Incyte
Ruxolitinib Cream: Phase 2 Data in Vitiligo
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Operator: Greetings, and welcome to the Ruxolitinib Cream Phase 2 Data in Vitiligo Webinar and conference call. At this time, all participants are in a listen-only mode. A question-and-answer session will follow the formal presentation. If anyone should require operator assistance during the conference, please press star, zero, on your telephone keypad. As a reminder, this conference is being recorded.

It is now my pleasure to introduce your host, Mike Booth, Head of Investor Relations. Please go ahead, Mike.

Mike Booth: Thank you, Kevin, Good morning and welcome to our conference call and webcast to discuss vitiligo: the disease, the medical need and the biological rationale for JAK inhibition as a potential therapy.

We will also provide some highlights from the presentation of the Phase 2 data from ruxolitinib cream as a treatment for patients with vitiligo that were presented at the World Congress of Dermatology, over the weekend.

The slides used today in today's webcast are available for download on the investor section of Incyte.com, as are the full data slides, as presented in Milan on Saturday.

I am joined on the call today, not only by Hervé and by Jim Lee, our Head of Inflammation and Autoimmunity Development, but we're also delighted to welcome Dr. John Harris from the University of Massachusetts.

Dr. Harris is a world-renowned expert in vitiligo. He is an Associate Professor and Vice-Chair in the Department of Dermatology and the Director of the Vitiligo Clinic and Research Center at the University of Massachusetts Medical School.

Hervé will begin the call today, with a few opening remarks, before Dr. Harris provides us with some important context on the disease of vitiligo, the evident unmet medical need and the rationale and potential for JAK inhibition to be the first approved therapeutic for the disease.

Jim will then provide some highlights of the ruxolitinib cream Phase 2 data set, before we open for your questions. During the question and answer session, I ask that you limit yourself to one question, and if needed, one follow-up, as this will enable as many of you to ask questions, as time allows.

Before we begin, however, I'd like to remind you that safe harbor rules govern our remarks today, and any forward-looking statements that we may make. I therefore encourage you to review the risk factors detailed in Incyte's SEC filings, including in our form 10-Q for the quarter ended March 31, 2019.

We will now begin the call with Hervé.

Hervé Hoppenot: Thank you, Mike, and good morning, everyone. So, Incyte's clinical portfolio is organized around three pillars. We have an oncology targeted therapies, and immunotherapies, and several years, ago, we built a new group of ten or fifteen scientists to review the use and indication for products coming out of the research and review where they could have applications outside of oncology.

And that was the goal we gave them; Of saying you have these immuno impacting type of a mechanisms coming from our research. Tell us where it could apply outside of treatment of cancer.

And that's what gave rise to our Inflammation and Autoimmunity Development Group, which is now headed by Jim Lee, here today, he's part of Steven Stein's organization.

So, we have small proof of concept trials already underway in several indications for our oral JAK and oral delta programs.

The most advanced programs in these IAI franchise are with ruxolitinib cream, so, we have Phase 3's ongoing in atopic dermatitis and are recruiting well. And we will have data from these Phase 3's in the first half of next year.

And now, we have a successful Phase 2 in vitiligo, which is the subject of today's call. So, if you remember, last year, we had an R&D day reviewing the full portfolioof Incyte. And this year, and this will be the first instance of that, we want to replace it with more thematic disease based on the news flow.

So, today will be around the proof of concept in vitiligo. And I would like to welcome Dr. Harris to the call to start the presentation.

John Harris: Good morning, everybody. And thanks, Mike, for that nice introduction. Just to remind everybody I'm a physician scientist who studies vitiligo. I see patients a half day a week in my Vitiligo Specialty Clinic and then I run a research laboratory to better understand what causes this disease.

And so, vitiligo is an incredibly common disease that affects about one to two in a hundred people. That's a lot of people in the U.S. and around the world. And half the patients who get vitiligo do so before the age of 20.

So, as a physician, I'm managing patients over many decades of life and we have to think about treatment in terms of decades. And as a scientist, it gives me an opportunity to study this disease over a long period of time.

Vitiligo has a lot of disease associations and so, as we study this disease, we know that, we believe that we're studying other, the mechanisms of other autoimmune diseases, as well.

So, this is a typical presentation of vitiligo, call it patchy depigmentation. This is on the hands, as you can see, here. It can become more widespread in some cases, as well. We'll talk about the surface area of vitiligo and how it can present in different patients, a little bit later.

The great news about vitiligo is that it's reversible. So, this used to be a white spot. You can see that there's repigmentation, here, coming back as little brown spots. And this is how it repigments. And the reason why the spots come back as they do is because the melanocyte stem cells live within the hair follicle. And so, this is where the vitiligo repigments from, as you can see here.

You can see, really, we can get very nice responses. It can take a very long time, however. So, this is a patient treated with narrowband UVB, top left to bottom right, is over a year. But she got very nice repigmentation of her neck and chest and was very happy with it. She said she was wearing low cut dresses again. It completely changed her life.

What I'm not showing you is the repigmentation on her face, which was complete, 100% to the point where I could not even remember that she had vitiligo on her face.

In talking about the effect of vitiligo on patients, it is huge. So, we published a paper called *Vitiligo Is Not a Cosmetic Disease* and the title just specifically did call attention to this because, sometimes in the past, it has been dismissed as such. But it's actually, it's a well-known mechanism. It's an auto-immune disease, similar to

psoriasis and alopecia areata, type 1 diabetes. We know that these run in families and so, we understand the mechanism.

It's clearly a disease where it's… Cosmetic treatments or cosmetic issues are things that we all struggle with, as we age, whether it's wrinkles or thinning of the hair, etc.

