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INCY - Q3 2017 Incyte Corp Earnings Call

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OVERVIEW:

Co. reported 3Q17 total revenue of $382m. Expects 2017 net loss to be $290-300m and adjusted net income to be $60-70m.

CORPORATE PARTICIPANTS

Barry P. Flannelly *Incyte Corporation - EVP and General Manager of U.S.*

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PRESENTATION

Operator

Greetings, and welcome to the Incyte Corporation Third Quarter 2017 Earnings Call. (Operator Instructions) As a reminder, this conference is being recorded. I would now like to turn the conference over to your host, Mike Booth, Vice President of Investor Relations. Please go ahead.

Michael Booth - *Incyte Corporation - VP of IR*

Thank you, Diego. Good morning, and welcome to Incyte's Third Quarter 2017 Earnings Conference Call and Webcast. The slides used today are available for download on the Investor section of incyte.com. And I'm joined on the call today by Hervé, Barry, Steven and Dave and Reid.

We would like to remind you that some of the statements made during the call today are forward-looking statements, including statements regarding our expectations for 2017 guidance, the commercialization of our products and our development plans for the compounds in our pipeline as well as the development plans for 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, 2017, and from time to time in our other SEC documents.

I'd now like to pass the call to Hervé for his introductory remarks.

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

Thank you, Mike, and good morning, everyone. So I'm very pleased to report another very successful quarter at Incyte with dynamic revenue growth driven by sales of both Jakafi and Iclusig and with significant progress in multiple places in our clinical development portfolio.

So let's begin with Q3 revenues. So you can see on Slide 5 remarkable growth in product-related revenue over the past 5 years, so that's revenue without the milestones, which has seen a compounded annual growth rate of more than 50%. 5 years ago, Incyte's product-related revenue was made of Jakafi sales and Jakavi royalties in myelofibrosis, and we have come a long way since then. Jakafi sales and royalties remain a key component of our revenue growth, and Iclusig sales and Olumiant royalties are now adding to it. We believe Incyte is in a unique position, combining strong revenue growth with a cutting-edge portfolio of projects at every stage of development.

And I will now spend a few minutes in our late-stage development portfolio.

So Slide 6 summarizes late-stage projects and the indications being pursued. Pivotal program for ruxolitinib is open in both steroid-refractory GVHD and essential thrombocythemia, and itacitinib is also in a pivotal program for GVHD. Recruitment is proceeding well in our 2 key FGFR trials, and our PI3 kinase-delta program is also moving forward where we are opening trials in 4 different non-Hodgkin lymphomas. And of course, the ECHO program for epacadostat continues to progress, and we are looking forward to the results of the pivotal ECHO-301 trial in melanoma expected in the first half of 2018.

I believe that over the next 5 years, these 5 late-stage product candidates have the potential to further accelerate our revenue growth, and we look forward to reporting on future developments.

So on Slide 7, you see our leadership position in immuno-oncology is driven by our roots in immunology research, and we consider our ongoing epacadostat plus PD-1 collaboration to be only the beginning for us in this field. Our discovery and development teams now have many candidates in the clinic to explore the I/O space, such as IDO1, obviously, arginase, JAK1, bromodomain and PI3 kinase delta inhibitors as well as our GITR and OX40 agonist.

We have recently announced 2 new collaborations that we believe will serve to further enhance our immuno-oncology portfolio, and I'll touch on this on Slide 8 and 9.

On Slide 8, you can see that we have agreed with AstraZeneca to expand our existing clinical collaboration and move into Phase III development in a trial which will study epacadostat plus durvalumab in patients with non-small cell lung cancer. This study builds on AstraZeneca's recent success in the PACIFIC study, and the objective of the study is to establish a new standard of care in the same patient population as was studied in PACIFIC. We will share the cost of the trial with AstraZeneca, and the trial is expected to begin in the first half of next year.

We are also excited to announce last week that we have entered into a global collaboration and license agreement with MacroGenics for its PD-1 antagonist MGA012, which is already in the clinic. Under the agreement, Incyte will hold exclusive worldwide development and commercialization rights in all indications, and Incyte will record all global sales for the compound. As you can see here on Slide 9, we have a total of 7 in-house assets today that have the potential to be combined with the PD-1 antagonist and are currently in a Phase I PD-1 combination trial, and we intend to proceed into combination trials with 012 as soon as possible. Yet, what is different about this collaboration is that the agreement also grants MacroGenics the right to develop 012 in combination with its own pipeline, and we believe that this innovative collaboration structure with MacroGenics provides us with significant optionality and may increase the compound's commercial potential.

Now on Slide 10. Drug discovery remains central at Incyte, and we have successfully added 2 large molecule discovery alliances to our small molecule expertise, one for monoclonals and one for a bispecific antibodies. These 3 platforms are expected to enable us to go after a multitude of future targets. We have 5 late-stage programs within our development portfolio. And in readiness for what could potentially be a good number of new product and new indication approvals, we'll now have an operation in the U.S., Europe and Japan as we continue to build Incyte into a world-class biopharmaceutical company.

As part of this process, we're also very pleased to have Jackie Fouse join our Board of Directors. Jackie has extensive experience in oncology and in the biopharma field, and she will be a wonderful addition to our team.

With that, I'll pass the call to Barry for an update on Jakafi.

