outlined, an extremely important program to us that's going very well. We view that approval that's important proof-of-concept for the pathway. We think the safety may ultimately be something that's important. We note the J&J label, and we'll see what our data shows in terms of safety down the pike.

I'll turn it over to Barry for your gross-to-net question.

Barry P. Flannelly - *Incyte Corporation - Executive VP & General Manager of U.S.*

Yes, Michael. So the gross-to-net, we estimate for the first quarter -- full first quarter, 17%. As you can imagine, that's much higher in January and then settles down in February and March. And generally speaking, it gets a little bit better each subsequent quarter after that. And as I said before, for the full year, we estimate the gross-to-net to be 15%.

Operator

Our next question is coming from Brian Abrahams from RBC.

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

What's the right way to think about the cost savings from the bari restructuring, I guess, for this year and beyond, once we net out the effect of some of those accounting changes for booking milestones? And how are you guys thinking specifically about allocating that funding? Will that be

for new projects, new indications for some of the late-stage programs, moving other earlier-stage pipeline programs forward into the late stage? What's the right way to think about that?

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

This is Christiana. So in terms of baricitinib, first of all, the revised guidance that we provided implies a 40% to 60% -- sorry, $40 million to $60 million reduction in R&D spend in 2019. That, as we indicated, includes the decision to opt out from baricitinib development and the partial reallocation in 2019 of some of the funds that we had earmarked for baricitinib to other internal programs. Also as we indicated, the decision to opt out was really driven by the opportunity that we see in some late-stage programs and the desire to accelerate or augment the development of those programs like rux cream. So in 2019 -- through the rest of 2019 and in 2020, we will be looking to reallocate the capital that otherwise would have been allocated to baricitinib to those late-stage programs.

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

Got it. And then one more question from me. What's the right way to be thinking about the bar for clinical meaningfulness in the vitiligo setting and the potential read throughs between vitiligo and atopic dermatitis pathophysiologically? Do you view this as sort of an additional endorsement of the potential for rux cream in atopic derm beyond the Phase II you've already reported in AD? Or should we think about this as completely separate from a scientific standpoint?

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

Brian, it's Steven. Thanks for your question. In terms of the -- what is clinically meaningful in vitiligo, obviously there's no approved therapies and there's actually been a dearth of clinical work to date. This is the biggest study done ever in vitiligo.

The primary end point in this proof-of-concept study was the percentage of patients treated with ruxolitinib cream who achieve a 50% or greater improvement in the facial assessment of the vitiligo area and severity index scores, called an F VASI score, compared to vehicle. And that measures the activity of the compound. In addition, as we've said and as the field keeps telling us, this is a disease with a large psychosocial burden on patients, and we'll be measuring that through appropriate patient-reported outcomes during the study because we'll have to document clinical benefit in that respect. The big caveat here is we need to discuss with agency what the primary end point will be for the Phase III studies. Will it be VASI? Will it be a face VASI? Will it be a total body VASI? And to what degree would they accept as the primary end point, in addition to measuring in our patient-reported outcomes.

It's a 150-patient study. You'll see the data at a major meeting in the middle of this year. And obviously we're very encouraged by it, we're going to Phase III. The read through for me is, in terms of inhibiting interferon-gamma signaling in vitiligo, stopping this cycle of melanocyte destruction and then getting the repigmentation in important areas to patients like the face and hand -- and hands, which are visible externally. And it's similar mechanism to AD, but I don't -- they're just separate indications that we pursue separately. There are potentially other diseases over the years we've looked at like psoriasis, which have some overlap in terms of pathophysiology. But the current program, in terms of registration direction, is towards atopic dermatitis and vitiligo.

Operator

Our next question is coming from Carter Gould from UBS.

Carter Lewis Gould - *UBS Investment Bank, Research Division - Large Cap Biotech Analyst*

Just wanted to, I guess, dig in a little bit more into the decision to stop the cofunding. Give some rationale for that. But I guess you've been pretty persistent on this front that you would keep up that effort. I know you had conducted a multiple internal analyses. So I guess sort of what changed?

And if there was any sort of shift, either in kind of how you guys were viewing maybe the systemic market for AD or specifically, you already mentioned some of the assets in your pipeline. Anything specifically you would call out?