And so, vitiligo is clearly in a separate category and the paper, second paper shown there, *The Burden of Vitiligo*, concluded that vitiligo is a serious skin disorder with an adverse impact on an emotional state, comparable with that of other major skin diseases. So, I think it's clear that vitiligo does not deserve a separate category as being any milder than the other diseases that we currently treat.

On the right, we have a study that looked at vitiligo patients and psoriasis patients and their quality of life, using the Dermatology Life Quality Index. And I like this study because it's a direct comparison and shows the effect on quality of life in both diseases.

And so, vitiligo patients who are affected, either moderate to severe to very severe is 51%. And in psoriasis patients, that number is 56%. And so, they're actually quite comparable in terms of the impact on quality of life, in both diseases. And so, both diseases deserve to be treated.

The unmet medical need in vitiligo is clear through the poor quality of life. As I mentioned, it's similar to psoriasis but also eczema. Actually, there's studies that show that the willingness to pay for a cure from

patients is higher in vitiligo than even in eczema. So, that's the amount that someone is willing to pay out of pocket to cure their disease. So, it just shows the impact of this disease.

There are no FDA approved medical treatments to improve vitiligo. There is one FDA approved medication called monobenzone. It's a cream that actually makes vitiligo worse. It's what Michael Jackson used to bleach his skin. And so, we certainly must do better.

We use off-label topicals, right now, and they have side effects that we'll talk about in the next slide, here. So, the current vitiligo treatments are listed here. The market is segmented and incomplete. We're not able to take care of all of our patients for the limited efficacy, the burden that it puts on patients in phototherapy [that] I'll show you and then, also, the side effects of these treatments.

So, the oldest treatments that we have are topical steroids. They can be effective. With continued use, they cause stretch marks, or striae, an atrophy of the skin. And dermatologists are very careful of topical steroids. Non-dermatologists are, actually, quite fearful of topical steroids and refuse to use strong steroids in their practice.

Topical calcineurin inhibitors are newer. They don't have the same side effects as steroids, although they are symptomatic. They can cause a burning sensation which can cause discontinuation. They also can cause hyper pigmentation around the edge of the border. And so, people have concerns about using them, as well.

Narrowband UVB phototherapy is currently the best therapy that we have but it requires a visit to the dermatologist's office two to three times per week for over a year, as you can see. A very time consuming [process], [and it's] very difficult for patients to take time out of their schedules to do this. And we have moderate efficacy. And we can talk about that.

Surgical transplantation is there just for completeness. It is only for patients who have very stable disease, which is a very small population of patients. But we can actually transplant pigment cells from one part of the body to another, as a treatment. But it only helps less than 5% of the patient population. And it is only conducted in three locations in the entire U.S. There's not a lot of access to it.

And then, depigmentation, I mentioned earlier. This is the monobenzone cream. We only use this if the disease is very severe. And this represents a very small part of the population with vitiligo. It actually worsens the disease, and so, it's not commonly used.

So, in summary, the current treatments that we have, they have pretty significant limitations, due to side effects in the population which they're useful. And so, at this time, without an FDA approved treatment, we believe we've penetrated only a very small part of the market. We estimate less than 20% of the total market.

Next, so, I put here just my simple treatment algorithm. This is how I treat vitiligo. First, I look to see if it's active. And if it is, I give some oral steroids for a short period while we get patients on something else. If it's

not active or after we put on the steroids, we look at the total body surface area. If it's greater than 5% body surface area, then, or if it's not greater than 5% body surface area, we'll use topicals alone.

And right now, we have to use clobetasol because it's the most effective treatment that we have. But because of the side effects, we have to use it in a discontinuous manner. So, we only use clobetasol for a week and then we use tacrolimus for a week, back and forth, and we continue alternating in this way.

It's very confusing for patients and tacrolimus doesn't have the same efficacy as clobetasol which is why we use it this way. But it's complicated because we can't use strong steroids, continuously.

For focal disease, we can also consider excimer laser as a phototherapy option and, as I mentioned, surgery. If the body surface area is covered greater than 5%, then we strongly consider narrowband UVB. If the patient has access to it, we'll do that. If they don't, we'll just continue to treat them with topicals in a smaller area of their body. If they'll use UVB and topicals, we certainly do that because we see better efficacy when you combine topicals with UVB. And if they're not willing or able to apply topicals, then we just use phototherapy.

So, the question frequently comes up in this avenue, this venue how many patients actually have less than 5% body surface area can be treated with topicals alone. And so, three specialty clinics around the world gather data, including mine: Amit Pandya's clinic in Dallas, Texas and Khalid Ezzedine’s clinic in Paris. And actually, we analyzed the body surface area of our patients in that breakdown. It was, really, very interesting. In these

different areas of the world, we had very similar numbers. And so, the number of patients who had less than 5% body surface area was 58% of our patients.

So, those are patients that we would, most of those patients, we would start on topicals alone. And then, the remaining population, 42% have greater than 5% body surface area. And those patients, we try to get on to narrowband UVB phototherapy. But then, we also combine topicals.

So, this is a summary of how we would use FDA approved treatments in the future, assuming we had a topical and a systemic available. First, we would look for signs of activity. If they were present, we would us a systemic plus topical. We estimate this would be 20% of the population. If there are no signs of activity and there was less than 5% body surface area, we would use a topical, alone. That would be about 48% of patients, we estimate.

And then, those without signs of activity would be more than 5% body surface area, we would use a systemic and topical, again. And that's about 32%.

The take home here, though, is that a systemic would probably be used in about half of patients. But a topical would be used in 100% of patients. This is what we do today. So, if I have a patient with widespread disease, then I'd put them on a phototherapy full body therapy. We add in topicals, as well. And so, those that would be eligible for a topical is every patient.

