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INCY - Q4 2018 Incyte Corp Earnings Call

EVENT DATE/TIME: FEBRUARY 14, 2019 / 1:00PM GMT

OVERVIEW:

Co. reported 4Q18 non-GAAP operating income of $77m.

CORPORATE PARTICIPANTS

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

Hervé Hoppenot *Incyte Corporation - Chairman of the Board, President & CEO*

Michael Booth *Incyte Corporation - VP of IR*

Paul Trower *Incyte Corporation - Principal Accounting Officer & VP of Finance*

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

CONFERENCE CALL PARTICIPANTS

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

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

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

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

Geoffrey Christopher Meacham *Barclays Bank PLC, Research Division - MD & Senior Research Analyst*

Ishmael Izakiel Gyimah Asante *Morgan Stanley, Research Division - Research Associate*

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

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

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

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

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

Ying Huang *BofA Merrill Lynch, Research Division - Director in Equity Research*

PRESENTATION

Operator

Greetings, and welcome to the Incyte Fourth Quarter and Year-end 2018 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 Fourth Quarter and Full Year 2018 Earnings Conference Call and Webcast. The slides used today are available for download on the Investors Section of incyte.com. I am joined on the call today by Hervé, Barry and Steven as well as by Paul Trower, our Principal Accounting Officer, who will deliver the financial section of our prepared remarks. I am also very pleased to welcome 2 new members of the leadership to the call today, namely Dash Dhanak, our new Chief Scientific Officer, who joined us in December; and Christiana Stamoulis, our new CFO, who joined us earlier this week.

Before we begin, 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 our 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-Q for the quarter ended September 30, 2018, and from time to time, in our other SEC documents.

We'll now begin the call with Hervé.

Hervé Hoppenot - *Incyte Corporation - Chairman of the Board, President & CEO*

Thank you, Mike, and good morning, everyone. So 2018 was another excellent year at Incyte as we delivered 25% growth in product-related revenues over last year. All 4 sources of revenues have shown good growth with 22% from Jakafi, 19% from ICLUSIG, 28% growth in Jakavi royalties, and Olumiant now becoming a material contributor to the top line.

Looking into next year, I see this revenue trajectory continuing given the guidance we have provided to, therefore, Jakafi to reach $1.58 billion to $1.65 billion, and ICLUSIG to reach $90 million to $100 million. Adding consensus estimates for our royalty income from Jakavi and Olumiant generates an expected growth rate for product-related revenue for 2019 of approximately 20%.

Slide 6 takes us beyond just revenue expectation for 2019 and outlines the most important pivotal news flow items we expect for the year. Please note that these items only include FDA decisions, FDA submissions and pivotal trial results, and the more complete summary of 2019 news flow will follow in the later slide.

We continue to work with the FDA regarding the priority review of the ruxolitinib sNDA for the treatment of patients with steroid-refractory acute GVHD. We recently announced a 3-month extension to the review and the revised PDUFA date is May 24. We expect to submit the NDA for pemigatinib for the treatment of patients with FGFR2-translocated cholangiocarcinoma in the second half of this year. And in the second half of 2019, we also expect Novartis to submit the NDA seeking approval of capmatinib for patient with MET mutated non-small cell lung cancer.

The first Phase III results from the itacitinib development program in GVHD are expected later this year, and if the GRAVITAS-301 trial is successful, itacitinib has the potential to be a global commercial opportunity for Incyte.

We also expect pivotal results from 2 trials for ruxolitinib in steroid-refractory acute and steroid-refractory chronic GVHD later this year. We are working in collaboration with Novartis in the development of ruxolitinib in GVHD.

Last week, we announced the initial Phase III result of the broad Phase III development program of baricitinib in patients with moderate to severe atopic dermatitis, and we look forward to additional results from that program later this year.

2019, therefore, has a potential to be a very exciting year for Incyte. And to share more details on Jakafi's performance and outlook, I'll turn the call over to Barry.

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

Thank you, Hervé. Good morning, everyone. Jakafi continues its strong growth. We have seen good revenue growth in Q4, which was due to new patient growth in both the third and the fourth quarters. This gives us excellent momentum as we head into 2019.

Slide 9 further emphasizes the consistency of Jakafi's performance on an annualized basis. In the fourth quarter, as shown on the left, Jakafi grew 26% over the same period last year. And for the full year 2018, Jakafi grew 22% over the full year of 2017, as shown on the right. There was no appreciable change in the level of inventory at the end of the year compared to the beginning. Today, we have provided initial Jakafi net product revenue guidance for 2019 as a range of $1.58 billion to $1.65 billion. This range includes both approved indications for patients with myelofibrosis and with polycythemia vera as well as potential third indication of steroid-refractory acute graft-versus-host disease. Should the FDA approve Jakafi in this third indication, we will be ready for an immediate launch and would expect good reimbursement coverage given our prior discussions with payers.

