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Q3 2018 Incyte Corp Earnings Call

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PRESENTATION

Operator

Greetings, and welcome to the Incyte Third Quarter 2018 Earnings 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. Mike, please go ahead.

Michael Booth ***Incyte Corporation - VP of IR***

Thank you, Kevin. Good morning, and welcome to Incyte's Third Quarter and 9 Months 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, Steven and Dave, who will deliver our prepared remarks, and by Reid who will join us for the Q&A session.

Before we begin, we'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 2018 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 June 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. I am pleased to report that Incyte continues to perform very well across all aspects of the business. We have recently delivered exciting data at both the EADV Congress and at ESMO, and we are looking forward to seeing many of you at ASH in San Diego.

Total product revenue continues to grow nicely and we recognized a 25% increase in 9 month revenue versus the same period last year. Revenues of over $1.2 billion in the first 9 months of 2018 included over $1 billion in Jakafi sales and over $160 million in royalties from Jakavi and Olumiant, reflecting strong demand for both ruxolitinib and baricitinib on a global basis. It's important to note that Q3 net sales for Jakafi were negatively impacted by inventory moves late in the quarter, and Barry will provide additional details in a few minutes. Patient demand for Jakafi remains strong and Slide 5 provides some historical data charting U.S. patient demand alongside U.S. revenue recognized for Jakafi.

Going back to the third quarter of 2012, you can see that Jakafi revenue and the total number of patients taking Jakafi show a fairly consistent rate of growth. Due to the strength in underlying demand and the growing number of patients on Jakafi, we are pleased to be increasing the bottom end of our guidance range so that our guidance for full year revenue for Jakafi is now a range of $1.37 billion to $1.4 billion.

Before I pass the call to Barry for more details on Jakafi performance, I would like to quickly mention recent updates from our portfolio. It has been an exciting few weeks for Incyte starting with a very encouraging data from ruxolitinib cream in patients with atopic dermatitis presented at EADV last month as well as data from capmatinib and pemigatinib at the ESMO conference last week.

On the regulatory front, we were pleased that the FDA accepted the sNDA for ruxolitinib in steroid-refractory acute GVHD for priority review and signed a PDUFA date of February 24 next year.

Looking forward, the GRAVITAS-301 study of itacitinib in patients with newly diagnosed GVHD is enrolling very well and both our PD-1 and PI3-kinase delta programs are on track. With Phase 3 baricitinib data in atopic dermatitis also expected in the first half of next year, there is much to be excited about in the coming months.

With that, I'll turn the call over to Barry for more details on the sales performance of Jakafi.

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

Thank you, Hervé, and good morning, everyone. Patient demand for Jakafi remains very strong, and we are seeing good uptake in both MF and PV indications. Slide 8 shows robust growth in patient demand for both MF and PV. As you can see, the total number of MF patients currently on Jakafi, shown in blue, continues to rise and the pool of MF patients on therapy continues to be greater than PV, shown in orange. The total number of PV patients on Jakafi is growing faster than MF, and we continue to expect that in time the number of PV patients taking Jakafi will overtake MF.

The sales bridge provided on the left-hand side of Slide 9 shows continued demand growth in Q3 and the effective inventory changes on net sales. We saw an unexpected destocking at several large customers late in the third quarter leading to a negative inventory effect of approximately $8 million in the quarter. The 9 month sales data, shown on the right-hand side of Slide 9, where effects of changes and inventory are normalized, shows a strong 21% growth over the same period last year.

The number of new patient starts is typically a leading indicator for sales performance, and Q3 new patient demand data are encouraging and provide us with good momentum as we enter the fourth quarter. Given our confidence in the full year outlook today, we have adjusted Jakafi guidance by lifting the lower end of the prior guidance range. Slide 10 shows the consistent yearly growth of Jakafi, adding more than $200 million in net product revenue each year since 2014. We are on target to continue that trend again for the full year of 2018, given that the midpoint of the new guidance range represents more than $250 million in increased Jakafi revenue versus the full year of 2017. I am very pleased that both indications are driving growth as we continue to secure new patients, while also maintaining current patients on therapy for longer.

Given the success of the REACH1 trial, we continue our readiness efforts for potential approval of Jakafi in steroid-refractory acute GVHD. Our team has made excellent progress in educating physicians about the benefits that Jakafi provides in both MF and PV indications. And I have every confidence the team will do an equally outstanding job for patients with GVHD.

We submitted the sNDA on schedule during the third quarter based on positive results from REACH1 in patients with steroid-refractory acute GVHD, and the FDA has recently accepted it for priority review. As we detailed last quarter, we believe our team's size and structure has already been optimized, and we are ready to launch immediately in this indication if approved.

With that, I'll pass the call over to Steven for an update on our portfolio.

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

Thanks, Barry, and good morning, everyone. We believe that JAK inhibition has significant potential as a treatment for graft-versus-host disease, and we have 2 pivotal programs that span several aspects of this devastating and often fatal disease. As Barry touched on, we were pleased to have the ruxolitinib sNDA accepted by the FDA for priority review based on the results of REACH1. Beyond REACH1, we have 3 ongoing Phase III trials that are all currently expected to yield results next year. REACH2 and REACH3 are evaluating the use of ruxolitinib in steroid-refractory acute graft-versus-host disease and steroid-refractory chronic graft-versus-host disease, respectively. GRAVITAS-301 is the first pivotal trial that is evaluating our JAK1 selective inhibitor, itacitinib, in patients with treatment-naïve acute graft-versus-host disease.