Currently, therapy for vitiligo is reimbursed at a high level, even though we don't have FDA approved treatments. We use narrowband UVB, it's reimbursed at $24,000 per year. Excimer laser is reimbursed at $42,000 per year. So, we do get coverage for patients, even though we don't have the approved therapy.

The opportunity in vitiligo, I think, is probably best appreciated if you compare it to psoriasis, which is another disease that has grown significantly over the last 25 to 30 years. So, 30 years ago psoriasis was in the same place that vitiligo is now.

We were treating with topicals, phototherapy, oral immunosuppressants, like methotrexate. Now, psoriasis is an $8 billion market, shared by 10 to 12 drugs, many of them biologics. And the market is expected to grow, significantly, in just the next few years. And part of the reason for that is the very highly effective biologics that have now been developed.

Psoriasis is in two to two and a half percent of the population. Vitiligo is similar to that, one to two percent. And so, we estimate a large unmet need, there, with the vitiligo population. And as I mentioned, there's no effective FDA approved medication for this disease.

So, to introduce the rationale for targeting JAKs in vitiligo, I put a few slides here on some of our work. We developed a mouse model of vitiligo, early on, about ten years ago, where we adoptively transferred autoreactive T-cells into a mouse that has black skin and black hair. And over six to seven weeks, we see white

spots occur up here. So, you can see them on the tail. They're on the feet, the nose and the ears of these mice. We're able to quantify that.

The mouse model, actually, is a great representation of human disease. So, if clinical and histological appearance is the same, gene expression, which I'll show you in the next slide, it's the same in mouse and human skin. It's the only mouse model that we have of skin depigmentation. Others cause hair depigmentation, which is a different animal, altogether.

It's the only reversible model of vitiligo that we have. So, to be able to test new treatments that reverse disease, we need to use this model. We have found that ongoing studies, including one we're going to talk about today, parallel observations in mouse and humans and the drugs that work in mouse [also] work in humans.

The mouse model has predicted JAK inhibitors that are now in clinical trials that they would be effective. And we use this model, actually, now for many companies that want to perform preclinical testing.

So, this is the gene expression profiling that we did early on in the mouse and human skin. We can see a loss of melanocyte transcripts, as you'd expect to see in vitiligo. And then, the other obvious pathway that's turned on is interferon gamma and the interferon gamma induced genes.

So, we see nothing from the type 17 immune response or the type 2 immune response. And this is where we have psoriasis drugs, and dupilumab for atopic dermatitis. And so, this really predicts that those drugs would be ineffective for vitiligo. And that's what we find. So, at least, psoriasis drugs have been thrown at vitiligo, many times, and they're completely ineffective.

So, we need drugs that target this interferon gamma pathway, which is the vitiligo specific and relevant pathway.

So, we had, based on this data, we hypothesized that interferon gamma was really the driver of this disease in mice. We found that was true, so if we knock down interferon gamma or the receptor for that, we were able to prevent vitiligo in the mice. If we knocked out a downstream chemokine CXCL10, which, on the previous slide, was one of the highest expressed gamma induced genes, we also found that that prevented disease.

But probably more importantly, we found that, even if we let disease continue, so this used to be a black tail on the top, turned completely white through vitiligo. And then, we blocked CXCL10, or interferon gamma, or other things with an antibody, we found that the pigment came back. So, we've got perifollicular repigmentation on the tail, as we see with treatments in humans.

So, we're very excited that we have identified the key pathway that drives vitiligo. And so, summarized here, interferon gamma initiates the pathway, signals through the interferon gamma receptor, JAKs 1 and 2, are required for intracellular signaling through this receptor. They activate STAT 1, and then turn on chemokines

CXCL9 and 10 and others that signal through CXCR3 and recruit more T-cells to the skin. So, this creates this positive feedback loop that drives the progression of vitiligo.

So, we have found, over the last ten years or so, that when we knock out interferon gamma, the receptor, STAT 1, the chemokines or the receptor to those chemokines, we're able to prevent disease, really, indicating that this pathway is important to development, progression of vitiligo.

We've also found that, if we use antibodies to the soluble factors of the receptors, we can not only prevent disease, but we can reverse it, which is fantastic and clinically relevant. And then, most importantly for today, we found that JAK inhibitors are effective in our mouse model. And I won't take time to show you the data. We have not published that data. They're highly effective in the model and prevent and reverse disease.

Next, we put ruxolitinib, oral ruxolitinib in a patient with vitiligo, as you can see here on the far right. You can see before and after treatment, five months of treatment, the amount of repigmentation he got. He had almost nothing left on his face and he nearly completely repigmented in just a few months. This is about 50% improvement, actually.

And we found we had saved up his serum over a year before this treatment, and we found that the CXCL10 level that interferon gamma induced chemokine was very high and stable for over a year in this patient, until he started the ruxolitinib treatment. And then it dropped.

And so, not only did we see that ruxolitinib was effective in a patient, but we saw that it seemed to be working the way we had hypothesized with blocking interferon gamma and dropping the chemokine.

And so, this has allowed for, this and other clinical studies, have allowed for three ongoing clinical trials, right now, by Aclaris, Incyte and Pfizer. We're talking about Incyte today, which is the furthest along, by far.

And so, we have one more question because those were systemic therapies. We wanted to know whether topical JAK inhibitors would be effective for vitiligo. So, we're back to the interferon gamma pathway. And the way we tested whether topicals would be effective, definitively and mechanistically, was to look at STAT 1.