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

Maybe I can start, and Christiana can complement it. I think it's important to realize that this decision is not about the way we see the future of baricitinib. It's about 2 other things. One is the ways or -- additional royalty rates is calculated. It's based on the cumulative investments in -- that we have already made in baricitinib. So you can imagine that the return on the marginal investment that we make is always lower than the return on the previous investment. So there is a point that we believe we have reached where in fact, we see that there is a better return on that investment in our internal projects as we have seen a number of them that requires or give us the opportunity to accelerate and expand like we discussed about itacitinib, pemigatinib and ruxolitinib cream. So we came to that conclusion that in term of marginal investment that we make in R&D, it would be a better allocation to do it through our internal programs that has been progressing very well and now very promising. So that's really how we came to that conclusion. As you know, we have told you already that we are reviewing -- all the time, every quarter, we are reviewing the way R&D resources are allocated, and that's basically the time came where it made sense for us to reallocate these resources to internal programs.

Carter Lewis Gould - *UBS Investment Bank, Research Division - Large Cap Biotech Analyst*

Great. And if I could just ask a follow-up. Appreciate all the color, Hervé. Just in terms of, I guess, there's been sort of increased talk around you guys potentially being an acquirer in the marketplace. And just in terms of your capacity for M&A based on your current cash position and future cash flows, kind of how you're viewing that.

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

I mean what we are looking at is really the 2 strategic goals are to -- are growth and diversification. So growing our revenue, which is obviously translating into the P&L and going to the bottom line in some way. But growth is important, and diversification is important. So that's why there is always this possibility for us to do some business development that will add to our top line over the next years. It's clear that we have -- I think at the end of the quarter, our cash position is $1.6 billion. So the P&L structure that you can see this quarter is very strong in term of cash flow, and that gives us more ammunition for potential business development opportunities. At the same time, our internal portfolio is also very strong and progressing very well. So we are basically looking at both as potential ways to get to our strategic objectives.

Operator

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

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

For vitiligo, in terms of the commercial opportunity, are the 2 million to 3 million patients in the U.S. all targets? And where should we expect that data set in 2Q?

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

Salveen, it's Steven Stein. So the incidence is around 1%. So if we -- 1% to, 2%, if you have 300 million population, that's how total many patients there are. And it's just -- that's just the potential opportunity. The amount to seek treatment currently is much, much smaller. It's around 150,000 patients we can best estimate that actually currently seek treatment. That could be for multiple reasons, as you all know, in terms of lack of available therapies, the fact that therapies that are available are somewhat cumbersome, hard to get and require, high compliance in terms of steroids and phototherapy and also for patients who just don't feel they need treatment.

So the population that is ultimately targeted will be for the ones that feel that they have to treat areas that are causing the visual disfigurement plus the psychosocial implications of the disease. Obviously, we'll have to demonstrate the efficacy benefit in the areas that are concerning, particularly as I said earlier, the ones that are visible externally like face and hands. And we're not the population that ultimately will need treatment for us could be in the range of 150,000-or-so. It's hard to estimate currently.

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

And just a housekeeping follow-up. Where did Jakafi inventory level stand exiting the quarter?

Barry P. Flannelly - *Incyte Corporation - Executive VP & General Manager of U.S.*

So this is Barry. Actually, they're normal level's below 3 weeks.

Operator

Our next question is coming from Alethia Young from Cantor Fitzgerald.

Alethia Rene Young - *Cantor Fitzgerald & Co., Research Division - Head of Healthcare Research*

Two from me actually. One, I know the PI3-kinase program doesn't get a lot of love, but I think there are some PI3-kinase coming back on the scene, including yours. So I just want you to talk a little bit about how you think your current molecule may be differentiated from others.

And then my second question is maybe just asking the question in another way. Obviously, you guys have a core JAK capability, and I'm just kind of wondering how long it would take for you guys to kind of generate a return on invested capital if you were to invest in dermatology. It seems like there are a lot you can do internally in the pipeline that you have, and obviously, you have the topical programs, which are ongoing.

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

So Alethia, it's Steven. I'll do your first question. So the reason, I think, we're quieter on parsaclisib at the moment as it's enrolling --- this is a year of enrolling the studies at a registration-directed in follicular lymphoma, mantle cell lymphoma and marginal zone lymphoma. And the enrollment, actually, is really going well this year. It will complete, and then will have data next year and hopefully be, again, of submission quality in those indications.

