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Galapagos NV R&D Update 2019

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PRESENTATION

Elizabeth Goodwin *Galapagos NV - VP of IR*

Thank you all for joining the Galapagos team for the 10th Annual R&D Update Event at Galapagos.

This is Elizabeth Goodwin speaking. I'm Vice President, Investor Relations. And I'm joined here in New York by Sofie Van Gijsel, Bart Filius, Walid Abi-Saab, Piet Wigerinck and about 100 investors and bankers.

This year's R&D update marks an important inflection point for the company as we stand at the cusp of our commercial phase with filgotinib, while embarking on an exciting new R&D collaboration with Gilead.

But before we begin, I do need to take care of a few logistics. You can find the webcast player via link on our homepage. And for those who'd like to join by telephone, please find the dial-in numbers and code on our homepage. A replay of this presentation will be available on our website later today and we'll provide a reviewed transcript on our site in the course of next week.

I need to start by reminding you that we'll be making forward-looking statements today. Actual results may differ from these statements. We refer to the full description of the risks of investment in Galapagos in our most recently filed Form 20-F.

Today, we're going to provide a snapshot of where we stand and where we're headed, zooming in on a few opportunities we'd like to highlight. Piet Wigerinck will speak on our delivery in R&D, update you on Toledo, and share his vision for future-proofing our productive research engine. Walid will cover filgotinib. He will then be joined by Dr. Toby Maher, who will provide a clinician's perspective on IPF today. And then Walid will finish up with an update on the 1690 program. Bart will then speak on organizational growth at Galapagos and our future outlook. We estimate that this presentation will take about 90 minutes, leaving us time for Q&A before we wrap at approximately 9:45 a.m.

And at this point, I'd like to invite Dr. Piet Wigerinck, our Chief Scientist Officer, to kick off. Go ahead, Piet.

Piet Wigerinck *Galapagos NV - Chief Scientific Officer*

Thank you, Elizabeth. Good morning, all of you here in New York as well as Good Afternoon for those in Europe, listening in on this call.

Let me start with showing a bit of what we've delivered in terms of R&D over the past 12 months. So for those who are longer with us and follow us for a number of years as we know every year, we show these 4 key moments in pipeline, which we believe if we keep on delivering on those are important for our long-term growth in success.

First of all, key for us is that we keep on looking and finding novel targets. So last year, we selected targets in the inflammation area, the metabolic area, fibrosis area and a new disease we added is osteoarthritis.

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Last year, as well as -- and I mean I'm making immediate jump over a couple of years. We've delivered 5 PCCs or preclinical candidates are in fact what we end up at the end of the drug discovery phase. 5, is, in fact, a new record. So you can all be sure our teams have worked day and night to push this company forward. 4059 is a metabolic PCC, I'll show a couple of slides. 4124 is a novel molecule, novel mechanism of action in fibrosis area. It's a synthetic compound. So the scale-up to the first batches will take a bit longer, which will move into the clinic after next year. 4259 is a backup in our inflammation pipeline. 4399 as well I want to spend a couple of seconds later. It's the third compound in the Toledo franchise we selected to move into preclinical development, has a unique profile, I'll touch upon that during my talk. And 4471 as well is a backup of one of the other compounds in the pipeline. And so all in all, 5 PCCs, 3 novel mechanisms of action, so we really keep on delivering sufficient ammunition to grow the pipeline.

Later in the pipeline, important for us is that we keep on doing novel proofs of concept. So out of these PCCs, a number will reach Phase II and the plan is for each of that one -- each of the compounds that reach Phase II, we set up 2 proof of concepts. So last year, we set up for 1205 the PINTA in IPF and with 1690 in Scleroderma, the NOVESA study.

And finally, we believe for long-term success, we need to keep starting one Phase III every other year. So if you can keep on that pace, we'll be set up for long-term growth. So previous year, we started 1690, this year our partner Gilead started a PENGUIN Phase III with filgotinib. Coming years, novel targets will get to that stage. But all in all, if you look to how much of novel targets, targets to PCC, PCC (inaudible), we really maintain our pace, and we are really set up for long-term growth and success.

I also always show effect in discovery. This is discovery area only, how much people work on an area, just to give you an idea, an impression on how important diseases are. The inflammation area with the Toledo project is by far the most important. So 40% of the people in discovery look for a new Toledo every day again. In fibrosis, about 30% of people who are up there are on complete novel mechanism of actions pushing forward for either lung fibrosis, either liver fibrosis.

Then we have the smaller areas as we call this. So inflammation, fibrosis are a strategic areas. We typically have as well 2 technical areas. Currently, we're switching between the diseases. So HBV is almost done. So you won't see it coming back next year. The new areas are OA and PCKD. PCKD is a polycystic kidney disease. And the metabolic area is an effort we started a couple of years ago is currently at its height and so will go down in terms of FTEs, but will keep on delivering a number of preclinical candidates planned over the coming years.

So these are our disease areas we focus on. With the expansion of the organization, we'll probably add one or 2 areas but that will come over time, and is not a topic for today. But all in all, we keep on being focused heavily on our strategic areas.

Portfolio R&D. Well, in discovery, we have around 30 projects. When I talk to my people -- my friends in academic area, they say, you're running a very hard model because you're stopping each year 6 projects. That's correct. We stopped 6 projects every year that as well gives us the room to start 6 to 7 novels. So we've been increasing the team slowly over the past years, the portfolio has grown a bit. Coming years as well as we go to the platform 2.0, this organization will substantially grow, will substantially deliver more over the coming years.