So, we were able to remove STAT 1, genetically, only from keratinocytes in our mouse model and then ask, did this have any effect on vitiligo. So, the keratinocytes, the question was whether the keratinocytes played a role in driving disease. So, this is how we did it. We put T-cells into the black mouse, again. The black mouse, we're able to completely remove interferon gamma signaling by removing STAT 1 only in keratinocytes.

And what we found was, if the keratinocytes cannot respond to interferon gamma, we were able to significantly protect from disease development and progression. So, this indicated to us, that all we have to do is turn off interferon gamma signaling in keratinocytes alone and we could have a big affect on disease progression and develop a treatment.

So, this is what topicals do. Topicals hit the keratinocytes first, and David Rosmarin at Tufts used this as rationale to perform a small topical clinical trial that was published in the JAAD 2017, where he saw significant repigmentation through topical treatment of ruxolitinib.

And that's the end of my presentation. I'm ready to transfer this back to Incyte.

Jim Lee: Great. Thank you, John. That was a great presentation. What I'd like to do now is to provide some highlights of the presentation by Dr. David Rosmarin at the World Congress of Dermatology. He presented the Phase 2 data, this past Saturday. And what I'd like to do is provide just some of the highlights of his presentation.

I think, as Dr. Harris mentioned, this was the first large randomized study in vitiligo. And on the next slide provides a very high-level overview of the study design and some key inclusion and exclusion criteria.

We evaluated three concentrations of ruxolitinib cream the 0.15, the 0.5 and the 1.5. With the highest concentration, the 1.5% concentration, we tested both once a day, and twice a day. And we compared it to vehicle cream. And that portion of the study against, the comparison against vehicle cream was done for 24 weeks. And that's the data that we're sharing, today.

After the 24-week visit, all the patients were crossed over to active therapy. Their crossover to either to continue with the two higher concentrations or the three dosing cohorts. And then, patients on the lowest concentration were crossed over to higher concentrations.

At week 52, all of the patients were started on the highest concentration of rux cream, the 1.5% BID. In terms of some of the key inclusion, exclusion criteria, we tested ruxolitinib cream in adult patients with vitiligo. They had to have approximately half a palm of body surface area involvement on their face and at least 3% of their total body had to have vitiligo.

We excluded patients that had other skin conditions that would have confounded any of the evaluations, as well as screening them or at least requiring a washout period for previous therapies of their vitiligo.

In the next slide, we highlight the key demographics and clinical characteristics of the patients that were enrolled in the study. You could see the average age was approximately 48, about a 50-50 split between women and men. And in terms of Fitzpatrick Skin-Type, about a third of the patients were darker skinned individuals, Fitzpatrick four through six. A third of Fitzpatrick Skin-Type three and a third Fitzpatrick Skin-Type two.

In terms of the disease, as Dr. Harris mentioned, some of the clinical characteristics of patients that he sees. I think the clinical characteristics, here, provide a view of the patients that were enrolled in this study. The total

BSA involvement was 22. So, 22 of that mean percent body surface area involved was 22%. So, it's quite a high number.

In terms of the length of disease that the patients had, the median duration of disease was 14 years. And Dr. Harris mentioned that there are other autoimmune conditions associated with vitiligo. We had about 25% of patients who reported another autoimmune condition.

And in terms of prior therapies, about half the patients had been treated with topical corticosteroids, another half treated with topical calcineurin inhibitors. And about a third of the patients had received prior phototherapy.

On the next slide, we present the primary efficacy variable, which was the Facial VASI50 (F-VASI) response. So, patients who achieved at least a 50% improvement from baseline in their F-VASI score. Couple points to highlight. One, as you can see, you can see over time, the response continues to improve and get better. But interestingly, we see a response as early as week eight. And then at week 24, we see that the best response are in the two highest dosing groups, the 1.5% dosed once a day and the 1.5% dosed twice a day.

One of the things that we've heard from feedback, and I think Dr. Harris mentioned, is that both physicians and patients truly want the best response for their vitiligo, as possible. So, another efficacy variable that we looked at was the VASI75 score, which is shown, here, on this slide. And this is the proportion of patients who experienced at least a 75% improvement in their VASI score from baseline.

And again, you see the same pattern. You see the response show up fairly early at week eight and improve over time. And in this case, you see that the best response was seen in the group that was dosed with the 1.5% cream, dosed twice a day. And about 30% of the patients achieved a F-VASI75 at the week 24 time period.

In terms of the safety that was observed in the study that's highlighted here in the next slide, we see that rux cream was very well tolerated. We do see some reports of acne in the study. A low percentage and none of them led to discontinuation from the study. Patients also reported some itch, both at the application site and other body parts.

In terms of the discontinuation, we had only three patients who discontinued due to adverse treatment events. We had one patient in the vehicle arm and one patient in the lowest concentration, the 0.15% QD arm, that discontinued due to headache. And we did have a serious adverse event occur in the 1.5% BID arm. However, that was not related to treatment. The patient actually injured himself and had to withdraw from the study. So overall, very well tolerated in the first 24 weeks of treatment.

So, the next slide is just a very high-level summary and the conclusions that we see from the study. We see that significantly more patients received a F-VASI50 improvement after 24 weeks of treatment with ruxolitinib cream. In terms of the specific arms that achieved the best response, we see that the 1.5% dose twice a day and the 1.5% dose once a day, both were significantly better than vehicle cream.

In terms of the F-VASI75, again, the higher, more robust end point, we see that 30% of the patients in the twice a day arm and 16% or 17% of the patients in the once a day arm were able to achieve a 75% improvement in the F-VASI score at week 24.

And again, from a safety perspective, we saw that the rux cream was very well tolerated.