Early next year, we expect to launch a second Phase III trial of itacitinib this time in patients with steroid -- with treatment-naïve chronic graft-versus-host disease. There are a significant number of new patients each year that would become eligible for treatment with either itacitinib, as the first-line treatment, or ruxolitinib, following treatment with steroids, if our trials are successful and we obtain regulatory approvals.

On Slide 14, we have included data for pemigatinib, our FGFR1/2/3 inhibitor, which was presented recently at ESMO in Munich. If you recall, we presented some initial data from this group of patients at our R&D day in June this year, which showed a disease control rate of 82%, an overall response rate of 24%, and a 6.8 month median progression-free survival. You can see here that as patients remained on therapy, responses have been more durable and more patients have become responders, such that the response rate is now 40% with a median progression-free survival of greater than 9 months. Importantly, all tumor response data are from central review. Recruitment into the FIGHT-202 trial in patients with cholangiocarcinoma is now largely complete, and we'll now wait for the data from the trial to mature. If the data continues to evolve as we expect, we intend to submit an NDA seeking approval of pemigatinib in second line FGFR2-translocated cholangiocarcinoma next year. We, therefore, expect cholangiocarcinoma to be the initial indication for pemigatinib, with the potential for an approval in FGFR3-mutated bladder cancer as well as the development program seeking a tumor-agnostic FGFR altered indication in the future.

Data on capmatinib were also presented at ESMO. Capmatinib is an oral reversible inhibitor of the MET receptor tyrosine kinase, and it has shown both high selectivity for MET and is extremely potent against MET exon 14 skipping mutation compared to all other MET inhibitors in development. Capmatinib was discovered by Incyte, was included in the 2009 license agreement with Novartis, and has the potential to be the first MET selective inhibitor to be approved, given the exciting data presented at ESMO this year.

Data at ESMO were from the GEOMETRY mono-1 study being run by Novartis, and these data were in patients with non-small cell lung cancer with MET exon 14 skipping mutations, which occur in up to 4% of patients with non-small cell lung cancer. The response rates seen in this 94-patient trial were clinically meaningful, with an overall response rate in second and third line patients of 39%, and in first line the response rate was 72%.

All data was centrally reviewed, and capmatinib showed a manageable safety profile in this challenging patient population. Novartis is guiding to an NDA submission for capmatinib next year, and we are very proud that another Incyte-invented molecule appears to be on the path to potential registration.

Let's move on to our development efforts in inflammation and autoimmunity. We were excited that data from ruxolitinib cream in patients with atopic dermatitis were presented at the recent EADV meeting in Paris and were very well received. As you can see here, the data showed rapid improvements in itch for patients on the ruxolitinib cream versus both placebo and steroid cream, which was seen as early as 2 days after the first use. These responses as well as other endpoints based on the Eczema Area Severity Index and the Investigator Global Assessment scales were durable, and the treatment was not associated with any notable safety or tolerability findings. We are currently in discussions with the FDA to design a Phase III program in adults with atopic dermatitis, which we expect to initiate shortly. Ruxolitinib cream also has potential as a treatment for patients with vitiligo, which is an autoimmune disease of the melanocytes, leading to disfiguring patches of hypopigmentation on the patient's skin, most notably on the face and hands. A small proof-of-concept trial of ruxolitinib cream has already shown promising results and a randomized double-blind vehicle controlled Phase II is ongoing. We expect to announce data from that trial next year.

I'll now pass the call along to Dave to review the financials.

David W. Gryska ***Incyte Corporation - Executive VP & CFO***

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 our press release.

For the third quarter, we recorded $450 million of total revenue on a GAAP basis. This is comprised of $348 million Jakafi net product revenue; $20 million in Iclusig net product revenue; $51 million of Jakavi royalties from Novartis; $11 million in Olumiant royalties from Lilly; and $20 million of contract revenues from milestone earned from Lilly for the commencement of the Phase III program in lupus. Total revenues for the quarter on a non-GAAP basis were $430 million and exclude the $20 million milestone from Lilly. Our Jakafi gross to net for the quarter was 13.5%, and we expect that our gross to net adjustment for full year 2018 will be approximately 14%. Our cost of product revenue for the quarter was $19 million on a non-GAAP basis. This includes the cost of goods sold for Jakafi and Iclusig and the payments of royalties to Novartis on Jakafi net sales.

Our R&D expense for the quarter was $251 million on a non-GAAP basis, primarily driven by clinical development programs, and our SG&A expense for the quarter was $85 million on a non-GAAP basis.

Moving on to non-operating items. We recorded GAAP and non-GAAP net interest income of $10 million in the third quarter. Our net income for the third quarter on a non-GAAP basis was $83 million, which is double that reported for the same period last year. Looking at our year-to-date results, our net income on a non-GAAP basis was $137 million. We ended the third quarter with $1.4 billion in cash and marketable securities, and we expect to end the year with approximately the same amount.