We -- this is a second-generation PI3-kinase delta inhibitor. The chemical changes that were done to this generation of compound seem to have dialed out the liver toxicity for the most part. So you don't see the transaminitis that you used to see with the first-generation compounds like from idelalisib from Gilead initially. But what is the concern with this degree of PI3-kinase delta inhibition over the long term are safety concerns like colitis, so we made a very conscious decision in a little over a year ago to try and thread that therapeutic benefit more cleverly. We know the compound's highly active. It's incredibly active in B-cell diseases. We've shown that data repeatedly. But to get that activity, at the same time to make it more tolerable, is to look at different ways of doing dosing and scheduling. So we do the high dose upfront, 20 milligrams weekly for the 8 weeks, to get to the efficacy bar we want. And then we looked at different ways of either weekly or daily dosing at lower doses. And it looks like early days that we've been able to dial out with many caveats, because of the small numbers, a lot of the longer-term toxicity that colitis. So that's a pretty exciting place to be from a therapeutic benefit point of view.

And now we're executing those studies to substantial numbers of patients in marginal, mental and follicular to see if we -- if it's true what we say. So having a high activity and much more tolerable profile and then filing those indications. All of those indications remain to date as not curable diseases. So despite there being BTK inhibitors, BCL2 inhibitors, CAR-T therapies, there's still a lot of unmet need in these entities, and that's why we're very encouraged by this program.

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

So maybe I'll speak about the ROI in dermatology. As I said, I mean, it's an open field for us. So we are looking at it and making decisions based on what seems to be aligned with our goals of diversification and growth, and that's important to look at this dermatology as very high potential indications for Incyte. When you look at the number of patients on both atopic derm and vitiligo, if you look at the therapeutic profile that we get from a topical administration, where the risk/benefit and the side effect that you can observe have a very different rate that what you have with systemic treatment, we believe there is a real opportunity and that could be very meaningful for Incyte, in both indications.

That being said, as we discussed, we are looking at the commercial cost of having infrastructure for dermatology. It looks like specialty dermatology products in the U.S. do not require an enormous size, type of team. So that one seems to be leaning in the direction where we would be doing it ourself. And as I said in Japan and Europe and the rest of the world, it's open and we would see what makes more sense.

And the ROI is certainly a very important criteria. The speed at which we can show cash flow positivity coming from the dermatology franchise, if you look at that way, it's very important. At the same time, being able to book the revenue and to diversify the top line is also very important. So that's the 2 criteria we would be looking at to make that decision.

Operator

Our next question is coming from Cory Kasimov from JP Morgan Chase.

Cory William Kasimov - *JP Morgan Chase & Co, Research Division - Senior Biotechnology Analyst*

I have just a couple of earlier-stage clinical ones for you. So first of all, at the Phase II tumor-agnostic study for pemigatinib, is there agreement with regulators or any sort of minimum number of different tumor types you need to enroll in that program?

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

It's Steven. So the precedent for it comes from both what other companies have done before in the setting, plus in an FDA opinion piece that was written recently around. This is a reasonable approach when you already have a drug that's approved in at least 1 or 2 indications that the pathway is validated, in this case, FGFR inhibition. And you can look at areas like MSI-high for the checkpoint inhibitors as sort of a proof of principle, if you will, for doing the study this way. So we don't have and we won't be obtaining strict regulatory approval for the exact numbers required each time, but what you want to see is in a particular disease like say, endometrial or glioblastoma, something where you have the selection for the particular FGFR mutation or fusion, a very high degree of activity that's robust and durable. In the setting, where you already have approvals elsewhere in a validated pathway. And that's the idea behind it. And as I said, there's regulatory precedent already.

Cory William Kasimov - *JP Morgan Chase & Co, Research Division - Senior Biotechnology Analyst*

Okay. That's helpful. And then for the second question, curious about your clinical plans for MCLA-145. Can you talk about the overall strategy there with the initial trials and how enriched those Phase I studies will be?

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

Yes. I think it's best to say we're working in collaboration with Merus. Yes, it's early days. As I said in my prepared remarks, it's a very interesting bispecific paradigm here. There's been precedent before with mono use of CD137, and unfortunately, quite a lot of toxicity in terms of liver toxicity and transaminitis. So the idea here is to direct it with a bispecific via the PD-L1 enrichment straight to the area where it's needed and try and subvert that toxicity and we'll see, right?

The second thing is should these both mechanisms work together as we expect from theoretic and our preclinical data, the potential plans for areas where sort of checkpoint refractory patients exist and that. But that's something we'll have to prove to you. I think it's too early just to talk about -- because we're only about to start dosing in -- whether we'll have a lot of activity data early on. We're not enriching early on for any particular, to answer your question directly, receptor or biomarker. It's more standard Phase I first-time-in-man just to get to a safe -- the safety principle first.