I'll finish my segment by reiterating our long-term revenue guidance for Jakafi of $2.5 billion to $3 billion. As you can see from the graphical illustration on Slide 10, we are now halfway to our long-term target, and we look forward to reporting future progress over the coming quarters.

Now it's over to Steven for a 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 projects, as summarized on Slide 12. These 6 projects include potential in 16 different indications and the estimated numbers of eligible patients for each project are also included in the slide. Each individual project has substantial potential on a stand-alone basis, and collectively they represent a set of late-stage project that has the potential to transform Incyte into a company with multiple-approved products in the United States, Europe and Japan over the next several years.

We'll focus attention today on 4 of them because these are the projects that we expect to generate important updates during this year. We are conducting 2 comprehensive programs assisting the safety and efficacy of JAK inhibition as a treatment for patients with graft-versus-host disease. The REACH program is investigating ruxolitinib and steroid-refractory disease. And the data shown in the left-hand panel of the pivotal REACH1 data and steroid-refractory acute graft-versus-host disease. These are the data that are currently being reviewed by the FDA. REACH2 also in acute and REACH3 in chronic graft-versus-host disease are being run in collaboration with Novartis and are due to report results later this year.

In the first-line or steroid-naive setting, the GRAVITAS program is investigating itacitinib in graft-versus-host disease. The data in the right-hand panel are from ASH, a couple of years ago, and which led us to initiate this piece of the graft-versus-host disease development program.

The GRAVITAS-301 trial is assessing the safety and efficacy of itacitinib in steroid-naive graft-versus-host disease and is due to report results later this year.

We are excited by the potential of JAK inhibition to treat this often deadly disease, and it's important to note that the opportunity includes approximately 15,000 new graft-versus-host disease patients that are diagnosed each year globally.

We also expect important news flow from pemigatinib this year, which we announced this morning was recently granted breakthrough designation by the FDA. The second-line cholangiocarcinoma trial is fully recruited, and we are now waiting for the data to mature before we run the updated analysis. Recall that in the initial data set we showed at ESMO last year, it took up to approximately 6 months for the maximum response rate to be seen. So we currently estimate that the NDA should be ready for submission to the FDA in the second half of 2019.

The continuous dosing cohort within the FGFR3 bladder study is also recruiting, and we expect the bladder sNDA for pemigatinib to be submitted next year. We are also planning a pivotal study in the tumor-agnostic setting, which should start later this year, and could further expand the number of patients eligible for the therapy, and therefore, the potential of the molecule.

I'll end my brief update with a slide on the ruxolitinib cream development program in atopic dermatitis and Vitiligo. The randomized Phase II data in atopic dermatitis as shown in the left-hand panel were very well received at EADV last year, and we have rapidly progressed into a Phase III program.

That program is already recruiting across 2 randomized vehicle-controlled trials, and we expect to be able to report data next year.

We expect data from the ongoing randomized trial in patients Vitiligo in the first half of this year, and if the Phase II data warrant it, we expect to move swiftly into a Phase III trial of ruxolitinib cream in this second indication. Vitiligo is a disease with significant psychosocial morbidity and is a condition where there are currently no approved treatments. Both atopic dermatitis and Vitiligo, therefore, represent important and near-term opportunities for our growing inflammation and autoimmunity research and development group.

I'll now welcome Paul to the call to review the financials.

Paul Trower - *Incyte Corporation - Principal Accounting Officer & VP of Finance*

Thanks, Steven, and good morning, everyone. The financial update this morning will include GAAP and non-GAAP numbers. For a full reconciliation of GAAP to non-GAAP, please refer to Slides 26 and 27 in the backup section of the deck and to the press release we issued this morning.

For the fourth quarter, we recorded $468 million of total product-related revenues, an increased of 25% over the fourth quarter of 2017. This is comprised of $380 million in Jakafi and $19 million in ICLUSIG net product revenues. $55 million in Jakavi royalties from Novartis, and $14 million in Olumiant royalties from Lilly.

Our Jakafi gross to net adjustment was 13.4% to the quarter and 14% for the year. Our total cost and expense for the quarter on a non-GAAP basis of $391 million increased 4% from the prior year quarter.

R&D expense for the quarter was $274 million on a non-GAAP basis, which did not grow over the prior year period and our SG&A expense for the quarter was $97 million on a non-GAAP basis. With total product-related revenues increasing 25% and total non-GAAP costs and expenses increasing only 4%, this has driven an operating income for the quarter of $77 million on a non-GAAP basis as compared to an operating loss of $4 million in the prior year period.

Looking at our full year results, our total product-related revenues were $1.7 billion, an increase of 25% over the prior year. Our total cost and expenses on a non-GAAP basis were $1.5 billion, an increase of 21% over the prior year period, including non-GAAP R&D expense of $1.045 billion, and non-GAAP SG&A expense of $387 million.

Our operating income for 2018 was $198 million on a non-GAAP basis as compared to $115 million in 2017. And we ended 2018 with $1.4 billion in cash and marketable securities.