Slide 21 provides a summary reconciliation from GAAP to non-GAAP metrics. And as I mentioned earlier, a more detailed reconciliation is provided in this morning's press release. My last slide provides a summary of our current financial guidance. Based on Jakafi's year-to-date performance, we are increasing the lower end of our net sales guidance by $20 million to a revised range of $1.37 billion to $1.4 billion. We're also decreasing the high end of our R&D guidance by $50 million to a revised range of $1.15 billion to $1.2 billion, and increasing our SG&A guidance from a range of $390 million to $410 million to a new range of $420 million to $440 million based on our run rate for the year-to-date. Our guidance for non-GAAP net income of $200 million to $250 million is unchanged.

Hervé will now conclude our prepared remarks by summarizing our expected news flow.

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

Thanks, Dave. And I would like to pause here for just a minute to say a few words of thanks for the invaluable role you have played in the Incyte leadership team since joining us in 2014. And I would like to take this opportunity to publicly thank you for all of your contribution and to wish you well in your retirement when we identify your successor.

So to end our discussion, I would like to share our key objectives between now and the end of 2019. On the regulatory front, we have 3 important goals. First, we expect to achieve FDA approval for ruxolitinib in steroid-refractory acute GVHD in the first quarter of 2019. It may come sooner, and, if so, we are ready to launch. Second, should the pemigatinib data continue to evolve as we expect, we intend to submit an NDA for cholangiocarcinoma next year. Third, Novartis has stated that it plans to submit an NDA for capmatinib in non-small cell lung cancer with MET exon 14 skipping mutations next year. Regarding key clinical data, we are currently expecting results from several registration-enabling trials before the end of 2019. Firstly, we expect to announce result of the Phase III program for baricitinib in atopic dermatitis. Then, data from 3 GVHD pivotal trial, GRAVITAS-301 with itacitinib and REACH2 and REACH3 with ruxolitinib are also expected to be available during 2019. We also expect to complete recruitment of the continuous dosing cohort for pemigatinib in patients with bladder cancer. If data from this cohort are positive, they could form the basis for a regulatory submission. We also anticipate initiating several Phase III programs before the end of next year. So GRAVITAS-309 trial is in preparation, and we will study itacitinib in patients with treatment-naïve chronic GVHD. And we are also planning on opening a Phase III program evaluating ruxolitinib cream in adults with atopic dermatitis, and if the Phase II is successful, a Phase III program in patients with vitiligo. Finally, we plan to start Phase III trials of pemigatinib in both cholangiocarcinoma and first line bladder cancer. We believe that there is a significant value

embedded in our portfolio and it's up to us to execute on these opportunities in the coming months.

By creating the right molecule and working towards clinical success, we aim to create value for both shareholders and society by bringing new and innovative therapies to patients. In doing so, we expect to drive Incyte towards sustained and significant profitability.

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 Salveen Richter from Goldman Sachs.

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

So, I have two questions on graft-versus-host disease. So firstly, in light of the upcoming PDUFA date for the REACH1 study, could you comment on the education required here on the sales side and any additional build you might require in terms of your sales force? And then secondly, in light of this positive data, how does that readthrough to the other rux studies in graph versus host as well as itacitinib? And then specifically for itacitinib, what is the benefit of JAK1 alone in the treatment-naïve setting versus JAK1/2?

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

Salveen, this is Barry. I'll take the first part of your question and hand it over to Steven for the second part of the question. So in terms of the build, so throughout this year, we added 25 sales representatives, 3 MSLs and 2 oncology nurse educators. And that was to get ready, in fact, for GVHD, but also to take advantage of continued growth opportunities for Jakafi in myelofibrosis and polycythemia vera. So those oncology sales representatives are actually positioned around the top centers that do stem cell transplants and where most GVHD would be found. So I think as we said before, the top 50 stem cell transplant centers account for about 70% of the transplants. So we think it's really targeted. Our training is beginning now -- so our training materials are all prepared in terms of educating our internal teams, including the sales teams. We call on many of these targets already -- about 50% of the physicians that are doing transplants because, remember, some of them are doing transplants for myelofibrosis patients. So we know the centers. We've been profiling the centers. We have another team that we call our Natural Account Managers that have been making sure that we'll be able to have Jakafi on formulary for steroid-refractory acute GVHD. So we think we're well prepared in terms of that education and then, of course, we'll educate health care professionals about the benefits that Jakafi provides in this patient population, and we're fully prepared in putting together materials for that. With that, I'll hand it over to Steven.

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

Thanks Barry. Thanks for the question, Salveen, So you asked about the readthrough from the REACH1 results to the REACH2 program, which is in steroid-refractory acute as well, but a randomized study against best-available therapy, and then REACH3, which is in chronic graft-versus-host disease and also a randomized study. Overall, the read is positive, given that it's JAK inhibition with a few nuances. Acute disease is generally an apoptotic disease, whereas chronic disease is more a fibrotic disease. But given that we have proof of concept in both entities, we obviously feel strongly about the likelihood and probability of success here, and thus we conducted these large Phase III programs. So overall, positive reads there. The same applies to itacitinib, even though it's more selective for JAK1. Again, JAK inhibition has been important across the spectrum of graft-versus-host disease. Let me just remind you of itacitinib's proof-of-concept data at ASH a few years ago, which showed a very high response rate in steroid naïve as well as in steroid refractory, but the steroid-naive response rate was 20 points higher. And thus, gave us proof of concept to go ahead with GRAVITAS-301. Why is it important? Because of the sparing of JAK2, there is expected to be relatively less cytopenias. And given that these patients are steroid-naïve acute to immediately post transplant, what they're struggling with in terms of morbidity is often cytopenias in terms of low platelets, low white cells, anemias. So the steroid -- the cytopenia sparing effect should be helpful and should translate to increased success and tolerability.