Barry P. Flannelly - *Incyte Corporation - EVP and General Manager of U.S.*

Thank you, Hervé, and good morning, everyone. Jakafi net sales were strong in Q3 of 2017 at $304 million, a 36% increase over Q3 2016 and a 10% increase over the second quarter of this year. Jakafi's performance in the quarter was driven by strong patient demand for both indications. We believe this demonstrates that our approach of educating physicians on the benefits of intervening early with Jakafi therapy and supporting patients through our educational and awareness initiatives continues to be very effective.

We did see that -- we did see some inventory build in Q3, which is now slightly above the high end of our typical range of 2.5 to 3 weeks. In dollar amounts, this inventory represents approximately $5 million of net sales.

As a result of our strong sales growth, we are revising our full year 2017 net product revenue guidance for Jakafi from a range of $1.090 billion to $1.120 billion to a new range of $1.125 billion to $1.135 billion.

I'd like to take a moment to remind everyone of the long-term revenue potential of Jakafi beyond MF and PV. Jakafi also has the potential to benefit patients with graft-versus-host disease, an underserved community of patients who may have been cured of their cancer by a stem cell transplant only to suffer a side effect of that treatment resulting in GVHD. Data from REACH1 in steroid-refractory acute GVHD are expected in the first half of next year. And if the results are positive, we expect to be able to file a sNDA for Jakafi in this indication in 2018.

We have also opened a pivotal study in patients with essential thrombocythemia. Jakafi has already transformed the lives of thousands of patients with MPNs, and we continue to work with doctors, patients, patient advocacy groups and the FDA to further expand access to those who may be able to benefit from this treatment.

With that, I'll pass along the call to Steven for a clinical update.

Steven H. Stein - *Incyte Corporation - Chief Medical Officer and SVP*

Thanks, Barry, and good morning, everyone. On Slide 15, I'd like to start by reminding you of the scope of our current pivotal program with epacadostat. As you are all aware, ECHO-301 is ongoing in patients with unresectable or metastatic melanoma. The trial has completed enrollment, and we are now waiting for events to accrue. We remain on track to announce results in the first half of 2018.

Earlier this year, we announced that we would be expanding the epacadostat program to include pivotal trials in 4 additional tumor types in combination with either Merck's pembro or Bristol's nivo. These studies are all on track to begin enrollment by the end of 2017.

As Hervé mentioned, we were pleased to announce that we are expanding further with a pivotal study in combination with AstraZeneca's durva in patients with stage 3 non-small cell lung cancer.

Our clinical development team, along with our partners at Merck and Bristol, are working hard to initiate the additional trials of epacadostat in combination with either pembro or nivo. The details of the renal and both lung studies with pembro are now available on ct.gov (clinicaltrials.gov), and we've summarized the trial schema for these studies on this slide, Slide 16. All 3 trials will be conducted in patients that are treatment naïve for their advanced disease.

ECHO-302 will study the combination of epacadostat in pembro in patients with renal cell carcinoma versus standard of care, in this case, either Sutent or Votrient in a simple 2-arm design.

ECHO-305 will study the combination of epacadostat and pembro in patients with PD-L1 high-expression lung cancer versus pembro monotherapy. Pembro monotherapy is the care standard in this population.

ECHO-306 will evaluate patients with lung cancer, irrespective of their PD-L1 status. The evolving care standard in this population is pembro plus platinum doublet chemotherapy. And therefore, this is used as the comparator arm.

We are also taking the opportunity in this study to investigate the possibility of a chemotherapy-free combination. And so we are not only including a triplet arm of epacadostat plus pembro plus chemotherapy, but also a third arm of epacadostat plus pembro. The co-primary endpoints for all 3 trials will be progression-free survival and overall survival.

Next, I'd like to spend a few minutes speaking about our other immuno-oncology assets and the significant progress we are making here. Our GITR agonist, '1876, and our OX40 agonist, '1949, have both completed dose escalation. Each of these candidates is now moving ahead in multiple combination cohorts.

'1876 is in combination with epacadostat and pembro and separately in combinations with nivo monotherapy or nivo plus ipi.

'1949 is currently progressing into combinations with either nivo monotherapy or nivo plus ipi.

Our first-in-class arginase inhibitor, '1158, is continuing with dose escalation and has recently moved into combination studies with pembro. We also plan to evaluate '1158 in both epacadostat and chemotherapy-based combinations.

On Slide 18, outside of immuno-oncology, we have what we believe is an exciting portfolio of targeted therapies. Over the last year, we have put together a broad program to study the effects of JAK inhibition for patients suffering from graft-versus-host disease. The program spans both acute and chronic graft-versus-host disease and will also evaluate various other treatment settings, such as prophylaxis for the condition, patients that are treatment-naïve and patients that are steroid-refractory.

The first pivotal trial of ruxolitinib in graft-versus-host disease, REACH1, is evaluating ruxolitinib in patients with steroid-refractory acute graft-versus-host disease and is expected to read out next year.

The GRAVITAS-301 study was recently initiated and will evaluate itacitinib in patients with treatment-naïve acute graft-versus-host disease.

On Slide 19, I'd like to cover our other 2 late-stage assets. Our selective FGFR1/2/3 inhibitor, '54828, is being evaluated in 2 key programs, one in metastatic bladder cancer and the other in cholangiocarcinoma. These studies are recruiting well.