Moving on to 2019, I will now discuss the key components of our 2019 guidance on both a GAAP and non-GAAP basis. Please note that the guidance we provide today does not include any potential future strategic transactions beyond agreements previously announced.

For the full year 2019, on both a GAAP and non-GAAP basis, we expect net product revenues from Jakafi to be in the range of $1.58 billion to $1.65 billion. For ICLUSIG, we expect net product revenue to be in the range of $90 million to $100 million. As in the previous years, we will not be providing guidance for milestone and royalty revenues. We expect our gross to net adjustment for 2019 to be approximately 15% for Jakafi.

We expect total GAAP cost of product revenues to be in the range of $112 million to $117 million and non-GAAP cost of product revenues to be in the range of $90 million to $95 million. Our non-GAAP cost of product revenues excludes $22 million of amortization of acquired product rights related to ICLUSIG.

We expect GAAP R&D expense to be in the range of $1.185 billion to $1.255 billion and non-GAAP R&D expense to range from $1.03 billion to $1.1 billion. Our non-GAAP R&D expense guidance excludes estimated stock-based compensation expense as well as estimated milestone expenses.

We expect GAAP SG&A expense to be in the range of $471 million to $521 million and non-GAAP SG&A expense to range from $420 million to $470 million. Our non-GAAP SG&A expense guidance excludes estimated stock-based compensation.

We expect the change in fair market value of the contingent consideration for the ICLUSIG royalty liability to be approximately $30 million on a GAAP basis and 0 on a non-GAAP basis.

In summary, taking our guidance for product revenue and expenses and taking account of current consensus estimates for Jakavi and Olumiant royalties, we expect this should generate non-GAAP operating income for 2019 in the range of $350 million to $450 million.

I will now turn the call back to Hervé for further discussion of the year ahead.

Hervé Hoppenot - *Incyte Corporation - Chairman of the Board, President & CEO*

Thank you, Paul. In our prepared remarks today, you have heard not only about the richness of our late stage portfolio with many opportunities to further accelerate revenue growth, but we've also shown how top line revenue momentum is beginning to translate into improved ratios within our P&L.

The chart on Slide 22 takes the guidance that Paul just outlined, and consensus estimates for 2019 royalties and it illustrates how our P&L is evolving as revenue growth is substantially exceeding expense growth.

Our last slide outlines the key news flow events we expect over the course of 2019. We're already off to a good start with earlier-than-anticipated initiation of the Phase III trial ruxolitinib cream in atopic dermatitis as well as the initiation of the first-line chronic GVHD study for itacitinib.

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

QUESTIONS AND ANSWERS

Operator

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

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

Two questions for me. First off, can you talk a little bit about your expectations for volume growth versus price contribution to your 2019 Jakafi sales guidance? And also wondering if you could give us some sense of how much GVHD is baked in there. And then I have a follow-up.

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

Well, as you know, from our guidance, we're expecting a 14% to a 19% net sales growth 2019 over 2018. As you know, we took a 4% price increase at the very end of 2018. We don't get all of that price, but you can see that most of that 14% to 18% is volume. Your other question was about GVHD. GVHD, we have some spontaneous use. It's a small percentage of the total use of Jakafi currently. We're anticipating once we get approval that, that could double, so that's somewhere in the range, including the current spontaneous use, of maybe around $80 million.

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

That's really helpful. And then, you didn't speak that much on updates on the life cycle strategies. So I'm wondering if you might be able to give us a status update there. Any specifics about data timing here for the PIM JAK1 combos or the SR formulation? And should we be thinking about these more along the lines of MF, solely MF extension strategies? Or are there concurrent PV life cycle extention strategies plan as well?

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

Brian, it's Steven. Thanks for the question. So obviously, the patent life of RUX extends in the U.S. through, at least, 2027, 2028, and. So it's a very active life cycle development phase. There are sort of 3 pillars to it currently. One is around new formulation work, and we showed at JPMorgan, work we have done in the past with an SR formulation that we have published in around 2011 that is very interesting in terms of what it does to the PK curve, and there's less peak-to-trough ratio with the SR formulation and there's ability potentially to ameliorate some of the side effects, namely the anemia. So that work will ramp up and progress and will be full steam ahead to take further SR doses forward and do the required bioavailability and bioequivalence work to do that.