Operator

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

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

One, kind of following up on Salveen, when we think about the itacitinib data in GRAVITAS-301, can you talk about what type of effect do you think you need to show to kind of justify moving an expensive therapy kind of into that front line in a more of a contract type of setting, like transplants? And is there just a response rate or is there some other aspect that we should really be focusing on to justify that?

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

Yes, thanks for the question. Again, it's Steven. Generally speaking, steroids have approximately a 40% to 50% response rate with the intended side effects, particularly when they are used over the long term, which are well known in terms of steroid side effects. So, from our point of view, a response rate that's one north of that and in absolute numbers can be quantified, but it should be higher than steroids. And then in terms of what we know in terms of tolerability, and you've got ample evidence of long-term use of ruxolitinib in MF and PV now. You know the profile is very different from long-term use of steroids. So the effect would have to be that higher response rate and a better tolerability profile that would enable people to get off the steroids, and that's what we're looking for in GRAVITAS-301 and that would be an additional clinical benefit to the actual treatment of graft-versus-host disease is the ability for patients to be weaned off the steroids.

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

Okay, great. And then just for Barry on the thing about pemigatinib and potentially launching your -- getting filed next year in cholangiocarcinoma, can you just talk about the build up that is going to need to be done, the timing of that for a commercial organization in solid tumors that doesn't really exist right now?

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

Well, we're hopeful that it will get approved as soon as possible, but we're just working on exactly the size of the team that we'll need for this patient population in cholangiocarcinoma with FGFR2 translocations. So those efforts are really ongoing, and we'll continue to update you as we get closer to an actual launch date.

Operator

Our next question is coming from Cory Kasimov from JPMorgan.

Shawn Fu ***JP Morgan Chase & Co, Research Division - Analyst***

This is Shawn on for Cory. Just a couple of questions on cholangiocarcinoma. So the updated results from ESMO looked to be quite promising. And actually, it looks like there was a significant portion of patients in whom the response took a bit longer to evolve. On your previous update, I think there was like 11 out of 45 responses versus 19 out of 47 responses at ESMO. So just kind of wondering did the kinetics of the response surprised you a bit? And as a follow up, maybe you could share with us some color around your filing plans? Is there a chance that we could potentially see a BTD and a priority review in this indication? And are those discussions currently ongoing with the FDA?

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

Shawn, it's Steven. Thank you for your questions. Yes, it's a good surprise, right? The ESMO updated data showed that centrally reviewed response rate of 40%, which is robust, and as you noted, increased with time. For reasons in one particular tumor versus others that we see that, it's not entirely clear, but obviously, the biology of that particular FGFR2-translocated cholangio is such that over time you can get increased cytoreduction. Probably a clue for that came if you look at the entire waterfall plot is the disease control rate is north of 80%. So just about everybody is having some degree of cytoreduction from the get-go and, obviously, over time those improved in a substantive way that were also really durable. So given the context, given that this is second line cholangiocarcinoma, given that chemotherapy in this setting has maybe a 10%, at a stretch 15% response rate with very short progression-free survival, we believe these results are now in the territory to meet potential regulatory approval-type data. And to further to your question, we will be discussing, of course, with the regulatory authorities does this meet breakthrough designation criteria and, as such, would it qualify for priority review? And again, we feel strongly that that's starting to look increasingly to be the case. I am focusing my comments on the FDA. We didn't

mention Europe because the route there for single arm studies is harder, but given this updated dataset, we will, obviously, be discussing these in Europe with the regulatory authorities as well, does this now meet potential regulatory approval criteria? So very encouraged by the dataset and surprised in a good way by the increase in response rate that's durable over time.

Operator

Next question is coming from Geoff Meacham from Barclays.

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

Dave, also I want to offer up some congrats on your retirement, seems like we've had this conversation before. Barry, another one on Jakafi. When you look at the GVHD opportunity, what do you think could be the initial uptake curve based on REACH1 in the unmet need? I guess, my sense is, do you think docs will want to wait ultimately until REACH2 or 3 data are fully out? And then I have one follow-up for Hervé.

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

No, Geoff. I actually think the uptake will be quite good. Obviously, you know what the patient population is. Steroid-refractory GVHD in the United States, we say it's around 1,500 patients. We think that the data we've shown so far are compelling, better than anything else, in this particular setting, able to get patients off of steroids. Obviously, these patients are very, very sick and they really need to get their GVHD under control right away, and it looks like we're able to achieve that with the profile that we have. So I am very encouraged about that opportunity. And then we're looking forward to getting approval for chronic GVHD. We think that will be a good opportunity as well. So we're looking forward to both of these indications.

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

Okay. And then Hervé, you've got a great franchise in Jakafi, which, obviously, could drive pretty robust profitability and how are you getting 0 credit for pretty much anything in the pipeline beyond what's in Phase III. So why continue to develop so many assets that are earlier stage? Do you think you'd add more value by, for example, narrowing the pipeline breadth and focusing a little bit more on profits today?