Our highly selective PI3 kinase delta inhibitor, '50465, is being studied in a broad program which includes trials for a number of non-Hodgkin lymphomas. Our program is additionally investigating dose and scheduling to maintain efficacy while hopefully ameliorating toxicity.

On Slide 20, I'll discuss some highlights from our upcoming news flow. As I've already mentioned, the additional Phase III studies with pembro and nivo are on track to begin by the end of this year. Also expected by the end of this year will be the first-in-man data from our lead BRD inhibitor, which will highlight the data we used to determine to prioritize development of '57643 over '54329. First-in-man data from our PIM inhibitor, '53914, is also expected later this year.

Heading into the first half of 2018, we are looking forward to the results of the ECHO-301 study as well as the results from REACH1, our pivotal study of rux in patients with steroid-refractory acute graft-versus-host disease.

Lastly and following the new go-forward decision with AstraZeneca, we expect to initiate a Phase III study of epacadostat in combination with durva for the treatment of lung cancer patients in the first half of 2018.

We've made significant advances in the clinic so far in 2017, and we have ambitious goals as we head into next year. We look forward to keeping you updated on our progress.

With that, I'll pass the call to Dave for the financial update.

David W. Gryska - *Incyte Corporation - CFO and EVP*

Thanks, Steven, and good morning, everyone. Our financial performance for the third quarter was very strong. We recorded $382 million of total revenue. This was comprised of $304 million in Jakafi net product revenue, $18 million in Iclusig net product revenue, $41 million in Jakavi royalties from Novartis and $3 million of Olumiant royalties from Lilly. In addition, we recorded a $15 million milestone related to the approval of Olumiant in Japan as contract revenue.

Jakafi's net product revenue of $304 million represents 36% growth over the same period last year. Based on Jakafi's performance for the first 9 months of the year, we are increasing our full year Jakafi net product revenue guidance to a range of $1.125 billion to $1.135 billion.

Our gross to net adjustment for the third quarter was approximately 12%. We expect that the total gross to net adjustment for the full year to be approximately 13%.

Our cost of product revenue for the quarter was $22 million. This includes the cost of goods sold for Jakafi and Iclusig, the payment of royalties to Novartis on U.S. Jakafi net sales and the amortization of acquired product rights related to the Iclusig product acquisition in Europe.

Our R&D expense for the quarter was $270 million, including $23 million in noncash stock compensation and a $12 million in-process research and development asset impairment charge due to the discontinuation of Iclusig second-line CML trial that began prior to the acquisition of the European ARIAD operations in 2016. The remaining increase in R&D expense over the previous quarter was driven by continued progress on epacadostat Phase III studies, the advancement of ruxolitinib GVHD studies and the expansion of studies in our large molecule programs. For the full year, we expect R&D expense to be in the range of $1.250 billion to $1.3 billion, of which approximately $360 million is related to the amended Agenus collaboration and the Merus, Calithera and MacroGenics collaborations. The increase in R&D expense guidance over the prior quarter is primarily related to the $150 million upfront payment under the recently announced license agreement with MacroGenics.

Our SG&A expense for the quarter was $91 million, including $12 million in nonstock cash compensation.

We recorded a $16 million net benefit related to the change in the fair market value of the contingent consideration for the Iclusig royalty liability. This net benefit included $8 million of recurring expense related to the change in the fair market value of the contingent consideration for the Iclusig royalty liability and a $24 million benefit related to the discontinued Iclusig second-line CML trial, as previously mentioned. As a result, we expect full year expense related to the change in fair market value contingent consideration for the Iclusig royalty liability to be in the range of $5 million to $7 million. This is a decrease in expense from the previous guidance last quarter.

Moving on to nonoperating expenses. We recorded a $23 million unrealized gain on our long-term investments in Merus and Agenus during the quarter.

Looking at the balance sheet. We ended the third quarter with $1.3 billion in cash and marketable securities and expect to end the year with over $1.1 billion. The increase in cash and marketable securities compared to the prior quarter is primarily related to the recent public offering of approximately 5 million shares of our common stock, resulting in net proceeds for the company of approximately $650 million.

On the final slide, you'll see our full-year guidance. Incorporating all the previously discussed changes, we now expect a net loss between $290 million and $300 million for the year. Subtracting the upfront and milestone expenses of approximately $360 million related to the amended Agenus collaboration and the Merus, Calithera and MacroGenics collaborations, our forecasted results for the full year 2017 would be net income of $60 million to $70 million.

To summarize, we are very pleased with our third quarter performance. We exceeded $1 billion in total revenue year-to-date. Our clinical development programs are advancing as planned. We continue to add to our development pipeline, and we have a strong balance sheet to support our continued growth for the long term.

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

QUESTIONS AND ANSWERS

Operator

(Operator Instructions) Our first question comes from Cory Kasimov with JPMorgan Chase & Co.

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

So I have 2 for you. I guess the first is probably for Steven, and it's on the overall strategy for epacadostat in lung cancer now that you've added durvalumab to pembro and nivo in terms of advancing to Phase III, and each seemed to be going after different segments or combinations in the market. And maybe specifically on this front, as it relates to ECHO-306, do you have evidence of additive effects for IDO when added to a PD-1 chemo combo? And then I have one follow-up.