The second pillar, as you mentioned, is around a combination that either enhance efficacy or improve safety or both. The one that is most advanced at the moment is the RUX plus PI3-kinase delta combination. We showed updated data on that last year in December at the American Society of Hematology. We're very encouraged by that data set. Despite patients being on at least 6 months of ruxolitinib, at least 2 months of stable dose and not coming off and then having progressive disease with the addition of the combination upwards of 60% of patients at 24 weeks and some spleen volume reduction, upwards of 1/3 of those patients had improvement in symptoms, despite that context, which is very different from other competitors. What was very interesting with that data set is when we withdrew from daily dosing to weekly dosing, there was some rebound in the spleen response. So the second phase of that study is going this year, which is looking at continuous dosing to arms, either a 20-milligram induction for 8 weeks and then 5-milligram continuous or 5-milligram continuous all the way through. Should that pan out that is our lead combination, very encouraging data. The other 2 you mentioned that we are running are the PIM combination and the JAK1 combinations, they recruit this year. Hopefully, over this year, they'll recruit substantial patients, and we will aim to present data on those 2 combinations for which the biology is really good, probably in 2020. The JAK1 combination there has 2 arms to it. There's an additive arm to RUX for patients who can't tolerate sufficient doses, and then there's a switch strategy for people who can't tolerate RUX at all. And then the third pillar of the life cycle is new targets. And there are a number of academic collaborations, which have been publicly announced, at places like Vanderbilt, Moffitt and Penn as well as with research groups like Syros to look for new targets. And your last question, obviously, we're interested both in myelofibrosis as well as P vera in that space to see if we can make improvements there.

Operator

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

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

One, just on topical RUX in atopic dermatitis, just maybe if you can talk about the position of this asset, so we think about it more in the neighborhood of Eucrisa. Or how do you think about kind of the peak potential there? And then just a quick one on Jakafi versus -- myelofibrosis versus polycythemia vera, I mean are we starting to get to the point where PV is slightly a bigger contributor, can you characterize that as well?

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

So Alethia, it's Steven. I'll do the first part of your question and Barry will address your second question. As we announced on the call, the atopic dermatitis Phase III, both studies are up and recruiting, and we'll recruit over this year. The group we were after is the mild to moderate with less than 20% body surface area involvement. And currently, the program is in patients 12 years and above. So you can see the difference in overlap, for example, some of the IV products which are more to moderate and severe with different body surface area, and the target population there is enormous in the U.S. There's millions and millions of these patients largely treated with topical corticosteroids at the moment. And then I'll ask Barry to address your second question.

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

Sure, Alethia. So MF versus PV, MF is still about 60% of the volume of the patient population that receive Jakafi for MF and PV. PV is about 40%, but the total growth of PV patients, for example, '19 versus '18 was 20% growth in total PV patients and 10% growth in total MF patients. So PV continues to grow at double the rate of MF patients, but it's going to take a while for PV to pass, just because MF patients stay on a drug for a very long period of time.

Operator

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

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

So with regard to the SG&A expense guidance for '19, could you help us understand the uptick here? Are you incorporating sales build outs ahead of expected launches?

Paul Trower - *Incyte Corporation - Principal Accounting Officer & VP of Finance*

Yes, so this is Paul. So our guidance does include launch preparations for, obviously, for GVHD. We have cost in there looking ahead to itacitinib as well as to pemigatinib, so that's all baked into to that guidance range.

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

And then just secondly, on your pipeline. So outside of the pivotal stage assets, you do have some earlier programs. Could you help us understand when we might see reads from these programs in 2019, as we look to AACR and other meetings?

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

Salveen, it's Steven, thanks for the question. So you're right. We have 17 compounds in development, 8 of them we consider post proof-of-concept assets all with very high -- probably have successful and hopeful future regulatory approvals, but the earlier programs are also firing very well. I think in terms of data sets, you may see at major meetings in the first part of this year, it will be around our oral PD-L1 inhibitor. We'd like you to show you some early data for the first time at a major meeting in the first half of this year. And then towards the second half of this year, it may be more updates in terms of Phase I data sets and data expansions across some of those earlier programs.

Operator

Our next question is coming from Ying Huang from Bank of America.

Ying Huang - *BofA Merrill Lynch, Research Division - Director in Equity Research*

I have a first one on housekeeping. Can you talk about the inventory levels for Jakafi in the fourth quarter? Whether there's a significant change in that level? And then secondly, maybe a big picture question for Hervé. Now you're starting to show significant cash on the balance sheet, what you think about the cash deployment from the balance sheet? And then given the industry consolidation we have seen recently, where do you think Incyte is positioned in that landscape?

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

Ying, it's Barry. Just addressing your inventory question. Inventory was in the normal range at the end of Q4. There wasn't any -- as we said at the end of Q3, I believe, is that we have a big drop off in inventory, but inventory ended normal for the end of the year. Hervé?

Hervé Hoppenot - *Incyte Corporation - Chairman of the Board, President & CEO*

Yes. So regarding the cash question obviously, one of the priorities we are pursuing is the growth of the revenue and the diversification of the top line. So you can imagine that one of the use of cash that we are always looking at, and it's a relatively challenging thing to do. But where we think they are some opportunities, would be to add to our late-stage or commercial portfolio in the next 24 months. And that's something we are -- that could be potentially strategically very important for the corporation and would be a very good use of the cash that we have now. Regarding the consolidation in the industry, as you know, we are in the process of building a long-lasting global innovative biopharma company, and what we presented today, is also reinforcing the multitude of late-stage internal candidates that we have and could be adding to the growth of our top line

and accelerate our growth in the next few years. So that's really the priority we are pursuing. As I said, we would be looking at opportunities to acquire additional assets, if there are good quality and fitting with our portfolio, and that really is the way I would describe the cash question and the consolidation question.