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

No. I mean, I think your question is really about our overall R&D investment. So what we believe is that the quality of the science we have here at Incyte the quality of the discovery team is now proven. I mean, we spoke about ruxolitinib and baricitinib already approved, commercially available. We are speaking of now pemigatinib, itacitinib, capmatinib. So that will be like 5 molecules that are coming from our own discovery group that have been now very close to crossing the line and showing a lot of very promising data. So it shows that R&D, done the right way, can be extremely productive. And before you have late-stage products, obviously, you have to have early-stage products, and that's why we have a portfolio of early-stage programs. We don't know yet from that portfolio, which one will be the breakthroughs that are moving very quickly, and which one may end up being more on hold. I must say in terms of investment, most of it is coming from the late-stage portfolio. So you should look at the way the investment is calibrated between early stage and late stage. What you see is that the pre-proof-of-concept programs usually have a relatively modest impact on the budget. I mean, it's a relatively smaller impact on the R&D budget. And our choice to develop these products is really based on the data and the science and the medical need and trying to improve treatment of cancer or outside of cancer. As you can see, there are now a number of fairly interesting programs we have. And I must say, the atopic derm and the vitiligo program for ruxolitinib cream, assuming we get good data from the Phase III, are going to be very productive for our corporation. So that being said, obviously, we are very cautious about our investments in R&D. And as I said in my remarks, the way we see the entire corporation evolve is increased profitability. I think Dave spoke about the profitability we have seen in this quarter, which was double what we had a year ago. And that's the trend over a period of time that you will see confirmed with the progress of our business.

Operator

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

Matthew Kelsey Harrison ***Morgan Stanley, Research Division - Executive Director***

I guess, one. Can you just comment briefly on the inventory drawdown, whether you expect that to reverse in coming quarters? Or if there was a specific driver of that drawdown this quarter? And then maybe secondly, can you just comment on what are the key issues that you're speaking with the FDA about the Phase III or atopic dermatitis with the ruxolitinib cream?

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

Okay, Matt. So I'll take the first part. No, we think this is one time. Well, inventory changes periodically. We've seen it over quarters, sometimes inventory is above the normal range that we experience, sometimes it's below the normal range, which is -- what we say is 2.5 to 3 weeks of inventory in the channel. And even if you move a couple of days one way or the other, now that's about $12 million. What's the driver of the inventory burn off this quarter? Well, we took a 3% price increase at the beginning of September. And historically, we've seen after we take a price increase that inventory does go down, but generally it's gradually over time. This was very quick and a little bit more dramatic that we saw some destocking. To be honest, even in October that's already reversed itself. We're on budget for October. We're on budget to hit the guidance that we just gave before. We're planning to deliver close to $250 million in 2018 above and beyond what we sold in 2017. So we're very confident moving forward. And I'll hand it over to Steven for the second part.

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

Matt, thanks for your question. This is Steven. They're the obvious issues, but I'll go through them. The type of things we discuss and given the proof-of-concept work we've conducted and presented already are the dosing, the need to study more than one dose or not; the number of studies that are needed in this setting in dermatology, conventionally it's at least 2 studies; the size of those studies, given that the safety databases in dermatology indications tend to be 1,000 patients or north of that; and whether or not an active comparator is needed or not in these studies. I think those are the 4 main issues. The good news is we're very close to closure on those. And we aim, as Hervé said in the call, at a minimum to get these studies going in the first quarter of '19 if not sooner. So we're in a good place. We have the right set of proof-of-concept data. We have agreement on most of these issues and we should be going soon.

Operator

Our next question is coming from Brian Abrahams from RBC.

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

Two questions on Jakafi life cycle. I guess, first off, I was wondering if you could talk a little bit more about the ongoing Jakafi combo studies? Perhaps put a finer point on the timing for upcoming readouts and maybe give us a sense for your view of the overall bar there. What you need to show from a symptomatic improvement standpoint from tolerability to warrant potential exploration here, not just in refractory patients, but in front line, as a potential Jakafi replacement? What would be acceptable in terms of additional AEs. And then I have a follow up.

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

So Brian, it's Steven. Thanks for your question. Obviously, the life cycle management of RUX itself is incredibly important to us, given that we have patent runway in the United States and beyond at least through 2027. So it's a large program with numerous efforts. You focused your question on one of them, which is combination work. We've various combinations ongoing. The one that you'll see that's currently the most encouraging to us, and you'll see data readouts on relatively soon at an upcoming meeting at the end of the year, which we already showed you a sneak preview in 10 patients at the R&D day is the ruxolitinib plus PI3-kinase program, the delta program with '50465. And in that early read we showed you in the 10 patients at the R&D day, you saw both, a further decrease in spleen volume in terms of actual reasonably objective measure of activity as well as symptom improvement. Remember, rux itself is such a fantastically successful drug that it's not easy to recruit these trials quickly and most people stay on rux for a very long time and do really well. So the additional need, beyond in terms of regulatory endpoints, aren't very clearly defined. We've been working with the FDA in the space, because we have numerous combinations ongoing, and trying to come to a very strict definition of what constitutes, if you will, "ruxolitinib failure" or "rux refractory-ness", and then put people appropriately on those studies to make sure we always have apple-to-apple comparisons across our programs and others. So they're not strictly defined yet, but we've been working very carefully to get those to you. We also have ongoing programs, just to mention, with the ruxolitinib plus our PIM inhibitor, which has really good preclinical data; and then a combination with JAK1 with itacitinib itself that's ongoing as well in patients who either can't tolerate doses of rux or have to come off it and then we have a switch strategy as well. So it's a very large combination program across all of them, with

the lead clinical evidence now for which you'll see updated data at a meeting at the end of this year is the rux plus PI3-kinase delta program, and hopefully the endpoints will be more clearly defined over time.