Operator

Our next question is coming from Christopher Marai from Nomura Instinet.

Christopher N. Marai - *Nomura Securities Co. Ltd., Research Division - MD & Senior Analyst of Biotechnology*

I'm just wondering if you could elaborate perhaps on the opportunity for topical rux in atopic derm. Would you be looking at expanding label perhaps to the pediatric setting?

And then secondly, with respect to the cream formulation, I recall previously there was a rather greasy formulation that you have been using and this may have been a problem in vitiligo. I was wondering, have you -- remind me, have you updated or modified that formulation to make it a little bit more patient friendly? And then secondarily, how does this cream differ from the ointment formulation used for Eucrisa?

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

Christopher, it's Steven. So it's good to bring up to pediatric part of the population here. So the studies that we're doing currently and we have permission to do from the regulators are in 12 years and above in mild to moderate atopic dermatitis, which covers the majority of the population. In terms of the population below 12, so 2 to 12 years of age, that's something we're still working on the regulators with things like safety margins, et cetera, and it's something we'll be interested in down the pipe. But the program at the moment is 12 years and above, and that covers the vast majority of patients who are interested in treating with mild to moderate atopic dermatitis.

In terms of the formulation question, we have not changed it. It's a cream. It's -- in terms of the data we have and we've used it extensively, if you just heard, in atopic derm already an in vitiligo. It's been very well received. There's no greasiness, no burning or stinging. When you allude to Eucrisa, one of the things we've been told and we've seen from real world data is that seems to be the problem with that particular agent and that it induces both burning and stinging and then maybe why it's not used as widely as people want it to be used. Then -- but we haven't had that at all a problem with our formulation to date, and we don't expect it to be given that we've already treated hundreds of patients.

Christopher N. Marai - *Nomura Securities Co. Ltd., Research Division - MD & Senior Analyst of Biotechnology*

Okay. And then with respect to perhaps the moderate to severe setting for atopic dermatitis, have you started -- or do you have any plans to explore the topical formulation there given, of course, also the potential for safety concerns or perhaps better efficacy there?

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

Our program is mild to moderate. The moderate to severe's, particularly more on the severe range, have been reserved for oral therapies. And as you know, baricitinib has a program there and others, and then other targets that are -- maybe have a different safety margin and are more acceptable for severes. That's not the population we're targeting.

There is some overlap in terms of the moderates, and we'll expect the clinical data will dictate how physicians and patients then use the therapies there in terms of degree of disease they have and what they're trying to achieve in terms of the clinical results. One very important end point we saw, which is a good surprise, was relief of itch with our product was dramatic and occurred very, very quickly, within 2 days. And that's something

that really is important to patients. So we think that's a particular goal of physicians and patients, and we document that in our clinical trials. That will be an important end point. But for the most part, we don't think there's overlap and, again, we target in mild to moderates with the cream.

Operator

Our next question is coming from Geoff Meacham from Barclays.

Jason Eron Zemansky - *Barclays Bank PLC, Research Division - Research Analyst*

This is Jason on for Geoff. Just real quickly on Jakafi, if you could give us a sense of your expectations for the mix of price and volume moving forward, especially considering the gross-to-net hit in the first quarter. And then I have a quick follow-up.

Barry P. Flannelly - *Incyte Corporation - Executive VP & General Manager of U.S.*

Sure, Jason. It's Barry. We continue to grow volume mostly. And as you can see from this quarter, in fact, or this year, Q1 2019 over Q1 2018, most of our growth, in terms of net sales, was for volume. And we see that continuing in the future.

Jason Eron Zemansky - *Barclays Bank PLC, Research Division - Research Analyst*

Got it. And in terms of duration of therapy and in terms of moving up earlier up line, is that factoring in as well? Or do you expect to see that more kind of as a longer-term influence?

Barry P. Flannelly - *Incyte Corporation - Executive VP & General Manager of U.S.*

Well, we always try to improve duration of therapy. We want patients to stay on as long as they continue to benefit from Jakafi, and that's true in both PV and MF. When we talk about duration of therapy, we really go back to the clinical trials, and we look at the COMFORT trials, for example, where at least 50% of the patients were still on at 3 years. And at the 5-year follow-up, the response, you have 66% of patients still on therapy at 5 years. So the duration of therapy, we always want to try to improve on and work together with our health care professionals. So they dose adjust those down based on increased efficacy or decreased toxicity. And again, we want them to stay on therapy as long as they continue to benefit from it.