Let me start now with a view on a completely novel activity. This is a metabolic area. GLPG4059 is a small molecule. It is being orally dosed, and it hits a complete novel mechanism of action, which is more focused around how the body handles lipids. So it has nothing to do with STLG-2s, nothing with PD4s or whatever, is completely something coming out of the lipid area. But my scientists really came to me and said Piet this is really a target for type-2 diabetes. It has every promise we need to make it successful. So we believe we are the only company working currently on this target. I'm not going to disclose this. So we've been working for years first in rodents. And our rodent models are, in fact, completely normal mice we use. We put them for 12-week on what we call a western diet, which is high fats and high sugar intake. And then after 6 weeks, we start to dose the mice with the drug for 6 weeks.

So here, you see the outcome at the end of the 6 weeks, at the end of the 12 week of the experiments and 6 weeks of dosing. So what you can see is that the effect on the lipids, we always see a very clear drop of lipids circulating in the plasma. That's what we have observed. That -- the compound is given the dark green bars. We've included that to the reference just to give you an idea, is this marginal activity?

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Or is this decent activity, metformin. The gray are the healthy mice which are keep on the normal diet. The orange bars are the ones that have been fed as well for 12 weeks.

But you have as well picked up quite early is a sustained decrease of body weight. So really, those mice lose a lot of fat and they lose body weight because they have much less fat in their body, similar to metformin here as well. Then as well finally, those mice, which is mice only, I agree with you, they handle much better all of the sugar content that they're getting. So they're fasting plasma glucose, that's what we measure in mice. It's much lower than in disease states. So really, by blocking this novel mechanim-of-action, we see a number of parameters, which we believe are important for type 2 diabetes, moving into the right direction.

Having been working for 3 years almost on, I said guys, It is time we confirm this as well in monkeys. So that's what we recently did. So now we are looking here to diabetic monkeys, they are older monkeys, and they have all of the symptoms of type 2 diabetes. So there are no healthy controls in this experiment, but we've added in yellow a box, where we combine our drug '4059 with metformin. The idea is if you move in type 2 diabetes, all patients will be on metformin and we want to illustrate that we don't block that activity. So it's not the idea really that with a single dose you see an increase in activity, it's just showing the principle when you combine them, patients will do well.

So again, on the left, the lipids there, a nice drop of lipids compared to the disease. In the middle of the body weight change again as well in monkey we see a nice drop the combo seems to be -- do a bit better in that, indeed in metformin. And here, we can measure HbA1c. So the glucose bond to hemoglobin. And as well, there, we see a nice effect. So that's one of the novel and the first projects in our metabolic program, which all in all is limited. But that has reached the stage where we currently are doing tox studies with it. Hope to move it into Phase I next year and then quickly move to type 2 diabetes patients, both as a monotherapy and on top of metformin. But just to give you a glimpse that we do more than just in inflammation and fibrosis only.

Most of you, of course, are waiting for Toledo update. I can understand that. So it's the biggest program in discovery. The biggest program in early development. And the whole thing keeps on being fired up every day. So in discovery, let me say, we're learning getting surprises every day. In development, we are moving nicely forward and getting close to the patients. So why are we so fired up on this mechanism of action? Well, let me try to explain you once more. So on the left, you see a normal healthy people like most of us in the room here. We have an immune system, which is ready to cope with infections, but which is kept under control by the purple dots, dots which are the anti-inflammatory cytokines. Even unfortunately, you're suffering from an autoimmune disease. In fact, what happens is that your pro-inflammatory cytokines are in a clear access, and you don't have sufficient of what you call here the the immuno cytokines. So what's happening now with most of current therapies. What we do is, well, we restore the balance. So as there is no excess anymore of pro-inflammatory cytokines, they don't attack the body, you don't get ulcers anymore, you don't get joints which are attacked you put it nicely into balance, so the disease stops. But unfortunately, we all pay a price at that moment because for the next infections, these people don't have a fully powered immune system. And that's what we in fact we observe with Toledo, and that's why we're fired up and so driven to bring these drugs to patients and to the market. In effect we again restore balance, but we see that effect we have an intact immune system. So these patients or patients in the future when taking the Toledo compounds, they should be much more ready to cope with infections we all get every year. So that's what tells us that if we can bring this to patients, we should come with a complete new wave of anti-inflammatory drugs here with Toledo.

So this we believe we have some data to support it. So let me show here. So with '3312, our first compound in the clinic, moving to IBD patients. We really went every layer we could, we could go to go and ask ourselves, is this not present. in the colon, is this systemic activities, is this local activity? So we really went down measures the compounds in every level, but also measured the cytokines in the colon. So it's not plasma, in the colon. You see exactly what I showed you on the previous slide is that in those disease models you see an increase of anti -- of TNF levels. And with Toledo, you push them back. And unique here is that indeed, the anti-inflammatory cytokines like IL-10 in disease you will see a drop. So the animals are not well prepared there or it's out of balance and Toledo pushes that up nicely. So according to us, it's the only approach there in the field that has this dual mechanism of action, and that will restore the immunity in a way that patients won't suffer from their autoimmune disorder and will be better prepared if there's an infection upcoming. So that's why we're so fired up. That's why we maintain the large team. That's why we maintain bringing novel PCCs forward.

We have 2 in the clinic currently, we have '3312. Moving to IBD patients. We have '3970, we started Phase I this year, it's moving to

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multiple ascending dosing. This compound, compared to '3312, shows activity of almost the same dose level across all the models. So this is a compound we will develop broadly across indications. So these are a couple of examples. We have much more data, but on the joint model. So for '3312, we have fantastic activity in IBD, but you need to dose much higher in the joint models. So '3970 is almost the same dose we're using there.