In terms of next steps, obviously, we're very excited about the data and we're moving very quickly to initiate the Phase 3 study. We hope to start the study sometime this year, and then, depending on enrollment, have the results some time in 2021 with, hopefully, a submission at that time point.

Mike Booth: Kevin, that ends our prepared remarks. If you could please give the instructions for Q&A. Thank you.

Operator: Our first question today is coming from Brian Abrahams from RBC, your line is now live.

Brian Abrahams: Hi, thanks very much for taking my question and congrats on the data. I was wondering if you could talk about any interim results you saw on T-VASI scores. Any reason to think that would trend differently? And, do you have any clarity from regulators on what registrational end points might be? And I'd love to hear Dr. Harris's views on that as well. Thanks.

Jim Lee: Sure, this is Jim Lee, great question. So, I'll start with your second question around the regulatory end points and just say that we are working with both the FDA and the EMA to finalize the Phase 3 study designs and we'll share those shortly when we start the studies. In terms of the total VASI, we did collect obviously, total VASI, as I mentioned the average body surface area was about 22%. Patients were restricted to treating only 20% of their body and we did collect the treated areas. And we'll provide that data at a future scientific meeting.

Brian Abrahams: Alright, thank you.

Mike Booth: Dr. Harris, if you'd like to add anything?

John Harris: Yeah, happy to add to that. So, in terms of the total improvement that patients are looking for, we published this. We've done panels with patients asking them how much improvement they want. And they consider 75% improvement successful therapy. So, but that is not 75% at six months. It's 75% eventually by a year or more. Ultimate improvement, they want 75%.

They said they would be happy with 25% at three months as long as they know that they're going to get more overtime. So, in this study, we found that 30% of the treated patients from the highest group actually achieved the successful treatment in only six months, which is very fast, and then the VASI50 with its upward projection at six months, we fully expect the 52-week data I would anticipate and guess just based on the trace on that, we improved significantly. So, I think we're completely within the realm of what patients want.

Brian Abrahams: Thanks so much.

Operator: Thanks. Our next question today is coming from Marc Frahm from Cowen & Company. Your line is now live.

Marc Frahm: Thanks for taking my question. Maybe, Dr. Harris, we can follow up on that last question and point. Yeah, I think in your studies and in talking to patients themselves, we see there is kind of a range of goals for patients. Maybe can you talk a bit about if you could bucket the patients into ones that are willing to accept say 50% to 75% versus people who really want, you know, how many patients really want just full or near full repigmentation before they would want a therapy.

John Harris: Yeah. There is a range of patients, so, some patients are very demanding, and they say, you know, it's 100% are nothing. They are the minority, for sure. But the good news is, actually, that the face is capable of responding to 100%. And what we see is the response, extensive response, really varies by anatomical distribution.

And so, as I mentioned early in my talk, the repigmentation comes from the hair follicles. And so, what we find on the body is the area that has the highest density of hair follicles respond the fastest and the most complete to therapy, any type of therapy. The face has the highest density of hair follicles. And so, the face, actually, is capable of responding hundred percent, as I mentioned, in my patient, and what frequently happens is after successful therapy, I'll forget that the face actually ever had vitiligo. So, that, fortunately, is the most important to patients, that their face is usually the most important area and that that location is capable of responding 100%.

At the same time, there are other areas that don't respond at all. So, fingertips with no hair follicles, or the underside of the wrists, and a very few other places that have no hair follicles typically respond 0%. And so, what patients need to be educated on and their expectations set about what can be expected. So, the good news is, even the patients who want 100%, the small number who demand that much repigmentation, can get that on the face. That is achievable. You

know, it will usually take a year, but patients, the good news too is, after three months, they've got 25% repigmentation. They are on board. They are excited. And they will treat for a full year to achieve the full effect. You know, so, it's not that it takes a full year to see anything. We see an improvement early on and that continues at a pretty slow clip for the whole time.

Marc Frahm: Alright, thanks.

Operator: Thank you. Our next question is coming from Tyler Van Buren from Piper Jaffray. Your line is now live.

Tyler Van Buren: Thanks guys. Good morning and congrats on the data. It looks great. I guess more of a commercial question. Can you guys speak towards your potential capacity to launch and strategically how you would do that and how much resources you'd have to put forth up front and how you would change that over time? And just briefly, maybe as a follow-up, is there the ability to price differentiate in vitiligo versus say atopic derm?

Hervé Hoppenot: Okay, thanks. I'll take this one. So, starting with your last question on the pricing obviously the Phase 3's are ongoing already for atopic dermatitis. There are two different concentrations that are tested in the Phase 3. So, we would be able to answer that, and we don't--have not yet started the Phase 3 in vitiligo. So, that's something that is [being] discussed. So, when we see the different concentrations and we have a question of the size of the tube in some way and see if it will be easy or less easy to have a price differentiation when we know the results of the Phase 3 in atopic derm.

Regarding the commercial aspect. So, obviously, we are seeing this as a very significant opportunity for Incyte. In the case of vitiligo, it is treated by specialists, mostly, or entirely, in fact. And the commercial deployment that will be

feasible from the financial standpoint are very different in Asia, Europe and the U.S. So, the way we look at it is literally three different analysis that we are doing. The program, in term of development is targeted at each of the three. And then, we have to answer the question of saying what does make the most sense to maximize this opportunity in Asia, in Europe and in the U.S. I can tell you for the U.S. that the number of people that will be required for launching it independently is around 200, and that would include commercial and medical affairs and the team required to do it.