Operator

Our next question is coming from Cory Kasimov from JPMorgan Chase & Co.

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

I just had a couple of quick ones for you on GVHD. So first, I'm just curious if there's any more color you can provide on the ongoing GVHD review for RUX in the additional information that was submitted to the FDA? And then secondly, as you prepare for that launch in GVHD, curious how your conversations in market research have evolved? And maybe better informed due to the potential ramp and more so peak sales opportunity for that indication between RUX and itacitinib?

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

Cory, it's Steven. I'll do your first question. The RUX sNDA for the steroid-refractory acute graft-versus-host disease indication is, to our knowledge, the first time that the FDA has reviewed an application for this indication, which is obviously a complex disease with a very complex treatment path. The FDA extended the action date to allow time to review additional data that we recently submitted in response to an FDA information request. This submission of additional information resulted in the extension of the PDUFA goal date by 3 months to May 24, 2019. Extensions, as you know, are not uncommon in the FDA approval process. And although we're obviously disappointed with this delay, we remain very confident in our data set. And that's the update I can give you on that at this point in time.

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

And so Cory, it's Barry. So just getting ready for the launch for acute steroid refractory GVHD. We think of this really as being the first launch of Incyte into treating more patients and helping more patients who have graft-versus-host disease whether in the acute or chronic setting. So while REACH1 is for the acute refractory setting, which we're fully prepared, and we believe we fully understand that disease. The opportunities there are -- you have about 3,500 patients with acute GVHD in the United States, maybe an equal number with chronic GVHD, about half of those have steroid refractory disease, but the real opportunity after that is, of course, with itacitinib with GRAVITAS-301 and GRAVITAS-309, worldwide, there's about 21,000 patients that suffer with GVHD after a stem cell or bone-marrow transplant. And we think that itacitinib in the steroid-naive setting will actually be able to benefit them a great deal. Our team has really learned a great deal about graft-versus-host disease. We learned a great deal about bone-marrow transplants and the devastating effects that GVHD plays on patients' lives by talking to health care professionals through advisory boards, through one-on-one meetings. And I think they're very excited about ruxolitinib and itacitinib, and moving it into the earlier-stage setting if in fact we prove successful in the current ongoing trials that we have.

Operator

Our next question today is coming from Matthew Harrison from Morgan Stanley.

Ishmael Izakiel Gyimah Asante - *Morgan Stanley, Research Division - Research Associate*

This is Ishmael on for Matthew. For Vitiligo, what would you consider to be clinically meaningful data from the Phase II? And what is your hurdle to move this into the Phase III?

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

Ishmael, it's Steven. Thank you for your question. As I said in the prepared remarks, this is a condition for which there are no approved treatments. There's many, many sufferers around the world. And a very underappreciated psychosocial morbidity. Having said that, you need an objective endpoint to conduct a study and deliver data. And the way it's measured is to quantify the amount of repigmentation in various areas, there are scales that are used for the whole body, they're called VASI scales, and the scales that are used for the face, which is one of the areas that is obviously most visible and causes a lot of the psychosocial morbidity. And its percentage improvements in those face VASI scores and total body scores that then give you the outcomes you need. You can get a 100% improvement, you can get 75%, 50%. You need to quantify those and present them. We're obviously still in discussion and will be when we complete our Phase II with regulatory agencies around what is the appropriate end point and what is the right number to hit. So having said that there's very little-to-no spontaneous remission of this disease. So anything is important in terms of the actual number achieved. Once we have the data in hand, which is going to be in the first half of this year, we'll find an appropriate place to present that. I will tell you in a very small data set, which gave us our proof of concept, was investigator-initiated work in 11 patients, 6 of those patients had very meaningful, more than 50% improvements in face repigmentation scores. So that's the sort of territory we've achieved with the drug to date.

Operator

Our next question is coming from Geoff Meacham from Barclays.

Geoffrey Christopher Meacham - *Barclays Bank PLC, Research Division - MD & Senior Research Analyst*

Just had a couple. To follow on a earlier question. In GVHD, it sounds like commercially you're ready in the U.S. for RUX, but looking beyond that, how would you characterize the incremental OUS commercial investment for itacitinib? How do you maximize the value of that asset? Then I have a follow-up.

Hervé Hoppenot - *Incyte Corporation - Chairman of the Board, President & CEO*

So the first step is ruxolitinib, as you heard, we are ready to go. We have deployed our teams. We are -- so that part is included in the P&L and the guidance that you have seen. I think for itacitinib, we will have, obviously, to look at the timing of when it's going to be approved, both for the U.S. for Europe and Japan. And as Paul said, I mean, we have included some potential prep cost in the guidance that you have seen for the U.S., where we anticipate it will be the first to launch. And then in 2020, we will be deploying additional resources for Europe and Japan.