Steven H. Stein - *Incyte Corporation - Chief Medical Officer and SVP*

Cory, hi it's Steven. Thank you for your question. So obviously, as you well know and others, too, lung cancer incorporates many different settings and different histologies as well. The whole premise behind immunotherapy has always pointed to the fact that its maximum benefit may be in areas of low disease burden or even in the adjuvant setting where you have maybe potentially micrometastatic disease to beat. So our studies encompass the high-expressing PD-L1 population in combination with pembro monotherapy, which is the care standard there. In the low-expressing settings, the chemotherapy combination with pembro is felt to be the care standard. Despite what happened last week with Merck withdrawing the application in Europe based on KEYNOTE-021G subgroup, we've always felt that the KEYNOTE-189 data was going to be the gating event. That data will report out way before our study finishes. And so we obviously incorporate in a Phase III study in combination there but also exploring a chemotherapy-free option as well. So there're 3 arms in that particular study. If you're asking me, do we have efficacy data in combination with chemotherapy that has enabled us, we have ongoing work looking primarily at the safety with chemotherapy combinations. And no -- and we have not presented efficacy data with that particular combination yet. In the adjuvant to early setting, the stage 3 non-small cell lung cancer setting building on PACIFIC data, which is post-chemotherapy radiation combination therapy for patients who are either in a complete remission, partial remission or stable disease, obviously, the durva data in PACIFIC was highly encouraging for a progression-free survival/ disease-free survival benefit. And this is again where immunotherapy, as I said upfront, is felt to potentially work best. And that is what we exploring there - the combination versus durva alone. Overarching everything that I'm saying is that our tolerability profile, as you know - we've presented now on a number of occasions with exposure data that now exceeds a year- we're very comfortable in our tolerability profile. And again, should there be the efficacy we want then the adjuvant setting would be a real win to have that sort of tolerability profile. That's our current strategy across lung cancer. We have not yet announced our BMS plans publicly.

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

Okay. And then the second question is for probably Hervé or maybe Steven as well. Can you just discuss the strategic thinking behind the MacroGenics collaboration for their PD-1 inhibitor? What was the primary driving force behind doing this deal?

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

Okay. So maybe a step back on the immuno-oncology. What we have seen over the past few years is really the establishment of single-agent PD-1 in multiple indications across multiple tumor types across many different companies, in fact. And that has been very steady. It has been making progress over more or less the past 5 years. If you remember, CTLA-4 was the first mechanism and then PD-1 more or less took the position of being the single-agent leader in multiple indications. What we believe, and that's shared by many, many people, is that the next wave, the next frontier for everybody is how do we establish IO/IO combinations either with or without chemotherapy, by the way. But how do we find a good combination that will improve the profile of PD-1 alone? We know in that field, the only existing combination is CTLA-4 and PD-1. And obviously, with our epacadostat PD-1, we are also trying to establish that across a number of indications. So what we see in front of us is a new effort, a new wave of clinical tests that will be trying to establish combinations of PD-1 plus other product. And as you saw on the slide we showed a little bit earlier, we have 7 of them already in the clinic. It includes very different hypotheses from the scientific standpoint. So some of them are large molecules, like GITR and OX40. Some of them are small molecules like arginase, JAK, PI3 kinase delta, epacadostat. And what we were looking at is saying as we are backing into this new wave of studies, what we would like is to be able to do it with our own PD-1. We have ongoing studies with pembro and nivo with all of these products. And with this deal, what we will be able to do is initiate in 2018 combination study with each of these 7 mechanisms. And then based on what we learn from the biology and the existing data, we'll be able to move this program to the next step of pivotal study after we have established that. So what it gives us is flexibility. It gives us speed. In fact, there's an economic benefit of doing it with your own PD-1 and it could potentially also be beneficial -- in fact, it certainly will be beneficial to the top line by having an additional product to our portfolio and amortizing the cost of development across 2 products instead of 1. So that was what was driving us. It's not very different from what we discussed over the past 2 years. But this opportunity came up, and we think it's a good product and we will be able to move quickly to combination trial in '18.

Operator

Our next question comes from Geoff Meacham with Barclays.

Geoffrey Meacham - *Barclays PLC, Research Division - MD and Senior Research Analyst*

I have a couple, I think, for either Steve or Reid. So the first one is on epacadostat. I know small numbers based on your Phase II, but I want to get your perspective on the opportunity in PD-L1 negative patients or minimal expressors, especially as you ramp up Phase III combo studies outside of melanoma. And then on rux in GVHD, I know data coming up next year for REACH1, but maybe what would you point to in doing this indication as a clinically meaningful result, either response rate or duration of response? And how is this different between the chronic and the acute setting?