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

That's really helpful. And then just a follow-up to that, in terms of next-generation ruxolitinib formulations, I know you recently published data on an earlier formulation, just wondering where you are with respect to optimization? How much cytopenia reductions and/or improvement in efficacy could you potentially achieve and might need to show for payers and KOLs to support use of a next-gen once a generic rux is available?

Reid M. Huber ***Incyte Corporation - Executive VP & Chief Scientific Officer***

Brian, this is Reid. I'll take your question. You're right we did publish some data on the -- on a sustained release formulation of ruxolitinib and there's actually some intellectual property around that as well, which has recently been locked down. Those are important efforts for us and they really dovetail with the remarks that Steven just had on the combination work. In some respect, that is kind of the first line of a life cycle strategy is to try to work on a more optimized pharmacokinetic profile of ruxolitinib that's beneficial in terms of patient usage, but also potentially brings important benefits in terms of their cytopenias or even the benefits that ruxolitinib achieves in terms of spleen volume reduction and symptomatic improvement. So that's sort of the first leg. I think the combination studies that Steven outlined is the second leg. And just for completeness, the third leg is a continued strong interest in active research programs we have internally, both fully in-house and in collaboration with academic and company partners, to try to identify new targets in this space that could be approached as, frankly, to obsolete ruxolitinib one day. And so these are all 3 active efforts within Incyte that, I think, help to underscore just how significant the commitment is that we have to MPN patients.

Operator

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

Katherine Xu ***William Blair & Company L.L.C., Research Division - Co-Group Head of Biopharma Equity Research, Partner & Biotechnology Analyst***

I just have a question on pemigatinib. Can you comment on the intermittent versus continuous dosing of the drug in both cholangio and in bladder? And then are you confident in terms of efficacy that you could attain with this increase in dosing? And then on the safety side, what would you expect with this more intensified dosing mechanism? And mechanistically, understanding that these are FGFR2 or 3 driven -- mutation-driven cancers, does that make -- does it make sense to find a combo partner to further increase the efficacy in these patients?

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

Katherine, it's Steven. Thank you for your question. It's a good one. So in terms of the dose we netted out at the end of Phase II trying to weave the therapeutic ratio between efficacy and safety, we had come up with a 13.5 milligram, 2 weeks on, 1 week off, dosing regimen, which many competitors at that time were doing as well, given the tolerability profile as regards to hypophosphatemia, GI side effects, et cetera. Our cholangiocarcinoma dosing regimen, as you've seen, is the intermittent one, 13.5, 2 weeks on, 1 week off, with the efficacy we just showed at ESMO and just spoke about. In the interim, in FGFR3-mutated bladder cancer, the lead competitor there, the JNJ compound, had switched from intermittent dosing to different continuous dosing regimens and had shown incremental improvements in efficacy from the mid-20% range up to the low 40% range, and had filed earlier this year and achieved a breakthrough status and that's the way they're doing their program in bladder cancer. So what we've done in bladder cancer is switch from intermittent dosing to continuous because, again, we look like we have a similar response rate with intermittent there, and we're just beginning that continuous dosing journey and should enroll, hopefully, our study at some point next year, as Hervé said in his remarks. What we want to see from that is an incremental improvement in efficacy, like they did, in bladder cancer. Your safety question is pertinent. If you look at discontinuation rates between intermittent regimens and continuous regimens, for our competitors, they're almost double. So you can go up with over 20% discontinuation rate, where you do continuous dosing and, obviously, that will have to be watched because you want patients to stay on therapy, you want durability of responses and you have -- you want long progression-free survival. So that's the sort of therapeutic ratio you have to weave when you do this effort. And it is likely that -- same with us with continuous dosing -- that the tolerability profile may worsen slightly, although our discontinuation rates to date with caveats on low numbers are actually much lower, so that's encouraging. In terms of partners across the spectrum, obviously, at the moment we've been talking mostly about monotherapy

efforts. But as you move up to first line, particularly in bladder cancer, we may be examining efforts in combination with I-O in terms of the checkpoint blockade that may be one of the relevant areas to attend to. And as you know, we have our own PD-1 inhibitor. So that's something we'd be interested in going forward. There are, as Hervé mentioned, other FGFR potentially driven diseases and there may be a way of doing a more agnostic approach across different tumor types just like what's done with checkpoint inhibitors with MSI-high tumors for example. And that's something we're going to be exploring actively next year. So that's the status of the program, and we have all the combination partners we need internally at the moment for the efforts we want to conduct. So thank you.

Operator

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***

In the release, you specifically mentioned a positive enrollment of the GRAVITAS trial. So as we think about the enrollment as a positive indicator of potential market uptake, could you elaborate on some of the factors driving enrollment in that trial? And then as a follow-up question to that, I believe the long-term Jakafi guidance includes the smaller acute steroid-refractory indication. So as you think about the expansion of that into both chronic and steroid naïve and the broader GVHD opportunity, could you help us put some numbers around the magnitude of that potential opportunity in terms of sales as you guys currently think about it?