So in terms of resources it's something that is somewhat feasible, and we are going to get the precise answer to the question more or less on time so that when we do the submission next year, when we get the results in atopic dermatitis, we would have a full commercial deployment plan in place. At this stage, we keep everything open, in some way, as we are trying to see what would make the most sense. There is, obviously, a probability of going alone and being able to book the revenue that is higher for the U.S., probably lower for Asia, which is a very complex market in the field of dermatology, and we are still not sure exactly how it's going to end up for Europe. but that would be the picture I could draw today. It's a higher probability to go alone in the U.S. or to go and book the sales [which would likely be] lower in Asia and still debatable for Europe.

Tyler Van Buren: Alright, thanks so much.

Operator: Thanks. Our next question today is coming from Evan Seigerman from Credit Suisse. Your line is now live.

Evan Seigerman: Hey all, thanks for taking the questions. When I look at the F-VASI50 score, I see that there's not much of a difference between the once daily and twice daily at the 1.5% dose. However, when you look at the 75, you see a much greater separation. Is it practical for patients to apply this twice a day and actually adhere to that longer-term to get that 75% resolution? And then my follow-up is, you know, we have this pretty encouraging data set, what do we

actually need to see in a Phase 3 for regulatory approval? And why is this dataset not sufficient given the unmet need in vitiligo? Thank you.

Jim Lee: Those are great questions. And maybe I can ask Dr. Harris to address the question around what patients would need comparing the VASI50 to the VASI75.

John Harris: Right, and the practicality of BID dosing.

Jim Lee: Right.

John Harris: Yeah, I think, I go through this every week when I see patients in the clinic. I explain to them, you know, the application. So, we use all topical's--I use all topical's, at BID dosing. So, everybody's using topical steroids and topical calcineurin inhibitors at twice a day. They don't always keep up every day. And I tell them once a day is better than zero, twice a day is better than one. And they are usually very happy with that, and they're motivated. And so, the majority of my patients actually follow the application of twice a day to get the results that they want.

Jim Lee: And to your second question regarding the FDA. Just maybe, could you clarify? I understood it as was there a thought of submitting this data rather than moving into Phase 3?

Evan Seigerman: I don’t know if it's actually a thought of submitting this data. But it's more that it seems there's such a high unmet need in vitiligo, I guess, what would you need to see in a Phase 3 trial? And would there be any situation where this data set could be used for some sort of accelerated approval?

Jim Lee: Sure. And I can speak to the regulatory requirements.

Evan Seigerman: Sure.

Jim Lee: So, in general, obviously, for a Phase 3 program, you need to show statistical significance - the difference between the active arm and the vehicle arm. But, in addition to that, you also--the FDA typically wants to look at response over time. They want to look at durability of response, and very importantly, the safety of a treatment over time.

And so, all of those components need to be included in a submission. And, obviously, this is a great study, a very robust study, but it was 157 patients. And so, we are including it and we'll have long-term data, but I think we need to expand the patient data set to increase the reliability, as well as, look at a large patient population from a safety perspective.

Evan Seigerman: Alright. Thanks so much for the questions. I appreciate it.

John Harris: Can I add one more comment, just in terms of the practical aspect of applying the cream? So, what we currently have available in steroids and protopic is that they are an ointment base in order to get the efficacy that we currently have. It's a very thick ointment like Vaseline. And patients really--they apply it, they do it, but they don't enjoy it. The biggest complaint about using these treatments that I didn't mention in my slides is how greasy they are. And the great thing about the new cream, the ruxolitinib cream is that it is, indeed, a cream and not an ointment. And the subjects actually really prefer this. And I think that--so if anything, I think they'll be more willing to apply this twice a day than what we currently have.

Evan Seigerman: Alright, thank you.

Operator: Our next question today is coming from Michael Schmidt from Guggenheim Securities. Your line is now live.

Kelsey: Hi, this is Kelsey on for Michael. First, I guess we're just kind of wondering in terms of the F-VASI 50 dose response, it looks interesting in that there isn't really clear separation until week 12. I guess, what are your thoughts on that? And then, follow-up, I guess what kind of duration of therapy should we expect should this hit the commercial setting? Thank you.

Jim Lee: Sure. And I can address the F-VASI. The F-VASI was developed a number of years ago. And in the publication, you know, one of the limitations is that it's a fairly blunt instrument. And so, with the 50% improvement, one of the reasons why we're likely not seeing a large separation between the various dosing arms, especially the 1.5 QD and the BID, is the sensitivity of the 50% improvement versus the sensitivity in the 75% improvement. So, if you actually look for a more robust endpoint, you can really clearly see the dose response between the various dosing groups. So, it's, I think, an effectof the 50% improvement versus the 75% improvement.

John Harris: I can comment on the duration if you'd like.

Jim Lee: Sure, yeah, go ahead--

John Harris: --The expected duration of therapy. So, you know, I fully anticipate that most patients would be on a year of therapy in order to achieve the results that they want. There are two options after that in terms of the potential for relapse. And so, patients currently, with current therapies, at least, we don't know the rate of relapse that will occur

with this drug. But with the current therapies, patients have a choice of either stopping their therapy once they achieve what they've been seeking to achieve and then waiting for relapse, which may happen a year or two years or later, and then restarting the therapy. So, a lot of patients do that.

I also have patients who really never want to see a white spot again, and they use a maintenance therapy of topical application instead of twice per day, twice per week. And I would anticipate that would be an option here, as well. So, patients for the rest of their lives could apply a topical just twice per week to maintain their benefit.

Jim Lee: And the only thing I would add there is that those are all very important clinical endpoints that patients and physicians would like to see. And we are trying to integrate as many of those into the Phase 3 program.

Kelsey: Alright, thank you so much.

Operator: Thanks. Our next question today is coming from Alethia Young from Cantor Fitzgerald. Your line is now live.