Steven H. Stein - *Incyte Corporation - Chief Medical Officer and SVP*

Geoff, it's Steven, thanks for your question. In terms of your question related to epacadostat and our Phase II data in both PD-L1 positive patients and PD-L1 negative -- and again, we need to be careful in general in terms of which test we're using, whether it's Merck or BMS, and what cutoffs we're using. So that's just as a general caveat. Obviously, to date, we have presented data in both those populations across multiple tumors. We have some intriguing albeit low numbers to date responses in PD-L1 negatives. And we have PD-L1 unknown data, which may include both. And so I think the jury is still out on whether we'll be able to further enhance the effect in low expressors in PD-L1 negatives and get T cells to do what they need to do there. But that's being tested across the programs, including, as you said, in melanoma where there's no selection upfront. There's merely stratification after the fact. And we expect the vast majority of patients with melanoma to be PD-L1 high or positive. In lung cancer, as we've outlined in the things we put out publicly to date, there's selection upfront in both those populations. And the question being answered at least in the ECHO-306 is also in combination with chemotherapy. But all we can point to, to date is the data we've shown publicly with some intriguing responses in the negatives. In terms of rux in graft-versus-host disease and across the populations, it's a little bit different for acute versus chronic in terms of what's considered clinically meaningful benefit as well as regulatory benefit. But for REACH1, there's an established primary endpoint of a day 28 response rate, which is defined by -- internationally defined bone marrow criteria, which will look at that response data. But it has to be coupled with durability of response as well. So in the shorter settings, in the acute setting, you look, for example, at 3-month durability of

response data coupled with the primary day 28 response rates. In the chronic setting, you look a little bit further out upwards of 6 months. And it's really the combination of both response as well as the duration of response for both those settings.

Operator

Our next question comes from Eric Schmidt with Cowen and Company.

Eric Schmidt - *Cowen and Company, LLC, Research Division - MD and Senior Research Analyst*

Maybe another one for Steven. It seems like there's increased interest in moving I/O into the adjuvant setting, and I'm wondering if it's too early to talk about epacadostat in such a role and whether you're planning such trials.

Steven H. Stein - *Incyte Corporation - Chief Medical Officer and SVP*

Yes. Eric, it's Steven. As I said upfront, in the adjuvant setting, what you're doing in those patients in that population is treating potential disease that you can't see, so micrometastatic disease, to try and increase cure rates. In those settings, it's where, in general, immunotherapy-based approaches are felt to be potentially most beneficial. So you see now reported out adjuvant melanoma studies with different checkpoint and checkpoint plus CTLA-4 combinations showing benefit already. So the next thing to do is in melanoma, if the ECHO-301 data points to it, is to test epacadostat in combination with checkpoint in adjuvant melanoma. And what you're seeing us doing in the lung cancer setting is trying to build on the durva data in a stage 3 non-small cell lung cancer setting, which is a much higher risk for relapse. So many of those patients untreated unfortunately will relapse. And you saw the very impressive progression-free and disease-free survival data with durva and now looking at the combination with epacadostat to see if we can further enhance that. And then I'll end by the comment I made earlier. Tolerability is key in an adjuvant population. These patients who are otherwise well, want to get on with their lives and don't, for the most part, want to suffer if they can avoid it any debilitating side effects. So our tolerability profile here is encouraging. Obviously, it has to be coupled with an efficacy win as well.

Operator

Our next question comes from Salveen Richter with Goldman Sachs.

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

With regard to the pipeline, can you provide us with the clinical rationale here for this JAK1 plus osimertinib combination study? And then when should we expect the pivotal FIGHT and CITADEL programs to read out?

Steven H. Stein - *Incyte Corporation - Chief Medical Officer and SVP*

So It's Steven. I'll start. If you look at EGFR inhibitor therapy in lung cancer in general and now this -- the newer generation EGFR inhibitors like osimertinib with their enhanced efficacy post-upfront EGFR therapy and potentially in earlier line setting, one of the potential mechanisms of resistance is up-regulation of the JAK-STAT pathway during therapy with those EGFR inhibitors. So it's looking at the addition of JAK to osimertinib in that setting to see if we can avert the development of resistance and thus improve clinical outcomes, namely time to event outcomes. I think your second question was related to timelines to pivotal data from the CITADEL and the FIGHT programs, is that correct? I'll address that and then you can correct me afterwards. So those are underway at the moment. The FIGHT program is our FGFR 1/2/3 inhibitor looking at 3 different settings, metastatic bladder cancer, cholangiocarcinoma and a rare myeloproliferative neoplasm. All of those entities are driven by genetic mutations involving the FGFR pathway that are oncogenic and felt to drive those diseases. In the bladder setting, it's FGFR3. In cholangio, it's FGFR1. And then the myeloproliferative neoplasm, it's an 8p11 translocation. Those studies are ongoing. They're enrolling really, really well. Despite needing genetic selection, we've been really encouraged by the enrollment. And we should be getting data over the ensuing 24 months. For the CITADEL program

in general, that's our PI3 kinase delta inhibitor across different non-Hodgkin lymphomas, diffuse large B-cell, mantle, marginal and follicular lymphomas. That program is looking at trying to avert toxicity by changing dosing schedule over time. And that is also -- we'll be enrolling patients over the ensuing 24 months. So it's a little early to speak about when we will be seeing pivotal data on those.

Operator

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

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

Specifically, I want to ask about the Phase III ECHO-301 primary analysis. Is it going to be done in all-comers or PD-L1 positive melanoma patients only? And then maybe another one for Steve. Have you guys enrolled any patients with stage 3 non-small cell lung cancer in the ECHO-203 trial in combination with durvalumab?