Geoffrey Christopher Meacham - *Barclays Bank PLC, Research Division - MD & Senior Research Analyst*

Okay. Makes sense. And for pemigatinib, I wanted to get you guys view of how much -- if it's changed at all, how much you view the cholangio data as a leading indicator for bladder? And obviously, urothelial looks -- is looking more competitive with erdafitinib and EV-201 from Seattle. So maybe just talk through the hurdles that you kind of clinical hurdles in urothelial cancer? And maybe what would be differentiated?

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

Geoff, it's Steven. I'll try to answer your question. So if we just look at first, at intrahepatic cholangiocarcinoma, that's FGFR2-translocated and driven by that. You know, obviously, we showed updated data at ESMO last year, independently confirmed 40% response rate with the PFS that was a little north of 9 months. And you saw those responses improve over time, which in my prepared remarks, we're saying we're waiting for that data to mature this year, and form part of our NDA submission. The testing for it, it seems to have increased globally as usually happens when people realize there's a drug that may benefit them. Places are starting to do molecular profile in certainly with the United States, Western Europe, and place like Japan and Korea, et cetera. You know, we think they're about approximately 3,000 patients available globally to the setting, second-line

cholangio that's FGFR2-translocated, and we're pretty sure we're clearly the leader there. And as we announced this morning, the FDA just recently gave us breakthrough designation with our data set. So it's a very encouraging arena. The readthrough to bladder, it's interesting. So bladder is different. It's FGFR3-driven, either mutated or translocated. J&J is clearly ahead. And as you said there's a comparative milieu in bladder cancer, in general, but not necessarily targeted to the particular mutation. The J&J data sets, initially they use intermittent dosing as well and then switched to continuous dosing regimens. And so an uptick in the response rates for the mid-20% range also to 40%. So we did the same. Last year, we switched from our intermittent data set to continuous dosing, and we're doing it now. We think we have a really good compound. We understand the PK. We're able to manage it well. And we think we have a best-in-class compound. So we think we'll be very competitive. And we will complete enrollment this year, analyze and hopefully submit an sNDA in bladder next year. The opportunity is obviously much, much larger, given the amount of metastatic bladder cancer patients there are. For the FGFR3 mutations, it could be upwards of 12,000 to 15,000 patients globally, obviously, with a much more competitive milieu. And then thirdly, as I said, now that you have validated clinically for FGFR2, FGFR3 in bladder and more recently, the myeloproliferative neoplasm we presented at ASH that's FGFR1, we think it's the right time to do a tumor-agnostic study, which we're busy opening and doing now. And the various entities there that are also, will end up being appreciable in terms of the amount of patients that may be involved. So, for example, endometrial cancer, the FGFR2 mutations, 10% prevalence, glioblastoma squamous lung, rectal, head and neck. If you add those all up, you get potentially to another 15,000 patients. So we think there are readthroughs across the board and potentially tumor-agnostic as well.

Operator

Our next question is coming from Carter Gould from UBS.

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

I guess one real quick one. Just in terms of clarification on a earlier answer around the PDUFA delay and any impact that might have to REACH2 regulatory strategy there? Or anything in sort of data preparation? And then separately, we saw you move your arginase inhibitor into a combination study with Darzalex. Just trying to see, if there's any -- if that has any sort of implications for what I guess you saw from the earlier Phase I, II studies you were advancing there? And when we might see some of that data?

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

Yes, Carter, it's Steven. In terms of read throughs and regulatory read throughs to REACH2 and 3, there are none. Those are stand-alone studies. They're yet to complete and deliver their data sets, and there should be no effect on any regulatory readthroughs in terms of REACH2 and REACH3. The arginase question is an interesting one. One of the areas where you see myeloid-derived suppressor cells that express arginase is in multiple myeloma. So it's a good disease to study it in. Daratumumab, the CD38 antibody is obviously an extremely active compound here, and we have worked with J&J Janssen to set this up as a randomized study to try and discern the additive effect of arginase in this area, and that study is just about to begin, as you saw it just appears on CT.gov. It's not from a learning in any other part of the program currently.

Operator

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

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

Maybe one question for Barry. With the guidance on the gross to net adjustments, it does seem to be creeping up year-over-year for the last couple of years. Can you just talk about what's driving that? Is that across the whole franchise? Is it one sector that's really growing the gross to net, or is it the patient mix thing? What's going on there?

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

Well, it's always the government rebates that we're required to do. So it's 340B, it's DoD, it's VA, it's Medicaid. So you can imagine Medicaid is growing a little bit because of the expansion of the Medicaid program by states under the Affordable Care Act. We have more use in hospitals, which drives up 340B usage. And then VA and Department of Defense is growing nicely, but we have to obviously give government rebates there. So that's the entire increase in gross to net.