Emma: Hi, this is Emma on for Alethia. So, in the commercial setting, which you expect patients to continue receiving phototherapy or other treatments in addition to rux cream? And if so, I guess, how would that factor into pricing and reimbursement discussions?

Jim Lee: Maybe, John, you can address the thoughts around combination therapy, and then, perhaps, we can try to address the pricing issue.

John Harris: Sure. Yeah, so, the way we use topicals now, as I mentioned in the slides, is we like to use them in combination for patients who have greater than 5% body surface area. So, if a patient comes in to me with less than the 5% body surface area, which is five hands worth of vitiligo all over their body, then we'll start with just topicals because it's practical to be able to--a practical amount of skin to be able to apply a topicals to twice a day.

Beyond 5%, it's just too much body surface area. So, the majority of patients have less than 5%, so we would use topicals alone there. If they have greater than 5% body surface area, we would want to put them on phototherapy, as well, because otherwise, they would have to bathe in the cream. And as I mentioned, though, we get better responses with topical and phototherapy than phototherapy alone. So, I would anticipate using them in combination for the subset of patients that have widespread disease.

Hervé Hoppenot: Again, so the pricing, maybe I can say what, I mean, obviously, we are in the process of working on how it would be covered. At least for the U.S. and Europe, we are in the process of - what we know is that phototherapy is fairly well reimbursed. It can be up to $24,000 a year. And, obviously, the question would be for different types of patients, how many of them would be using combination of the two versus single agent with the cream. Overall, the view isthat the medical need is well understood. It would be the first approved product for this condition. And we think reimbursement would be achievable, and it would take some evidence to get there, but we think it could be well covered. At which level is probably something we would not discuss until the day of the launch of the product.

John Harris: Just to add one more thing to that in terms of practicality. When we add phototherapy and patients continue on topicals, they usually are not treating a large body surface area. So, patients will often, when they go on phototherapy, they may just treat their face and their hands at that point. And so, they would probably use less cream if they are on phototherapy. So, the total reimbursement might end up being similar.

Emma: Great, thanks.

Operator: Thanks. Our next question today is coming from Salveen Richter from Goldman Sachs. Your line is now live.

Maryana Breitman: Yes, hi. Thank you for taking the questions. This is Maryana Breitman for Salveen. I have a quick question. In the study, the meeting duration of disease was 14 years. Do you think it will be advantageous to start treating earlier in the course of the disease? And also, do you get any additional benefit from some kind of phototherapy or a light therapy? I mean, would great exposure to light have an effect on keratinocytes. Thank you.

Jim Lee: Sure. Maybe Dr. Harris, John, could you handle that?

John Harris: Yes. Sorry, could you repeat the question again? I had it and I was ready to go and then the second question.

Jim Lee: Yeah, so, the duration, the meeting duration that we saw in this study was 14 years.

John Harris: Oh, right. Yeah.

Jim Lee: And we saw patients with less long--or lower durations of disease.

John Harris: Right.

Jim Lee: What do you think would be the impact, if any, in the Phase 3 study?

John Harris: Yeah, so, the good news here, and it confirms what we've seen previously, that the duration of disease itself does not indicate the response to treatment. So, I've had patients with twenty-year duration disease respond just as well or better than patients with shorter disease duration. Certainly, there's a huge advantage to starting early, and it's not because of the binary response. The treatment will work or not work if it's treated early or late, but really, the amount of body surface area affected directly correlates with how long disease has been present.

So, if you've had disease for 10 years, you're going to have much more body to treat and repigment than if you started earlier. And then also, remember, some parts of the body don't respond to treatment. And so, those can be protected if started early and cannot be if started late. There is a clear result though. So, the longer duration of disease, the more likely it is that the hair growing in the spot will also turn white. And when that happens, we generally don't see repigmentation. So, there's that risk. It's more of a binary risk.

So, if you've had disease for 20 years, it's more likely that the hair within your spot will be white, and in that case, you won't respond. But, if you've had disease for 20 years and the hair is still pigmented, then there's no problem.

Jim Lee: Great. Thank you for that. And I can address the second part of that question around the potential for combining light therapy with ruxolitinib cream in the Phase 3 studies. I can say that the Phase 3 programs will be designed as monotherapy. So, ruxolitinib cream versus vehicle, but obviously, we're thinking about future studies beyond the Phase 3 program that will look at a combination of rux cream and light.

Maryana Breitman: Got it, thank you.

Operator: Thanks. Our next question is coming from Matthew Harrison from Morgan Stanley. Your line is now live.

Matthew Harrison: Hi, this is Kostas on for Matthew. Can you elaborate a little bit on the dose selection for Phase 3, and how high the bar is for success in Phase 3? Thank you.

Jim Lee: Yeah, at this time we're still finalizing the Phase 3 program. We'll obviously have that with a press release, but also, in clintrial.gov, the details released then. But, at this point, we can't comment on it.

Kostas: Okay, thanks.

Operator: Thanks. Our next question is coming from Carter Gould from UBS. Your line is now live.

Andrea: Hey, this is Andrea on for Carter. Thanks for the question. How does this Phase 2 data shift how you are thinking about your inflammation and autoimmunity portfolio and strategy around business development, both in licensing and out licensing standpoint?

Hervé Hoppenot: Yes, I'll take that. We can, you know, discuss it. When we started this program, was really agonistic to any indication. We were really working on the biology where does it makes sense, where is there a medical need. Obviously, vitiligo is a great example of, you know, the strategic aspect of it. And when we reach proof of concept, which is what we have done now for both atopic derm and vitiligo is where the question becomes like, do we partner this? Do we find somebody who would be better fitted to make it a success in Phase 3 and then on the commercial side? So, as you have seen for atopic derm and vitiligo, we decided to do the Phase 3 ourselves. And now, we are at the

stage where the same question comes up for the commercial side of could we have the benefit of some help, or could we benefit from licensing out the project.