Steven H. Stein - *Incyte Corporation - Chief Medical Officer and SVP*

Ying, it's Steven. The Phase III ECHO-301 melanoma study is in all-comers. There is stratification for PD-L1 status. So PD-L1 positive and negative is captured upfront, and they'll be balanced between the treatment arms for each of those groups. So both the standard of care arm of pembro and the experimental arm of pembro plus epacadostat will have the same representation proportionally of PD-L1 positives and negatives. So again, just to be clear, it's a stratification factor, but the primary analysis is in everybody. In terms of stage 3 non-small cell lung cancer patients in the program to date, no, we have not enrolled those sorts of patients because of their potential curative nature to date. So our program is focused to date on latter stage patients.

Operator

Our next question comes from Brian Abrahams with RBC Capital markets.

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

A couple of questions on the epacadostat-pembro lung cancer Phase III designs. I guess, I'm just wondering if you could talk about any potential dose ranging you might need to do for the chemo study for the epacadostat PD-1 chemo arm whether you're looking for superiority or non-inferiority for the chemo-free checkpoint IDO arm versus the checkpoint chemo arm. Which epacadostat arm would need to hit to constitute success of that study? And then if you might be able to give us any sense of timelines for potential interim or full data from those recently announced non-small cell lung cancer programs.

Steven H. Stein - *Incyte Corporation - Chief Medical Officer and SVP*

So Brian, it's Steven. I'll try and answer all 4 of your questions. So the enabling safety work for the chemotherapy combinations has been going on in the background for months now. The intent is not to have to change dosing at all and use our Phase III doses that we have been using across the program and the ones we have announced to date, all at 100 milligrams b.i.d. So as long as safety stands up to what it's been to date, that's the dose we'll be using in the announced programs, for which we have greater than 80% to 90% inhibition of the enzyme, which we've shown in our Phase I data. Your question 2, all the analyses are superiority in the announced programs to date. All the comparisons are superiority comparisons. There is no non-inferiority comparison in anything we've announced to date. In terms of success, the study is all undertaken with equipoise upfront, looking at a standard of care and then comparator, either one or in the other announced study, ECHO-306, 2 different comparator arms, both looking at superiority. Success will be hitting the endpoint in terms of efficacy that is clinically meaningful and statistically significant for any of those arms, either the chemo-containing or the chemo-free one. And I think in terms of timelines down the pike, it's really too early given that the

studies haven't initiated. The aims on the publicly announced ones in terms of the enrollment numbers are there for you on ct.gov (clinicaltrials.gov). And we hope we have the success we had with the melanoma study already in terms of enrollment. And then we'll be waiting for the endpoints. And then -- so you can do your own calculations there in terms of when we may see it, and I think those were all 4 of your questions.

Operator

Our next question comes from Alethia Young with Credit Suisse.

Alethia Young - *Crédit Suisse AG, Research Division - Research Analyst*

One, just around the trends you're seeing now that the NCCN Guidelines have changed for PV and just kind of wanted to see kind of how -- do you feel like you're kind of in the midpoint of the education process? Or is there still sufficiently more wood to chop? And the last one is just philosophically on CTLA-4. Do you think there's a need for better CTLA-4? Or is that something you're interested in, in future I/O combinations?

Barry P. Flannelly - *Incyte Corporation - EVP and General Manager of U.S.*

Okay. Alethia, this is Barry. I'll take the first part of your question about the NCCN Guidelines in PV. We continue to grow very nicely in PV. The NCCN Guidelines obviously helped, as we said before, that PV total patients continue to grow faster than MF total patient growth, but both MF and PV total patients continue to grow. The education process continues for PV, but we think it's going very well, and we continue to penetrate the available patient population.

Reid M. Huber - *Incyte Corporation - Chief Scientific Officer and EVP*

Alethia, this is Reid. I'll take your question on CTLA-4. I think, obviously, with the first-in-class mechanism really that established immune therapy and serves as the foundation for the wave that we're in right now, it's fundamentally limited by its systemic tolerability profile. But clearly, it's an efficacious agent. And when added to backbone checkpoint inhibitor therapy like PD-1, access blockade can be highly active and unfortunately also highly toxic, at least for some patients with irreversible inflammatory conditions. So it's important, I think, for the field that we try to learn from that experience with CTLA-4, and that can come from a few different directions. One is understanding the importance of selecting targets that have a mechanism of action that's constrained to the tumor microenvironment and not necessarily systemically acting drugs. And I think we've seen now a wave of new mechanisms coming into the clinic, which are designed to do just that. Certainly, epacadostat and IDO1 inhibition is one of those mechanisms, but there's many others in our pipeline and in others. I think there's another question as to whether or not we can be better at constraining CTLA-4 activity to the tumor microenvironment through other approaches. Bristol is taking a few different approaches, such as enhancing effector function of the antibody, trying to mask activity and release it only in the tumor microenvironment through another technology within CytomX. There may be bispecific approaches to CTLA-4 that could be interesting as well. There's still a lot we don't know about the basics of why CTLA-4 is active in one cell type it's active in and why its systemic toxicities are the way they are. But I think a lot of these approaches are going to design to determine whether there could be a better CTLA-4 antibody and one that still contains its tumor-directed efficacy but avoids the systemic toxicity. So it's a work in progress, but it's absolutely an important one for the field to continue to study.

Operator

Our next question comes from Ian Somaiya with BMO Capital Markets.