So you can see on the left in the CIA model for RA, a nice drop of the disease activity on the right in IL-23, psoriatic arthritis model also a nice drop of disease activity. So this compound really works in skin, in joints, in the GI track across all of the models, and I'll show you that later again.

So we have different compounds there, and we keep on improving upon all of their properties. So the family has 3 related targets. The disclosure of the target, I said, is not for today. So you can keep on guessing and doing whatever you like. But so '3312 is hitting each of these 3 targets. We call it a PanTOL compound. '3970 is only hitting TOL2 and TOL3. But '4399 is a TOL3 selective. It shows only the drop of TNF does not show the IL-10. So it's a bit of a stranger in the family, but we're going to see them push this forward into proof-of-concept to see how well only this part of the activity as well is working. If then, it's a fantastic drug, w'e can still decide. But 4399 does not have the full promise I want to stress that of what the '3970 or '3312 has.

As you know, we test these compounds across multiple indications in the autoimmune space. And we go beyond the classic borders of autoimmunity. The compounds don't work everywhere. None of the compounds works for example in OA, that's clear, very clear. '3312 and '3970 has very similar profile with the difference that '3970, as it's going better into all the tissues also shows some good activity in osteoporosis models. Fibrosis has been a surprise for us. We are driving deeper into that and might take the compounds to that area later, if we fully understand what's happening there. So Tol3, as I said to you, '4399 the tol3 it be selective company has a different profile. We don't see activity in IBD. So that IL-10 is really needed for that activity. We don't see activity in skin models again, that's part of the activities for some of the diseases really essential, but in the joint models, '4399 is as good as any other compounds we've ever seen. We keep on pushing further, we're making TOL2 selectives we're mixing TOL2, TOL3, we always get surprises. So -- but we keep on bringing novel chemistries, novel compounds forward, and we'll keep on doing that next year. And then next year -- and this year -- next year we'll have patient data, and I'll show you what studies we plan. So for '3312, we start the UC study that's going well. We developed a compound as well for Crohn's later. '3970, we'll explore much broader.

So we'll start 3 waves of studies. First start a couple of short-term PoCs to validate what we see in animals, we can translate into humans, will be the classic or short-term PoCs in inflammatory disorders. Middle of the year, we plan to start dose-ranging. We really want to pick a right dose earlier in the program as well. We might start some longer-term Pocs studies as well there. And finally, those other indications, which are beyond autoimmune probably will start around year-end next year. So they are shifting back also you really first want to understand fully what is this compound doing across the autoimmune spectrum and move it forward quickly there, but not forget that we also see activity in the fibrosis models and in the OP models. So those indications are our plans, so far my update for the Toledo today.

Since we have that huge deal with Gilead, unfortunately the question I get everywhere is not how good is your science, what are you going to do with the money? Which, is in fact, a quite boring question for you, what are you going to do with the money? Just want to find novel drugs is the answer. But we've been thinking for a long-term, how can we do things better because working on novel mechanism-of-actions, we had a limited pool of genes that we're targeting. How -- and what's the smart way to expand here? So I want to share with you our plans there as well.

So our current approach in drug discovery has been for 20 years the same. We find novel targets. We drug them. And when we have a safe drug to put in the clinic, we do a proof-of-concept, and when a proof of concept is fantastic, Walid can take it further into Phase III. And dose-rangers and we'll bring it into the market and we start to sell it. That's a very simple 3-step approach.

One of the limitations we saw in this over past years is that finding novel targets in that selective pool of 6,000 drugable genes was becoming harder and harder. So at the beginning, we had only 15 and then 10. Takes 3, so we started to do, say, well, this pool probably, it's a bit too small. So first that we're going to do is really enlarge the pool and not going to the drugable only, but to the protein coding genome. So we'll expand our pool from which we're going to start fishing.

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There's one risk if you start to expand the pool. The risk is that at the end of the screening, we're looking to a galaxy of all targets that are lighting up, you have no clue how are we going to start here. So what we need to do to keep science on track there is to really as well develop the pathway. So the pathways tell in fact within the disease how the different, or some of those normal targets might be connected to science we know might be interlinked as well.

On the left, you see here, if you just work on novel targets, and sometimes it's a scary picture, I can share that with you, that for some of those targets, we discovered, we have no clue what is going to work. Even then sometimes we start, but these are really the very difficult than the slow-moving programs. If you have an idea of which part where they're working, drug discovery efforts have become really much more efficient, and you a have goal and need and a way to move forward. So you really want to map this much better out other than wait for others to bring us a map.

But in fact what you really want to approach is that you have the complete disease network. So you want to understand what's helping the patient, what are the symptoms, the science or the biomarkers, how is all this playing, how is this traffic coming together in certain nodes so that you know if I hit it there, I'm going to see that if I hit it somewhere else, this is going to be the impact.

So we are going to much more focus on novel targets we can link to pathways and build the disease that's around us so that we can really select the better pathways out of diseases. So those pathways, that's something I invented to give a short talk here. Well in fact pathways is what we've learned over the past years how it works in patients. If you look here, if you would take an old school book on autoimmune disorders, they would order them by tissue. You will have the disease of the joint together. If you have had the disease of the skin together, you will have the diseases of the GI together. And the vascular is a group of its own.

After developing multiple drugs, in fact, we've learned that, in fact, you better group them by pathway. Some of these diseases are sensitive to IL-23, some on to IL-17. There is a difference between IL-6 and IL-1. So what we plan to do is what we've learned over the past 15 years to really get that info much earlier out of the patients and out of the cells.