Jason Eron Zemansky - *Barclays Bank PLC, Research Division - Research Analyst*

Got you. Thank you for the color. And then with regards to REACH1, now that we're in the homestretch here, and -- to the extent that you can, can you provide some color on how those discussions with FDA are moving? And kind of what are your expectations for read through for REACH2 and REACH3 when we get to that point?

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

Jason, it's Steven. So you're right, the PDUFA date, as Barry said, is May 24. We're still extremely confident in our data, and we look forward to the PDUFA date. We don't give granular details on back-and-forth discussions with the FDA, but we are in a place where we're confident in our data and look forward to the PDUFA date.

Of course, because of what I just said, we expect the read through to REACH2 which is the same population, steroid-refractory acute graft-versus-host disease, to be similarly positive. It's a randomized study against best available therapy. And then in terms of chronic graft-versus-versus host disease,

REACH3 against randomized against BAT, we have strong proof-of-concept in that area. And we will have data by the end of this year in both REACH2 and REACH3 and similarly confident in it and wait for the data.

Operator

(Operator Instructions) Our next question is coming from Tyler Van Buren from Piper Jaffray.

Tyler Martin Van Buren - *Piper Jaffray Companies, Research Division - Principal & Senior Biotech Analyst*

Thanks for the updates, and the reallocation of baricitinib funding makes a ton of sense. I guess the -- my question is related to the long-term Jakafi guidance that you provided in February of last year of $2.5 billion to $3 billion by 2027. Are you guys -- can you reiterate your confidence in that based on what you're seeing MF and PV and the development of GVHD programs? And also with respect to ET, how should we think about that program that's ongoing and when that indication could come to market?

Barry P. Flannelly - *Incyte Corporation - Executive VP & General Manager of U.S.*

So yes. We're fully confident in $2.5 billion to $3 billion, and that's, as we've said before, includes MF, PV and GVHD indications. We didn't really estimate for ET. We're fully confident. We have almost 10 years actually left on the patent, and you can see the growth year-over-year and the contribution that we give to the top line. I think we can make it there. I don't know if Steven wants to comment on ET.

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

Yes. Obviously, that's the remaining myeloproliferative neoplasm after you have myelofibrosis and polycythemia vera that's not BCR-ABL driven. And because of the pathophysiology again, every expectation that JAK inhibition should work there, and we know we have some spontaneous use there. The issue with the study there is it's very difficult to enroll. Dominant first-line use is hydroxyurea, and the study requires, as you can see on ClinTrials.gov, for patients who have high white blood cell counts at initiation of the study and then to be randomized to the approved therapy for essential thrombocythemia, which is anagrelide. So both the high white count and the anagrelide randomization continue to make the study difficult to accrue. And we'll continue to examine ways to try and improve that recruitment and may end up being an entity that we end up doing a publication on -- before completing the entire recruitment, but an important disease for JAK inhibition and obviously one we're trying to address with a formal study.

Operator

Our next question is from Ying Huang from Bank of America Merrill Lynch.

Unidentified Analyst

This is Alec on for Ying. I guess I just have one on the differences between the various REACH studies. You alluded to this, the SG&A for Jakafi in steroid-refractort acute GVHD was based on the single-arm REACH1 study. Do you see any risks in REACH2 and 3 comparing Jakafi to best available therapy in terms of superiority? And some patients do actually respond to BAT, and were the studies powered with this in mind?

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

Yes. It's Steven again. Obviously, whenever you conduct a study, there's risk attached in that you may have a negative outcome. And as you alluded to the fact that best available therapies and there's a different list for REACH2 and REACH3 are active therapies and can have upwards of 30%, 40% response rate. They tend though not to be durable. And so we have confidence in the data we have seen to date in our proof-of-concept where

we can differentiate, both in terms of the upfront activity and then the durability of response. But the outcome will be on how the studies report out, and obviously there's always some risk with randomized studies.

Operator

Our next question is coming from Jay Olson from Oppenheimer & Co.

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

I was curious if there is any update on Jakafi life cycle management. I know in the past you've talked about extended-release formulations and potential fixed-dose combinations. So any update there would be great.