Ian Somaiya - *BMO Capital Markets Equity Research - Analyst*

Two questions. First on just the MacroGenics PD-1. I'm just trying to understand what the larger goal is. Just given the ongoing studies with PD-1s, whether it's pembro, OPDIVO or now with durva with epacadostat, your goal is obviously to establish a new standard of care, which would also

make it more challenging for you to be able to succeed in those settings with the MacroGenics PD-1. And I guess, what I'm trying to understand is, is the goal of the MacroGenics deal to establish simply new triplets? Is that where we should -- how we should be thinking about the future development? And then I have a question on Jakafi.

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

Okay, let me try to answer the question about PD-1. Epacadostat is not the key driver of the PD-1 agreement. I know it sounds a little bizarre because, obviously, epacadostat will be a potential beneficiary of this, having our own PD-1 in the long run. But the way we were thinking was more the other 6 products we have currently in Phase I combination trial with pembro and nivo and how to make that clinical development faster, economically easier and potentially giving us the economic benefit of having our own PD-1. So that was really -- the key driver was not to have some sort of short-term epacadostat impact but to have an impact on the other 6 products we are now moving through the process. And that could be done by starting the safety studies in 2018. And then where we feel we have information to move forward, we will be able then to get each of these projects moving forward. Concerning epacadostat, obviously, someday there could be a benefit of having our own PD-1. There are 2 scenarios. One of them is that pembro and nivo and durva plus epacadostat are established standard of care in multiple indications. So that would be one where the question is can we do it with our own PD-1 also. But there is something that probably has a far higher probability of success is that we will be also moving through triplets as you were describing, where as we are identifying other combinations that include epacadostat and potentially some of our other products, we will be able to do it with our own PD-1. So there is a strategic aspect, there is a tactical, clinical development aspect, and there is a commercial aspect. And that's why I think it's very important for us to have this product in our own portfolio.

Ian Somaiya - *BMO Capital Markets Equity Research - Analyst*

Okay. That's very helpful. And the other question I had on Jakafi and maybe one I've asked before, can you just speak to the line expansion? The investor base -- investors generally are obviously focused -- more focused on company's lead assets and the sustainability of that revenue stream. We appreciate, obviously, lack of near-term competition or any sort of visible competition. But just if you could speak to how you can maintain this revenue stream, what line extension opportunities you're working on and is there any timeline which you could share.

Barry P. Flannelly - *Incyte Corporation - EVP and General Manager of U.S.*

Ian, it's Barry. So I'll just try to expand. So I think we've said before -- we certainly said before that we'll exceed $2 billion in total revenue for Jakafi mostly just with MF and PV and adding in GVHD. When we talk about GVHD as a line extension, we're really talking about acute and chronic GVHD together, right? And then obviously, we have essential thrombocythemia. But we really think the drivers continue to be myelofibrosis and polycythemia vera patients and then add-ons are acute and chronic GVHD and essential thrombocythemia.

Ian Somaiya - *BMO Capital Markets Equity Research - Analyst*

Well, Barry, I guess, how do you replace Jakafi when...

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

Yes, so let me -- and maybe you can -- Reid can help on the mechanism, but we have like basically 2 phases of development where we are trying to improve over Jakafi for both MF and PV and maybe potentially some of the other indications. One of them is working on a combination of mechanisms, and this is already in the clinic where we are testing combination with delta. We are testing some alternative schedule of JAK. A lot of that is already ongoing. On top of that, we are also looking at new mechanisms that could be helping patients with MF and PV, and maybe Reid can speak about some of these collaborations.

Reid M. Huber - *Incyte Corporation - Chief Scientific Officer and EVP*

Yes. Ian, this is Reid. I think it's an important area for us to continue to innovate in. We're very proud of the efforts that we've done in the MPN space and I think have brought a very important therapy now to patients. But there still are patients that unfortunately don't receive an optimized benefit from the available therapies. And there's still other aspects of benefit that we may be able to achieve with new approaches, new combinations, new therapies. So this is an active subject of research here. Hervé mentioned the doublet studies in myelofibrosis. I'll remind you that really the selection of targets like PIM, delta, BRD and even LSD1 were in part because of their potential activity downstream of the JAK-STAT pathway. And in fact, for every one of those mechanisms I just mentioned, there exists preclinical or translational correlative data that support their potential utility in combination with ruxolitinib. So that will be something that Steven's group will be executing on over the coming months and several years. The delta study is already ongoing. Beyond that, it's an active area of research within Incyte as to how we think differently about myelofibrosis, what do we think about new targets, how do we think about achieving different types of benefit in patients. And that's a very early stage research effort, but it's one that's very important for us to maintain if we're going to continue to have a leadership position in MPNs and continue to drive patient benefits forward. So that's a longer-term endeavor, but it's absolutely one that we, as a company, are very committed to.

Operator

Our next question comes from Katherine Xu with William Blair & Company.

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

If you could indulge me with three questions. Number one is on the Flexus feud. I'm just wondering whether you could give us an overview and your strategy there and potential scenarios that we could expect. Number two is on the ECHO-302, -305 and -306 studies. I'm just curious about your rationale and basis for designing those studies in terms of powering and others, in particular just based on the evidence that we have so far and then just what gives you the confidence about those designs. And number three, assuming -301 is positive, epacadostat and pembro become the standard of care, what is the next step that you are thinking about taking to take the frontline melanoma cure to a higher level?