So we're really going add to the whole system, a level of patient data. So recent years, the technologies have become available that allow you to look 3 levels lower than what we did until now. Let me give you an example here, these are how we today look into the joints of RA patients. We have always worked with tissues out of RA patients where we took the tissue as a whole and looked to the mixture. Today, with single cell sequencing, you can degrade a tissue up to a single cell level, then you're going to sequence a couple of thousand cells. And now you can cluster those cells according to their gene expression into functional times. So you can separate out the monocytes, the T-cells, the B-cells the fibroblasts, whatever. And you can measure the amount. That's the first and that's an easy level.

We can go a little deeper. If now look to what JAK is in all these cells available. We could have saved ourselves 10 years of debate between JAK1, JAK2 and JAK3. There's only one JAK, which is present in all of those cells. So if you really want to block in the joint, IL- 6 signaling, a choice is made in a minute here. So by looking to those cells, how they are active and how the different cell types work, you come to the right choices, much more quicker than you ever did today.

Well, of interest is a bit the blue gray clustering there, where people, in fact, never talk about. When we talk about our drugs in autoimmunity we talk about T cells and B cells, and that's not as difficult as it is. We never talk about the fibroblasts. So you have different types of fibroblasts, really because informative if you can now cluster these or you can bring them back to how a joint really look like. So see 4 colors for the 4 different types of fibroblasts. You can see you have a green and red, an orange and blue. And so one type of fibrosis is the lining, second layer is blue one. You have the red ones which are in the blood vessels, and you have the green ones, which are just around the blood vessels. So we with all this type of information and now looking what's going wrong in patients, what's going wrong in patients that don't respond will be much better fit to select the promising targets and developing better drugs for even RA where we stand today. So that's the first level on how we're going to upgrade our target of the platform.

Next to that, we've always been -- not always, we've been -- we are extremely proud of our small molecule platform, but we've also had a couple of targets where we blocked the enzyme, and nothing happened in the disease, where we could not block the enzyme, where it was the target let's say we do everything right, but we don't find a way to modulate. So we're going to as well expand on the type of

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drugs we want to develop.

Let me explain quite simple. Industry always worked on the right of this cartoon, we always made compounds that activate or block targets. So these are the small molecules that has been the origin of this industry, has been the focus. They've supplemented that with peptides and antibodies, cell therapies, but we've always worked on the right-hand side.

In theory, for every target we drug today, you could go to the genome, knock it out, you could say, okay, let's keep the genome intact, we could be -- we go and work at the RNA level, doing an siRNA or an antisense.

While we work on the protein, but we don't want to influence the function of the protein, we want to influence the concentration of the protein. If you just make it a protein disappear as well, you, in theory, could have a good type of novel drugs. So what have we selected out of these modalities? So we've highlighted them in orange. So we will keep our work on small modules, so don't panic, here and out of the room, they're going to change everything, but we're going to build further on our expertise. Plus we're going to add on what we've been working on in the lab for a number of years, is to as soon as we have binders to proteins, direct those binders to the enzymes that degrade or the cellular components that degrade proteins as well. So that's what they call PROTACs. We also can do the inverse trick what we learned in the CF area. You can add compounds that influence the confirmation of the protein, so the protein is much prone to the enzymes.

The other hand, if you see what our platform does, our platform, in fact, is a knockout platform or knockdown platform. We're knocking down our target. So we as well are going to invest into siRNA type of works, where we're going to work at that level to decrease the amount of protein. Quite honestly, what we've seen in the HBV field, it tells you this technology is ready for more diseases than HBV and a number of muscle diseases only.

In an overview, we'll keep on doing small molecule discovery, don't worry. So those targets where an inhibitor and activator doesn't work, we're going to use other tricks to degrade the amount of protein is going to be on first waves the PROTACs later to small molecules because it takes time to build that platform.

And then finally, in order to also much more efficient drug discovery going to do siRNA type of -- going to bring in, siRNA type of work to really from our knockdown platform immediately map the pathways, immediately select the models so that we much faster can select out the promising targets in the drugs. And eventually, if you're good enough even bring in siRNA to the market or to the clinic ourselves.

So that's the expansion we are planning, we are actively looking and searching. So we are going to build, collaborate, acquire a number of -- what we need to do to indeed get this ready within a couple of years.

Looking at the highest level. So currently, we work on about 6,000 genes. Yearly, gets more or less 6 more molecule targets out of that. And that translates then into 3 PCCs, on a yearly basis. That's currently, if you look on how we plan at the organization. Over the coming years, we're going to expand the pool from 6,000 to more than 20,000. We'll have more hits, so we'll need the pathways to guide us, to help us selecting the targets. But with siRNAs and all of that we can take a number of targets immediately to the right track here. And we as well have more starting points for small molecules. So idea is we'll be able of starting more small module programs and deliver more PCCs, either as the classic small molecules, either as PROTACs that degrades the proteins, either as siRNAs that inhibits the formation of the proteins.

That's all for my talk. I now invite Walid to tell us on filgotinib, our latest views.

Walid Abi-Saab ***Galapagos NV - Chief Medical Officer***

Okay. Good morning, everybody. Good afternoon for some of you who are on the phone, joining from other parts of the world. Thank you, Piet, for walking us through this early part.

So let me tell you a little bit about filgotinib and where we are heading. So we've been talking about filgotinib. It's really been a pipeline in the drug. We're very happy with the way this program has been progressing very nicely, and it's essentially profile and its risk-benefit

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profile has been becoming more and more crystallized with every new data that we get.