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

Tyler, it's Steven. I'll go first, and then hand it over to Barry. So just to mention the GRAVITAS-301 program that you referenced is with itacitinib, JAK1 inhibitor, and then you turned over the rest of question to rux. So I'll let Barry address that part. But for steroid-naïve acute, I think it's numerous factors. We've been really encouraged by the rapidity of enrollment and the enthusiasm around it. And I think it's related to the fact that there's a large unmet need in this area, with a disease that can be of high morbidity and actually high mortality at 6 months, so that, that need to address, plus now the knowledge through numerous publications that JAK inhibition is highly effective, so people want to get on to these studies and have it tested, and I think those who -- and then the global nature of the way we're conducting the study across the U.S. and Western Europe as well as some Japanese enrollment. So those are all driving very encouraging enrollment, and we're really happy to see where that is. I'll pass it over to Barry for your commercial question.

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

So Tyler I think you were asking 2 separate questions, one is the long-term guidance that we have on Jakafi, which includes acute steroid-refractory GVHD and chronic steroid-refractory GVHD as well as ET. And that brings us to the $2.5 billion to $3 billion guidance that we have given before. In terms of itacitinib, obviously it would be used mostly in what we're currently studying in treatment-naïve acute GVHD and treatment-naïve chronic GVHD and globally, so that is global product, so that is separate from our guidance on Jakafi. So globally for itacitinib, we see about 15,000 patients that would have both treatment-naïve acute GVHD and treatment-naïve chronic GVHD, and then you can do the numbers from there. And obviously, we haven't done pricing and other forecast around that, but we know what the opportunity is. It's bigger than the perhaps the steroid-refractory setting, and we'll advantage of that.

Operator

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

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

Can you talk us or walk us through kind of your thoughts regarding the data from competitors in terms of pemigatinib? And how you are viewing that data in terms of indications perspective? Whether you are actually competing in things like bladder or you think certain indications are going to be free and clear? And related to that, can you talk about the importance of Foundation Medicine companion diagnostics or companion diagnostics in general, and how that could impact your uptake?

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

It's Steven, I'll go first. I just may want to add to my comments. I think when you start getting more competitive, it's sort of validation of that you're chasing a target, although there is no approved FGFR inhibitor yet. But that's recognized as an oncogenic driver for which you have compounds that are active and you've seen activity data now in cholangiocarcinoma, which is FGFR2 translocated, FGFR3-mutated bladder. And in fact a myeloproliferative neoplasm that we're studying as well that's FGFR1-driven through an 8p11 chromosomal

translocation. And then potentially other areas, where FGFR may be a driver, but it's a little more unclear because you are often looking at amplification, rather than mutations. So in terms of talking directly about competitors, which I won't do, but it's interesting as the field is as busy as it is. It's encouraging, it's good for patients and we can learn where others are hit, and I just give you the perfect example earlier of the JNJ switch with their inhibitor from intermittent to continuous and getting that efficacy bump, which we can clearly learn from and catch up pretty quickly. So we don't view bladder as gone in any way. We think we have a superb molecule. We're going to do the continuous dosing experiment. As I said, we should finish enrollment sometime next year, and we want to be very competitive there with what we think is an excellent compound. In cholangio, our view is we're ahead of everybody else. And as we said with the dataset, we will take it to, hopefully, a regulatory filing next year. In terms of the companion diagnostic, the way it works from a regulatory point of view, is one has to have that attached to your study. We're working with the lead developer in this area, Foundation Medicine, with their tests. It's important from the regulatory's perspective in getting the study completed, done and attached to your label. From an uptake point of view, I'll make a clinical comment, and then I don't know if anybody wants to add anything in that, what happens in the real world thereafter is a bit of a mix, is that people often have local testing available through their centers under clear certification in the U.S., so other means in the rest of the world. And as long as it's done appropriately to measure either the FGFR2 translocation or FGFR3, you know they'll often go ahead and treat patients without waiting for the one that's actually per label from an uptake point of view. So -- and that's increasingly being done across the globe now in various places. And certainly, once you have a validated pathway with an approved drug, you start seeing testing become routine. So you can go back 20 years to HER2 in breast cancer, then EGFR in lung, et cetera, et cetera. So they become routine diagnostic things. So from a clinical point of view, uptake should sort of, in some way, take care of itself. I don't know if anybody else wants to make other comments?

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

All right. Then just maybe as a quick follow-up -- or a separate question for Hervé. When we think about it from a company perspective, there's this growing franchise in what appears to be nononcology and specifically dermatology. And so how should we be thinking about that going forward? Is this something that is really a focus? Is it something that could be packaged and kind of sold off and monetized? Any sort of thoughts regarding that?