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

So let me start with Flexus, it will be short, but there are obviously public documents that are available. We had press coverage, which was surprising, coming last -- in the last days or last week we were -- I'm not sure exactly why it came at that point, but we cannot comment further. So I think the best is to refer to the existing publicly available documents.

Steven H. Stein - *Incyte Corporation - Chief Medical Officer and SVP*

And then Katherine, in terms of your second and third question. Your second one mentions ECHO-302, -305 and -306. The renal cell study is looking at a combination of PD-1 plus IDO, beating the current care standard of a VEGF inhibitor based, tyrosine kinase inhibitor, so either Sutent or Votrient. We needed to execute that study briskly because it's an evolving care standard there. We have data from our own program in combination with Merck in ECHO-202 that's already been presented that enabled that decision to be made. In terms of ECHO-305 and ECHO-306, the lung cancer studies, again, the enabling data comes from ECHO-202's lung program in general. It's the PD-L1 high. And again, looking at the combo versus PD-1 alone in the high expressors and then in the all-comers are looking at the care standard of triplet-based therapy -- excuse me, PD-1 plus chemotherapy and then comparing the triplet, PD-1 plus IDO plus chemo, versus PD-1 plus IDO alone. The somewhat controversial area there is the withdrawal in Europe of that application, but that has not impacted our design, and their KEYNOTE-189 study will report out before the study finishes. So we remain confident. We do not address powering of our program at all or those design characteristics publicly. We view that as proprietary information between us and Merck, which we use to design the program, but we don't put that out publicly. If ECHO-301 is positive in melanoma, that would be the care standard there. As I mentioned earlier, the natural next place to go, to address your question, to enhance cure rates is the adjuvant setting to look at the combination in an adjuvant population to increase disease-free survival and overall survival. And that would be the intent after that study.

Operator

Our next question comes from Carter Gould with UBS.

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

I guess one for Hervé and maybe Steven. On the strategy for OX40, GITR and, I guess, with the next wave of I/O assets, is the message really that we should only expect pivotals with your own PD-1? Could we still see pivotals with other approved PD-1s? Just want to be -- I guess, it's a clarifying question there. And then also when you just think about the MacroGenics PD-1, any reason to think that you might still move that forward as a monotherapy either for regulatory or strategic purposes as you broaden out the indications you might go after?

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

Yes, maybe I'll start on the -- I think -- obviously, as I said, I mean, the goal is to get this combination done with products from our own portfolio. So you should expect if we go in pivotal study with a PD-1 with OX40 or GITR or any other products in the I/O portfolio to see that include an '012 plus that product in the pivotal studies. Would it be only with our own PD-1? It will depend highly on the indication we will be pursuing because, as I said, in some of these indication, pembro or nivo or durva PDL-1 inhibitors could be the standard of care. But obviously, at the end of the day, we want that pivotal program to include '012 plus GITR or '012 plus OX40 or plus arginase, et cetera, et cetera. So that would be the way to think about it. In terms of monotherapy, obviously, you know there are indications where there is the option to receive an indication in monotherapy for PD-1. It could be either of the so-called niche approach, which we have heard a lot from many different companies. So that could -- that is an option so we are looking at that as a possibility or it could be frankly in a less niche indication where we would be trying to establish it as a single agent across a larger indication. We don't know that yet. So what we are doing in the short term are 2 things. It's the so-called niche approach with a single agent, '012. And as I described, we will be initiating a number of combination studies in 2018 so that we can be prepared for the next step in combination with our portfolio.

Operator

And our final question comes from Michael Schmidt with Leerink.

Michael Schmidt - *Leerink Partners LLC, Research Division - MD, Biotechnology and Research Analyst*

A couple of quick ones. Number one on ECHO-301. What is the number of events needed to trigger unblinding of the study? And number two, maybe for Reid, can you comment on how important potential differences are among the various IDO inhibitors in development in terms of the PK, PD profile and whether -- or how that might translate into differentiated clinical profiles?

Steven H. Stein - *Incyte Corporation - Chief Medical Officer and SVP*

Michael, it's Steven. Just quickly upfront, we do not disclose the event number that would be -- would trigger the ultimate unblinding. So that's not public information.

Reid M. Huber - *Incyte Corporation - Chief Scientific Officer and EVP*

Yes. Michael, this is Reid. On the IDO inhibitor question, the key thing for this target, as we know, is near complete or complete inhibition. We can do that safely with this mechanism, and that's going to be the bar by which we judge compounds. And I think if any compound can safely, with appropriate drug-like properties, achieve those levels of inhibition, then that should drive the pharmacology irrespective of any biochemical

nuances. At the end of the day, it's about inhibiting the enzyme to a maximum degree. Differentiation between agents will come from their ability or inability to do that as well as any other off-target liabilities they may have.

Operator

I'll now turn the conference back over to Hervé Hoppenot for closing remarks.

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

Okay, thank you. Thank you for attending this meeting today and your time. A great quarter, progress on the pipeline, some new entries into our portfolio with the deal with MacroGenics and also a new board member. So a lot of good progress from the Incyte side, and we look forward to seeing you -- some of you at the upcoming investor medical conferences including at ASH. But for now, thank you again for your participation in the call today. Bye-bye.

Operator

This concludes today's webcast. All parties may disconnect. Have a great day. Thank you.