As I said, there is so much value we can see here that we are looking at it over a good period of time, and we are also looking at how we could do it ourselves. And for other indications, and you could see from the list of the ongoing POC studies, we would be going through the same process as we see the data coming. We have studies ongoing in ulcerative colitis. We have studies ongoing in hemolytic anemia, HS and Sjogren's. So, all of that will be subject to a very specific maximization business development kind of approach. And, frankly, there is no rules that apply to all of them. It will be really case-by-case.

Andrea: Thank you.

Operator: Thanks. Our next question is coming from Pete Lawson from SunTrust Robinson Humphrey. Your line is now live. Mr. Lawson, perhaps, your phone is on mute. Please pick up your handset.

Pete Lawson: Thank you. Dr. Harris, just on the drug. If it's approved, what percentage of your patients would you think about using a topical rux on?

John Harris: So, I think, assuming it's an FDA approved treatment, I anticipate that the coverage will push us toward that drug. Right now, if we get denial for coverage, it's because there's no approved drug for vitiligo, and everything is being used off label. In terms of looking at the efficacy and side effects, I think that it would be very high on our list. If covered, I would anticipate going straight to rux, you know, if the insurance companies didn't require us to go through other drugs first. And I think it would be hard for them to do that because there are no FDA--if it's the only FDA

approved drug, it would be strange for them to say, well, you have to try all these off label things first, although, we would still know what the insurance companies are going to say.

But the efficacy of this is, you know, in my estimation, much better than any of the topicals that we currently have. And the side effects are certainly much lower than the other topicals that we have. You know, the side effects really, in my view, for the drug at least, are limited to acne, which was pretty well tolerated. 10% to 15% had acne really as the only side effect, and then the remaining had none. So, I think that this--the safety profile, the efficacy profile is so good here that if we can get coverage, that it would be one of the top, if not the first.

Pete Lawson: Great, thanks so much.

Operator: Thank you. Our next question today is coming from Jay Olson from Oppenheimer & Company. You line is now live.

Jay Olson: Good morning. Congrats on the data and thank you for taking my questions. I have two of them. At the beginning, you described the quality of life impact. And I was wondering if there are other long-term dermatological or systemic morbidities associated with vitiligo if left untreated? And then, separately, I think you mentioned, there are two systemic therapies in development for vitiligo. And I was wondering if you could please talk about the pros and cons of a topical treatment for vitiligo versus a systemic therapy? Thank you.

John Harris: Sure. Go ahead. Was there a comment?

Mike Booth: No, sorry. Dr. Harris, do you want to take both of those questions for us?

John Harris: Yeah, in terms of the topical versus systemic, I'll take first, I think that it's important to have both, as I mentioned, just the extent of disease really dictates the need for topical and systemic. And honestly, I think we need both. And so, for small areas of disease, we love the side effect profile of the topical, and feel very comfortable with that. A systemic would--you know, we really eventually, I think, need for the widespread disease, which is a minority of patients, or patients with rapidly spreading disease and active disease. So, I really think there's a need and a place for both. And then, sorry, can someone remind me of the first question?

Mike Booth: Yeah, the first question was the quality of life measures indicated. But what are the other co-morbidities in life if left untreated?

John Harris: Yeah. So, for patients and their family members with vitiligo, they are at a much higher risk of developing other autoimmune diseases, and particularly, Hashimoto's Thyroiditis, about 15% to 20% of vitiligo patients develop Hashimoto's, which is unrelated to the vitiligo. So, if you treat the vitiligo, we don't necessarily know that that will affect the Hashimoto's, although, and certainly not a topical, but a systemic might be able to decrease the incidence of that.

In addition, what's more directly related to the vitiligo, we think, is hearing loss in patients. So, there are probably four to six studies that have been done in vitiligo patients looking at hearing loss in showing that there's a greater incidence of hearing loss in vitiligo patients. None of the individual studies was very well done or in a large proportion or well-controlled, but just a number, the fact that all four or five of them or six showed that there is some hearing loss is a good indication that that's true. There is some vision loss as well, again, the data is weak, but there are a couple studies out there suggesting that long-term vitiligo predisposes you to worse vision as well.

There are rare forms of vitiligo that clearly affect vision and hearing. Patients with syndrome called Vogt-Koyanagi-Harada Syndrome actually can become blind from this very severe form of vitiligo. But I've only seen one in my career so far. So, it's very rare.

Jay Olson: Thank you very much.

Operator: Thank you. Our next question is coming from Gang Li from SVB. Your line is now live.

Gang Li: Hello. Hello, this is Gang Li on for Andy Berens. Just to have a quick question regarding this study for the follow-up study for the 52 weeks and the double-blinded for 28 weeks for the randomization. When do we expect the data? And how do you expect that the data is? More like close to what we have for this study? Or just it's going to have more info regarding the double-blinded study and the open label study? Thank you.

Jim Lee: Thanks for that question. We plan to present and share the week 52 data at a future scientific meeting. And I, unfortunately, I can't comment on the data now, obviously, until we present it publicly. So, just you have to wait until the next scientific meeting where we'll be able to share that data with you.

Operator: Thank you. We've reached the end of our question and answer session. I'll now turn the floor back over to Mr. Booth, for any further closing comments.

Booth: Thank you all for your time today and for your questions. We look forward to speaking with you at our second quarter call in a couple of months time, as well as, see you at upcoming investor and medical conferences. But for now, thank you again for your participation in today's call. Thank you, and goodbye.

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