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

Okay. And then maybe following up, Steven, on your comment a couple of questions ago. The 15,000 patients that you think might be amenable to the tumor-agnostic approach. Can you break that down between translocations and mutations? Because we've seen in this space, translocations translate very well to efficacy; mutations, it's a little less clear.

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

Marc, I just -- this is Barry. Again, I just want to clarify. And remember, the gross to net for Q1 is affected by the additional amount that we have to pay through the Donut Hole, so it went from 50% to 70%. So I forgot to mention that, but now pharma is picking up 70% of the Donut Hole from Medicare Part D patients. Now I'll pass it over to Steven for your other question.

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

Marc, it's Steven. So I'll backtrack a little bit, for a second. You're absolutely right. The FGFR field's been going for a long time. Initially, companies that had FGFR inhibitors targeted amplifications. And as you know, that didn't really pan out. There's no approved FGFR inhibitor, and that doesn't seem to be a driver, but if you hit in the amplification setting that you get the efficacy needed. But with the switch now with us and others to, for example, in cholangio, it's an FGFR2-translocation in bladder, it's an FGFR3 mutation or fusion. In the MPN 8p11, it's an FGFR1-translocation. You now see these efficacy bumps that should translate hopefully to approved products. In the tumor-agnostic setting, again, it's not amplifications, you're right. I can try to break it down for you, but I will give you some examples because it gets a little busy, but endometrial carcinoma is an FGFR2 mutation or fusion, that's 10% of those patients. Glios is an FGFR3 mutation or fusion, that's 10%. I'll give you one other example, which is pretty well-known one is squamous non-small cell lung cancer. And that could be either FGFR1, 2 or 3 mutations or fusions. The main point to make is, it's moved completely away from amplifications to the mutation translocation fusion setting, where you're likely to see those as the oncogenic driver. And if you aggregate that part where you get the efficacy you need.

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

Okay, great. And then one last one, just on the pemigatinib time lines. Is the gating to the filing purely the -- more follow-up on patients? Or is there also some nonclinical stuff that needs to be completed in parallel?

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

Yes. It's really around the maturity of the data set and follow-up. We saw this very encouraging sign when with more mature follow-up, the response rate over time went up. And remember, this was an independently confirmed response rate. So when we first presented the data, we were sitting in the mid-20% response rate range, and then the ESMO update, you saw a 40% independently confirmed response rate with really long duration of response and long PFS. So in that particular tumor type, that's around maturity and needing about 6 months of follow-up to get the maturity you need. There's nothing else that's on critical path here in terms of our NDA submission. There's no CMC issue or anything else.

Operator

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

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

Just, Hervé, maybe -- I wonder if you can make any comments around any of the off-label use you could be seeing for RUX that you've already seen in GVHD? And then, I guess the follow-up question is around pacing of data for GVHD in 2019, when would we see REACH2, 3 versus GRAVITAS?

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

So, it's Barry, Peter. So I'll try to answer. So we have some spontaneous use, and we've said it before, I think of the total amount of Jakafi used maybe 2% to 3% of that is spontaneous use of Jakafi in acute and chronic GVHD. And the second part of your question was?

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

Was just on the timing of around the date for GVHD in 2019, so for REACH2, 3, GRAVITAS, et cetera?

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

Yes, Peter, it's Steven. It's hard to give you exact timing. Obviously, it's event-driven, but REACH2 is steroid-refractory acute and REACH3 is steroid-refractory chronic done in combination with Novartis, our partner. Global studies enrolled really well, and we fully expect data in the second half of this year for both of those studies. GRAVITAS-301, itacitinib steroid-naive acute, our global study is enrolled also superbly well. And, again, data-driven in terms of the endpoints, but we also expect data in the latter half of '19 for all 3 of those 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'm curious about the decision to move into continuous dosing in the Phase III cholangiocarcinoma study for pemigatinib? And Steve, you mentioned earlier, your observations from changes to the bladder study. I was just curious if you could share with us your expectations around how the move to continuous dosing might potentially impact efficacy and then also tolerability? And then I have a follow-up question.

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

Jay, it's Steven. Very good questions. I think, both J&J and we've demonstrated that you do get a bump in efficacy with switching from intermittent, which is 2 weeks on, 1 week off to continuous dosing. Clearly, you also pay a price in terms of tolerability. So the J&J published data set went from a 10% discontinuation rate to a 20% discontinuation rate. That happens across drug development. You have to create the therapeutic ratio there. We felt that for our first-line cholangiocarcinoma study that's FGFR2-driven that it's head-to-head against the chemotherapy doublet in terms of gemcitabine and cisplatin. And that has appreciable response rates that we're going to have to beat in that study. We clearly think we'll beat them on durability, which is why we're doing the study. In the end, though it's about individual patient titration, right. So you'll be able to -- the protocol will be written and allow people to dose titrate based on tolerability, either up or down, or even take treatment breaks as needed. Because you make a population decision on dosing, but it comes down to an individual decision on tolerability. And so we elected to obviously do that in the cholangio first-line study for the reasons I mentioned. And then the bladder work, we were largely driven for what J&J showed in terms of the

uptick in response rate. We have done appreciable work with intermittent dosing in bladder already, and we were in the same territory as them with our intermittent dosing, which is why we did the switch there.