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

It's a good question. And it's part of -- related to an earlier question about value creation through research and development. I think that's a very good example of a project that we have been working on, in general, now for more than 2 years of looking at non-cancer related application of the technology coming from research. So we have a group of biologists working on that and it's starting to translate into clinical programs. And these clinical programs are going in many different indications. We have, obviously, the dermatology group of indications where there are a number of projects, but we have also a program in ulcerative colitis. We have a number of pre-proof of concept small programs trying to establish these products. So as we get these proof of concepts, we will have to make decisions on doing the Phase III ourselves or to find a partner. In the case of dermatology for atopic derm, and I can say already for vitiligo, we will do the pivotal Phase III studies internally. And as we are seeing this data maturing, and as we get the result of the Phase III, that's where we will have decisions to make on how do we plan to do the commercialization for each of these products. At this stage, these decisions have not been made. You can imagine that there are differences depending maybe on the geographies also. So we are looking at it at as Asia, Europe, U.S., and we are looking at it as do we go and do it ourselves or is it better value for the corporation and the shareholders to do it with a partner. And all of this is up in the air now. We are in the process of identifying and quantifying our options to make sure we choose the one that is the most productive.

Operator

Our next question today is coming from Christopher Marai from Nomura Securities.

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

Maybe to follow up more on the topical rux. So with respect to atopic dermatitis, could you perhaps comment on the potential size of the Phase III that you're going to be required to run? And then secondarily, any other safety studies beyond the typical Phase III that will be required for that? And then secondarily on vitiligo, actually the Phase II is ongoing, is that a registration-worthy trial? And I have a follow up.

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

Yes, it's Steven. Christopher, thank you for your question. So on the size of the Phase III program for atopic dermatitis, I alluded to a little earlier, but the FDA requirements on safety are the main driver here. We need at least 1,000 patients worth of data probably across 2 studies. It could end up being slightly north of that. The good thing is these studies are relatively easy to do and really quickly, as you've just witnessed from the baricitinib atopic dermatitis program. So there's no concern there. We'll get the right sizing and get the right safety database to do that. For vitiligo, we have a very well-constructed proof-of-concept study, similar to the way we did atopic derm, with the dose ranging, the right control, et cetera. Would that suffice -- your question was, on a stand-alone for regulatory approval? It's somewhat unlikely in the derm space. You usually have to conduct the studies I just mentioned. But given that we will have a large safety database from atopic dermatitis, it's certainly something we would discuss depending on the results. But just to manage expectations, the likelihood is that we would have to conduct, as Hervé said, the vitiligo Phase III program to get it across the finish line there.

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

And then just a follow-up, thinking on about the commercialization for pemi. It's, obviously, someone else brought up outside heme/onc, and in solid tumors. I was just wondering could you remind us of the option that you have to co-promote capmatinib? And how that option to co-promote might work into plans to also commercialize -- or set up commercialization of pemi?

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

Hervé here, I will answer. On the worldwide basis, we have no intention to go in co-promotion of capmatinib at this stage. I think the contract we have with Novartis on capmatinib gives them the right to promote it. And so that's not part of the plan. I would say on hematology versus oncology, you have -- depending on the countries, you have separation of the 2 specialties or not. I mean, most of them are practicing in the same building, in the same hospital. So you can imagine that there is, from the hematology commercial organization, already synergies for launching an indication in oncology like, for example, cholangiocarcinoma if it is the first to come up. Cholangiocarcinoma is relatively rare. So it's an indication where we believe we could fairly easily be promoting it by ourselves in a way that will not involve a very large increase of our sales force. So we -- I mean, depending on other indications that would be coming after cholangiocarcinoma, I think, bladder cancer will be a specific different type of customer base. In fact in -- with some of them being in the urology department, so we will have to adjust as we go. My experience with hematology-oncology and a mix of products in both specialties over a number of countries -- a large number of countries over a number of years is that there is lot of that ways you can organize it geographically or by specialty depending on the density of your customer population. And that's probably what we will be doing.

Operator

Ladies and gentlemen, in the interest of time, we have one final question from Carter Gould from UBS.

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

Dave, congrats on your retirement. I wanted to ask on the rux program in AD. I want to understand better a little bit of the stage gates to starting some studies in pediatrics. How do you and, I guess, FDA feel about the safety profile potentially in that population? And I guess, how critical is that to how you see the value-creation opportunity in AD? And then as a follow-up, Hervé, I appreciate your comments around the relative spend coming from early-stage programs, any intention to increase your disclosures around where R&D spend is coming today?

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

Carter, I'll go first and then Hervé will take your second part. It's Steven. So the rux program, in total, will look at patients initially from 12 years of age and above, and with mild-to-moderate atopic dermatitis. And that will address the vast majority of that population. In terms of the pediatric setting, the 2- to 11-year age gap, per the definition, that is what we're discussing with the FDA at that moment. It's an area we'd like to address. We need to just work out with them what they would consider safe dosing in terms, again, of the therapeutic ratio, and that should follow thereafter. But the program should start initially in ages 12 and above and that will address most of the mild-to-moderate population with which we want to go off to with the ruxolitinib cream.

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

So on your question about R&D allocation, as you say, I think, it's an important question, in fact, because as you can see, I mean, there are a lot of aspects of what we do that is very much quantified and rational and based on our projects, and the more clarity we can give on how resources are allocated I think the better it is. So we are looking at what is the sort of the norm in our industry. So we have been looking at how other companies have been giving more clarity on the R&D allocation, and we will be considering doing some of that or all of these in the future at the time we are reporting next year.

Operator

Thank you. 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?

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

Okay, thank you, for your time today, for your questions. We look forward to seeing you at upcoming investor and medical conferences, including at ASH. 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.