As you know, earlier this summer, we submitted the dossier in Europe. More recently, we submitted the dossier for approval in Japan. And we're working relentlessly on finishing up the dossier and submitting it to the U.S. before the end of the year.

Our Phase III program in IBD is progressing very nicely. This -- both studies in UC and CD, Crohn's disease and also ulcerative colitis -- also the ulcerative colitis program, as we've been communicating before, finished recruitment. And now we're going through the in-life phase of the trial, and we expect to have top line results by the second quarter of this coming year.

We have also going beyond -- in other rheumatology indications beyond RA, in particular, psoriatic arthritis and ankylosing spondylitis. Our psoriatic arthritis program, I'll talk about it a bit later today is actually active now and our ankylosing spondylitis program is getting ready for a start early next year.

When you look at the RA space, you realize how large of a market inflammation is expected to be by 2027, we're talking about $65 billion. And if you look at the indications that we're in beyond RA, particularly, IBD and ankylosing spondylitis, psoratic arthritis, those would represent more than 60% of the market. And in those spaces, particularly in the IBD space, which is the lion's share of that additional space, we will be in a very competitive position or being either first or second to market. We believe this will put us in a very good shape considering our efficacy profile that continues to manifest itself and also the very favorable safety profile that we have, giving us the potential to be best in

(technical difficulty)

In psoratic arthritis, we're getting ready to move on into the Phase III program. This is a disease with a high unmet medical need. These are -- this represents about 1/3 of the patients of psoriasis, they have joint involvement as well. And these tend to be more difficult to treat than RA. Usually, the response rates are a little bit lower than RA. And this is the EQUATOR study that we shared with you last year, we were quite impressed by the level of efficacy that we've seen in this trial. This is a trial of about 65 patients per arm. So 130 total. Given filgotinib 200 milligram or placebo in a 1:1 ratio, treated for 16 weeks. And you can see the ACR20 response here are in the upper 80s. ACR50, more than 50% and even ACR70 in a short duration in these more difficult-to-treat type of population is getting close to 30%. These data look very promising. And based on that, we continue development of this compound.

Just recently at ACR, we shared the data from the long-term extension of this trial. So at the end of those 16 weeks, those who are on placebo will get given an open-label fashion, filgotinib 200. And those who are on filgotinib 200 will continue their treatment. And here, you can see how the effects have been sustained, both on ACR20, ACR50 and ACR80. The numbers continue to look very good and are maintained throughout the year.

But also the safety story continues to be as impressive and consistent with what we've seen before. On the left-hand side, these are the safety that were seeing in the first 16 weeks of treatment with filgotinib and placebo, so you can compare. And we here, we selected the adverse events of interest like serious infections, opportunistic infections, zoster, DVTs and so on and so forth. And what you can see on the right-hand side, which comprises all the data up to week 52, that there's been no significant additional events that we've seen. So no DVTs or PEs, no additional death. There was 1 additional MACE, maybe couple of serious infections. And what you see on the right-hand graph for the totality of the safety is we express it as event per 100 patient years because that also would be helpful to compare to the rest of the data that we generate from RA program. And as you can see, those rates continue to be looking very favorable and very consistent with our RA program. So 1 of the key things for me for filgotinib really has been very -- performing in a very consistent manner regardless of which indication you put it in, which makes me feel very good about the likelihood of success in the future, when it becomes available to patients.

So let's talk a little bit about the Phase III program that we're moving forward with in ankylosing spondylitis. It's called PENGUIN. It's going to be similar to our RA program but at a high level, and that we will explore both doses of filgotinib, 100 and 200. PENGUIN 1. High level, it looks like FINCH 1, if you want to. This is in methotrexate IR. It's a 24-week, double-blind, placebo-controlled and active control. So adalimumab is also the active control. The primary endpoint will be at week 12. There will be 2 doses of filgotinib. And then at

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the end of those 24 weeks, the patients will be then either continue on their original dose, if they were randomized to filgotinib 100 to 200. But if they were on placebo or adalimumab, they will be re-randomized to filgotinib 100 to 200. And they will continue equivalent to a FINCH 4 to -- with a long-term extension, where their treatment assignment to dose will be blinded, but everybody will be on filgotnib.

PENGUIN 2 is the -- in the biological IR population. It will be 2 doses versus placebo. The double-blind portion of the study will be 16 weeks. Primary endpoint will be at week 12. And primary endpoint, by the way, for both studies will be ACR20. And again, at the end of the 16 weeks, the patients who are on placebo would be re-randomized to filgotnib 100 and 200. And those who were on 100, 200 will continue in a blinded manner in terms of dose assignment

(technical difficulty)

So we've been talking from the beginning that we want to go after JAK1. That's been something that is driven from the science, and you've heard Piet talk about it earlier today as well about how we go about looking at these things. So from the get-go, our hypothesis was you need to block JAK1. That's the only thing you need, to bring inflammation under control. And sparing JAK2 and JAK3 pathways will allow these pathways to continue to be active and functional as they should be in the body, if you don't need to block them. Otherwise, we are going to start earning off-target activities and increase in side effects. And we designed filgotinib specifically with that in mind, and as you can see on the panel on the right, we've shown this data before in our whole blood assay, and those have been validated from some external work from McInnes and others have been published, that our compound has been highly selective for JAK1 versus JAK2, on the left-hand side graph. And also highly selective JAK1 versus JAK3 in the right-hand side graph, which -- with about 25-fold in both cases. So this is specifically designed so that you have enough headroom so that when you go in the clinic, you go as high as possible, so that you can achieve maximum JAK1 inhibition in the majority of patients without hitting JAK2 and -- or JAK3 and stay away from any liability.