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

It's Steven again. Yes, as Barry said, despite there being 10 approximate years of patent life left, it's an extremely important compound to us with a very large team working on active life cycle management. Currently, there are 3 pillars to that. There's the formulation side, as you allude to, and we've already published data with one strength of ruxolitinib XR. And we're busy developing other strengths to go forward in that arena that may be along a BA bioavailable, bioequivalent route, plus/minus a safety play because it may have a different profile in terms of anemia induction. So you'll have to just wait on that, but it's very active and it's underway as we speak in terms of the XR formulation.

In terms of combinations, both us, Novartis and the external world, are investigating multiple combinations in the second-line setting and beyond for which this theoretic and sometimes very strong preclinical evidence and some clinical evidence. The combination that we are investigating are rux plus PI3-kinase delta. We presented the first set of that data at ASH last year, and we're doing that experiment further this year with continuous dosing rather than the weekly dosing. And we were encouraged by the activity we saw in patients that had been on rux for a long time, hadn't withdrawn from it and then had splenic responses as well as symptom improvement that there were some withdrawal of that when we went to weekly dosing. So we want to do that continues experiment this year.

The 2 other combinations we're doing are rux plus PIM, which has a very strong preclinical rational, and then ruxolitinib plus our JAK1 inhibitor, itacitinib, in patients who can't tolerate sufficient doses of rux or can't tolerate it at all and then switched to itacitinib. So those are all ongoing. Novartis have combinations that are ongoing and in the external world as well. But -- so combinations' are very important and it's both an efficacy play and a safety play.

And then the third arm of that is more -- and Dash can speak to this, is around the research arena and targets. So we have a very important collaboration with Syros in terms of looking for further targets here and then internally ourselves. Obviously, it's an area we know extremely well and are there better ways of potentially tackling the drivers of these conditions. I don't know if Dash wants to add anything here.

Dashyant Dhanak - *Incyte Corporation - Executive VP & Chief Scientific Officer*

Thanks, Steven. So absolutely right. There are a number of approaches one can think about going further than what were already done in terms of -- as Steven was talking about, the first 2 aspects of the pillars. And we have a number of discovery programs ongoing, both internally and in collaboration with academic institutions as well as biotech -- so nationally and internationally around probing really the fundamental underlying mechanisms in addition to JAK inhibition that one could go after.

Operator

Our next question is coming from Pete Lawson from SunTrust Robinson Humphrey.

Peter Richard Lawson - *SunTrust Robinson Humphrey, Inc., Research Division - Director*

Just on the oral PD-1, what's next readout is next year, what could we see? And where would you be positioning that drug which indications?

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

Yes, Peter. It's Steven. We filed our IND in October. We went into patients in December last year. It's going really well. There's a lot of interest and excitement in the compound being that it's oral with this potentially very interesting mechanism of action and internalization of the receptor and that translate to a clinical differentiator. But this year, its execution of the Phase I, getting to a recommended Phase II dose, and it's going well in that regard. Looking at benchmark areas of like lung cancer and melanoma to see what kind of activity there to see if this is efficacy-differentiator, and we -- that'll take the most -- better part of this year. And we would love to show you some clinical data next year. As soon as we have a safe dose and schedule, we'll also be pursuing combinations that are relevant in terms of having an oral PD-L1 inhibitor, but you will not see data until 2020.

Operator

Our next question is coming from Ren Benjamin from Raymond James.

Reni John Benjamin - *Raymond James & Associates, Inc., Research Division - Senior Biotechnology Analyst*

I guess just regarding GVHD. The way I kind of look at it is itacitinib coming on board after rux, which will likely be used off label quite a bit. Do you guys envision a launch where rux is kind of laying groundwork in GVHD? And when itacitinib comes on board, it just takes over, both at the steroid-refractory and steroid-naive? Or can you keep the 2 indications quite separate to each individual drug? How are you thinking about the commercialization?

Barry P. Flannelly - *Incyte Corporation - Executive VP & General Manager of U.S.*

Well, we think we have an advantage because we're able to launch -- we will be able to launch ruxolitinib/Jakafi in GVHD. So we're understanding that market very well right now. So we've gotten to know the BMT treaters. We've gotten to understand exactly what drugs they're currently using. But then itacitinib, when it gets approved, it really does, in fact, should have a better profile, at least in terms of cytopenias. So we really think that we could continue to develop rux or people will use rux in that setting. But ultimately, itacitinib should be the drug of choice in steroid-refractory and acute GVHD.

Operator

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

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

Okay. Thank you all for your time today and for your questions. We look forward to seeing you at upcoming investor and medical conferences, but for now, we thank you again for your participation in the call today. Thank you, and goodbye.

Operator

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