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

That was very helpful. And congrats again on getting the breakthrough designation. I had one follow-up on your small molecule. Oral PD-1 inhibitor, you mentioned earlier that you might have some data earlier this year. And I was wondering, if you could share with us any initial thoughts you might have around what sort of clinical development options you might be considering, such as adjuvant therapy or other settings where a small oral molecule might have significant dosing advantages over an antibody?

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

Sure. Thank you. It's Steven. I'll take the question again. So you know we went into the clinic at the end of last year in December. We announced that at JPMorgan, it's an oral PD-L1 inhibitor, which what we think looks like a very interesting mechanism of action in terms of bonding PD-L1 and then internalizing, which we showed work around that preclinically. Just to manage expectations though and I should have been clear earlier. The major meeting data set for the oral PD-L1 compound will be preclinical data, obviously, initially because we've just been in the clinic, and we're just dosing now and getting PK and PD. In terms of the compound itself, that's interesting, so the mechanism of action I alluded to, what will that translate too. Obviously, our hope is that there will be an efficacy differential based on that because of its unique mechanism of action. We're going to have to show that clinically. Should that be the case that will drive very different development than from a PD-L1 inhibitor alone, if there's an efficacy differentiator based on the mechanism of action, and we'll work that out. In terms of its oral nature, it may potentially give us some advantages. One is in the safety realm. When you run into trouble with checkpoint blockade, it can be quite devastating complications like colitis, and obviously with an IV, it's going to be on board for a long time. With an oral, you can immediately stop dosing and potentially ameliorate safety there. The other areas of oral-oral combinations, it will be very useful. Maintenance settings particularly, the adjuvant setting when patients don't want to come into IV -- to the clinic to get IVs and just take an oral long term, so you can think of areas adjuvant like in melanoma, potentially adjuvant like in non-small cell lung cancer. Obviously, AstraZeneca with Durva is already showing that there is a benefit to checkpoint blockade in an adjuvant setting in lung cancer there. So those are areas we're really thinking about and we'll work on. Internal combinations will be important. Obviously, we have FGFR in bladder now, and that may lend itself to a very good internal combination. But there may be external combinations that will be really important, for example, with VEGF inhibitors and renal carcinoma, et cetera. It's really too early to tell you, what the totality of the clinical development program will look like. So we know a little bit more about what we have in the clinic.

(technical difficulty)

Operator

Our next question is from Tyler Van Buren from Piper Jaffray.

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

Okay. Yes. I just want to follow-up on a comment you made earlier about adding late-stage commercial revenue. Specifically, could you speak about what therapeutic areas you guys are most interested in? And also your capacity to do a deal? And what size of deal you guys could potentially do? Clearly, you have cash growing to $1.4 billion and improved profitability. Would you also be willing to take on some leverage, and what that may look like?

Hervé Hoppenot - *Incyte Corporation - Chairman of the Board, President & CEO*

So there are always like 2 types of products, or franchises we are interested in. I mean, the one would be early like we have done historically like early technology and Phase I type of products because they would be complementary to what we have. So you can think of life cycle management

in the field of MF and PV. So you can think of that, I mean, what could be the early products that are helping us manage the portfolio and from the early stage. The other part is what I spoke about earlier is saying, if we can identify opportunities to diversify our revenue line in the short term, we know from the 6 projects we have in our own portfolio that, that diversification would be happening. But if there is a way to add to that with external growth, that's something we would be doing. The targets obviously in the field of oncology and hematology because as you can see the late-stage portfolio from the internal pipeline is clearly where we will be very active in the next few years.

Operator

Our next question is coming from Katherine Xu from William Blair.

Michael Booth - *Incyte Corporation - VP of IR*

Are you on mute? Kevin, let's move to the next one, and we can come back to Katherine.

Operator

(technical difficulty) Ladies and gentlemen, we are experiencing technical difficulties.

I would like to turn the floor back over to management at this time.

Michael Booth - *Incyte Corporation - VP of IR*

Kevin, will we able to take any additional questions or should we close the call at this time? I think we should. In that case, I think we should close the call. Apologies to those analysts who weren't able to ask. We'll follow-up with you immediately after the call, and Hervé, would you like to make any closing remarks?

Hervé Hoppenot - *Incyte Corporation - Chairman of the Board, President & CEO*

Yes. Thank you. Sorry for the technical difficulties. Thank you for your time today for your questions, and we look forward to seeing you at upcoming investor and medical conferences. But for now, we thank you, again, for your participation in this call today. So thank you, and goodbye.