And actually, that's kind of what we see when you look at the totality of the data, I'm not going to recap this because we've been published, we've been talking about it for some time. We've seen that the JAK1 inhibition, filgotinib, is sufficient to address inflammation. If you look at our efficacy across the board, you see that we work early on, we have deep and sustained efficacy that is maintained. And also, we work across the board, whether you have early RA and you're naive to methotrexate, whether you are methotrexate in complete responder, or even, on the other end of the spectrum, biologic and completed responders. And as a matter of fact, we've also shown recently some subgroup analysis at ACR, where it doesn't matter whether you've been exposed to 1, 2 or 3 previous -- or -- 3 or more of previous biologics, and you have not responded, your response to filgotinib is the same. So very robust, very sustained efficacy. And you see it very early. Importantly, this comes without additional liability of off-target activities. So these are the data summarize the safety of some key important elements that if you think about the JAK class, in general, people have raised questions, well, we are not sure a little bit about the risk -- increased risk of serious infections, increased risk of herpes or increased risk of thromboembolic events? Well, here they are. These are data from our FINCH program, more than 3,500 people, more than 2,000 exposed to filgotinib on the far right-hand column. You have the people on adalimumab, in the middle, about 300 patients. And those on the left are the placebo and methotrexate active treatment from FINCH 1, FINCH 2, FINCH 3 lumped together for about 1,000 patients. And here, you can see the risk of serious infections, herpes, DVTs and death. They're really similar across the board. There's no significant uptick in the case of filgotinib, and they look very competitive when you look at the -- what's been published out there, what's known now out there from other JAK inhibitors.

And here, you look at the data from our DARWIN 3 study. This is a long-term extension of our DARWIN program. We've been reporting on it on an ongoing basis as we accrue more data. A few days ago, we showed this data at ACR. And you can see up to week 156, we have more than 2,200 patient year exposure. And here, I'm showing the data in events per 100 patient years. Again, you see these rates for serious infection, zoster, DVT, PE and death, the rates are quite low. I point your attention for DVTs and PEs. I'm sure you've spotted it as well, the rate is 0.1, and this is very, very low if you've been looking at data from other JAKs out there as well.

So to conclude, we believe that filgotinib has been designed with that selectivity in mind. And we're very happy to see that clinically, it continues to display JAK1 selectivity. It brings us strong efficacy across all the signs of symptoms of RA, across a wide range of RA patients from the mildest to the most severe patient. It does that in a way that does not interfere with other JAK signaling. And you can see that clearly by the fact that we normalized certain laboratory parameters that are abnormal inflammation, specifically, I'm thinking about hemoglobin changes and platelet changes. And in addition, it has a clear safety profile, which is, in our opinion, a result of this

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high selectivity. And you see that across the board and continues to be confirmed, the more data we add.

So I -- with that, I'm going to finish my talk on filgotinib and switch gears. And actually, we are very fortunate today to have with us professor, Toby Maher, who's been actually with the program, '1690, longer than I have, since he's been involved in the design of the FLORA study with us, from the beginning he's been the lead PI on that study. And he's been also with us with the ISABELA and lead program -- the lead PI on this. I'll just say a couple of words about who he is, and then we'll tell you much more about it in a minute. So professor Maher, he is a professor of interstitial lung disease at the National Heart and Lung Institute at the Imperial College in London. He's also Director of Respiratory Research at the Royal Brompton Hospital in London as well. And we've been very fortunate to be working with him for the past several years and many more to go. Toby?

Toby Maher

Just far too many words about me. But I'm going to talk to you about idiopathic pulmonary fibrosis, which obviously has been a large focus for Galapagos over recent years. Just to tell you a little bit about myself in my own words. I work here at the Royal Brompton Hospital, was built in 1844, which makes it quite old, I guess, by American standards.

It was originally a TB sanitorium. It became a thoracic diseases hospital. And the lady there, Dan Margaret Turner Warrick, actually set up our lung fibrosis units in the 1960s, a long time before anyone else became interested in fibrosis lung disease. As a consequence, I currently -- or my service currently looks after about 1,500 new patients with pulmonary fibrosis each year. We have about 5,000 patients under our care at any one time. That's given me a great opportunity to run clinical trials. And we've recruited more than 500 patients into clinical trials over the last decade. So we've got extensive background in running clinical studies. And as Walid said, I got to know Galapagos. I think it was 2013 or 2014. So a fair while ago now.

And so what is IPF. So IPF is a progressive scarring disorder of the lung. It tends to affect older adults. In many ways, you can think of it as the sort of lung equivalent of Alzheimer's disease. It's -- the lung prematurely aging in advance of the rest of the individual. And as the lung scars it becomes less effective as an organ of gas exchange. Obviously, our lungs are working to get oxygen into our body, carbon dioxide of it. As that scarring process progresses people become breathless. They ultimately slip into respiratory failure. And ultimately, they die as a consequence of their disease.

It's a pretty nasty condition to have. Without treatment the median survival is about 2 to 3 years from diagnosis. 5-year survival is around 20%. And the graph here just compares the 5-year survival of idiopathic pulmonary fibrosis to a variety of cancers. And I think one thing to notice is that the 5 years slope of many of these cancers is a lot better now than it was 20 years ago. The same cannot be said for IPF, where we've seen little change in outcome until very recently. And moreover, IPF has a prognosis that's very similar to adenocarcinoma of the lung. So whilst it's not a malignant disease, it has an outlook akin to malignancy.

What's important is that it's becoming more common. So at the moment, FDA, European Medicines Agency consider IPF to be an orphan disease. Truth be told it isn't. In the United Kingdom, 1 in every 100 people who dies, dies as a consequence of IPF. Same is probably true in the U.S. Probably 100 of us in this room, so at least 1 of us is going to go from IPF. So probably not an orphan disease, but we won't tell the FDA that.

At the moment, there are probably 40,000 to 50,000 new diagnoses of IPF in the U.S. each year. There are probably 250,000 or more people living with the condition as it stands. As I told you, it's a disease of aging. Our average patient is a man in his mid-to-late 60s. We suspect that men are more effective than women, probably because of past smoking habits and also because of exposure to dust in the industrial setting.

That said, IPF doesn't really respect social class, and it's a disease that we see affecting a wide range of individuals.

We've begun to understand a lot about the pathogenesis of the disease, which is obviously important when it comes to thinking about developing new treatments. We recognize that there's a genetic component. So about 5% to 10% of our patients will have a family member who's also suffered with pulmonary fibrosis.

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And we are increasingly recognizing the genes that are responsible for making individual susceptible to developing the disease. The second thing that's important is a lifetime of injury to the lung. So obviously, we're breathing in 5 liters of air every minute, that air contains dust, contains other people's cigarette smoke, it contains viral and bacterial particles, and all of those things are causing little bits of damage to our lungs day in, day out. And it seems there is a threshold at which once you increase the level of damage that you experienced during a lifetime, you become more likely to develop IPF. And then the final piece of the jigsaw is getting older. And I think those factors are important because we are seeing the disease increase in incidents. We have, in the last 20 years, seen a doubling in the number of new cases. And we haven't seen that plateau yet. And that's partly because we have an aging population. It's partly, I suspect, because we are seeing changing patterns of air pollution. We're seeing damage from microparticles, diesel fuel, which may well be triggering damage that leads to fibrosis. And I think the third important thing is we're getting better at treating all these other diseases, like cardiovascular disease and malignancy. And as a consequence, our patients are living long enough to get IPF. Once the disease triggers, we see activation of multiple pathways involved in the normal wound healing response, and that leads to fibroproliferation and fibrosis. It's the same process that would happen if you scare the skin after injury or surgery. But it becomes uncontrolled and self-perpetuating in the lungs of patients with the disease. As I've alluded to, clinically, we see our patients become progressively breathless. At the start of disease, they're only breathless when they heavily exert themselves. By end of disease, they'll be oxygen dependent. And it's worth reiterating that the majority of patients who develop IPF die from IPF. This is not something like prostate cancer, where 80% of the population gets it, but only a small proportion die from it. Instead 80% of patients who get IPF die from respiratory failure as a consequence of their disease.

From a clinical perspective, we do see different patterns of disease behavior. We typically measure disease progression using force vital capacity, which is a measure of lung volume. Get patients to blow out from a maximal inspiratory effort all the way out. And that gives you a measure of lung volume.

We've used this technique to sort of measure patient day-by-day disease behavior. The graph here represents 1 individual who's done his forced vital capacity every day for 18 months. You can see the gradual rate of progression in his disease. He lost about 10% of his lung function in 12 months. This is another individual, much more rapidly progressive disease. He died 220 days after entering this study. And then this is the third pattern that we see. So this patient had an acute deterioration. And actually, patients with pulmonary fibrosis are uniquely susceptible to lung injury. So when they develop something like an infection, they get widespread inflammation and damage of the lungs. And once that happens, they've got a 50% chance of being dead within the next month.

This patient actually started off with well-preserved lung function. And you can see after the deterioration his lung function plateaued for a while. Nonetheless, these episodes affect about 1 in 20 of our patients each year and are 1 of the leading causes of death that we see.

We can use forced vital capacity to understand disease progression in the individual patient. We've also used force vital capacity to help develop better trials. And the FDA are now very happy with using a rate of change in forced vital capacity as their primary endpoint of choice for approval studies in IPF.

Just -- I want to keep hammering on how bad this disease is. So in case you haven't got the message, bad disease. None of us want to, but one of us probably will get it. This is just what happens to the patients I see in my clinic.

So if I see 100 new patients in a month, I can pretty much work out what will happen to them over the next 3 to 5 years.

Unfortunately, people still present quite late with this disease so even at diagnosis, about 15% of patients will already be oxygen requiring. If I go a year down the line, during that first year, we have some of those patients with very rapidly progressive disease, about 20% of patients will be dead by the end of 1 year and some of the remainder will have slipped into respiratory failure. After the first year, the death rate sort of settle down at about 15% a year which means that by the end of year 3, half the population are dead and a proportion now are oxygen requiring.

And if we fast forward to 5 years, somewhere around 20% of my patients will still be alive 5 years after that initial diagnosis, but only a small proportion of them will be off oxygen and actually leading any semblance of a normal life.

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So we have seen the development of treatments. There are 2 FDA approved therapies. There is pirfenidone. This was the pivotal trial, which showed that pirfenidone slowed the rate of disease decline as measured by FVC by about 50%. And then the other drug is nintedanib, again, a similar magnitude of benefits in terms of slowing FVC decline.

Those drugs were both approved in late 2014. So we've now got 5 or more years' experience in using them, and we are beginning to see some improvements in survival for our patients. Both the European and Australian registry have being able to show that even when you normalize for baseline disease severity, there appears to be an improvement for patients beta with antifibrotic drugs. But I'll highlight this graph here. So this was some work we did with data available from open-label trials of patients on pirfenidone. And these patients have been on treatment for 10 years or more. Comparing them to historic severity matched patients, we found that pirfenidone probably gives 2 years extra life expectancy to our patients. But the third line on the graph is the normal life expectancy for the average 67 year old in a western population, 67 being the average age of the patients in the clinical trial.

So you can see that patients even on antifibrotic drug still have a deficit in life expectancy of approximately 12 to 15 years. So although we've seen some advances, we've still got a long way to go to try and make life normal for our patients with this disease.

And then I think the other thing that's been important is that we've now seen the use of these antifibrotic drugs in other forms of lung fibrosis. So whilst we focused on idiopathic pulmonary fibrosis as the worst of the fibrosing lung diseases, we actually, for every one of our IPF patients, see 2 other patients with different forms of fibrosis. So it can arise in the context of connective tissue disease or rheumatoid arthritis, systemic sclerosis. We also see a range of other conditions, things like asbestosis or chronic hypersensitivity pneumonitis. And all of these core scarring of the lungs and the majority of them go on to cause death sometime a little more slowly than with idiopathic pulmonary fibrosis.

But this was the data from the pivotal study done with nintedanib in patients with Scleroderma associated ILD. And the FDA have now approved nintedanib for this indication, and they've given it breakthrough designation for chronic fibrosis of any form in the lung. And so the hope would be that if we can identify another drug that treats IPF, we will be able to demonstrate that, that is effective in that even bigger population of patients who also have fibrosis.

As Walid said, I was fortunate enough to be involved with the FLORA study, the Phase II study of GPLG1690 and IPF patients. We presented the data, I didn't choose this picture, by the way, I wouldn't normally put pictures of myself in a presentation, it was done on my behalf. But this was us presenting the data at the ATS meeting a year ago. And Walid, I think, is going to talk to the results in a second.

So I'll just wrap up. These are pictures of my patients attending open days that we held. I still see lots of people dying very sadly of respiratory failure. It's a nasty way to go. As I've told you, it's not truly an orphan disease. It's becoming increasingly common. We've shown with pirfenidone an nintedanib that fibrosis can be treated, and there is a pathway to approval. But those drugs have tolerability issues, and we've still got a long way to go to restore normal life expectancy to the patients I see in clinic. So from my perspective, it's fantastic that Galapagos are working on this disease.

Walid Abi-Saab ***Galapagos NV - Chief Medical Officer***

Very good. Well, thank you, Toby. It's a very sobering talk. But at the same time, it's also very motivating for those of us who are working on this disease. As you know, Galapagos really is putting IPF in its crosshairs, and we have a number of approaches to try and tackle this disease. So let me tell you a little bit about our program with 1690. I think Toby touched on this a bit, the fact that the drugs that we have currently have significant limitations. Although they do reduce FVC decline by about 50%, the problem is also that they have some tolerability issues and in real-world settings about 1/4 of the patients do not take these medications, and as they discontinue about at a rate of about 25% per year because they don't tolerate it or they don't see effects from it.

Despite that, the market size in 2018 was more than $2 billion for these 2 drugs pirfenidone and nintedanib.

So maybe by a little bit of background, just bear with me, I'm just going to walk you through a bit our story there.

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So where does -- how does '1690 work. So we need to take a step back and look at the autotaxin as a target. So on the left-hand side of the graph, you see a cartoon, which is taken from our New England Journal paper by David Lederer. Where he was reviewing the various negative actions of these compounds. And you can see the pathway that we're talking about here highlighted. So the autotaxin enzyme is widely expressed. It is responsible for converting lysophosphatidic choline to the bioactive lipid lysophosphatidic acid, which in turn then works through a number of different receptors of at least 60 protein coupled receptors to produce its activity. It's known to essentially regulate diverse cellular processes such as proliferation, differentiation and migration. And these have been involved and have been linked to a variety of diseases, particularly in inflammation and fibrosis.

So one of the things about '1690 is that it has a dual role in the way it blocks autotaxin. So essentially, it blocks the Type IV enzyme, which is not only responsible for blocking the enzyme itself, but it also blocks the transport of LPA1 as foreign. So it has a dual mechanism of action, which is -- which we expect that it will render it much more potent in controlling LPA levels.

And based on that science, and there is a lot more which I'm skipping over that were done in Piet's labs. We embarked on the FLORA study, where we studied the small proof-of-concept study of about 23 patients, the effect of '1690 and 600-milligram once-daily over a period of 12 weeks. This trial was randomized 3:1 drug versus placebo. And we looked at a number of endpoints, including changes in LPA levels in the blood. And in addition, we looked at FVC. And the study was not powered to detect changes in FVC because of the size of it, it was mostly designed to look at safety and tolerability as well as pharmacodynamic effect, but we were very surprised by what we were able to see, which you can see here on the graph. It seems like stabilization of the lung functions and patients receiving drug. And about -- at the end of the trial of 12 weeks, there was about 100 ml difference between drug versus placebo in this office based spirometry. Actually, those data were corroborated by home based spirometry, and you can see these data in the last paper that was published, where also the difference over time is about 100 ml between the 2.

When you couple that with the clear effects that we've seen on imaging. We used functional respiratory imaging where we showed that the drug essentially stabilized the disease completely as opposed to the placebo patients who continue to decline, and a safety profile that looks very promising. We were very excited to embark in further development of this compound.

And as we are moving and preparing for it, we had a very nice surprise in that -- BMS actually validated the autotaxin pathway in patients with IPF. This is a study from BMS. This is a compound, if you remember on the previous slide that I showed with the cartoon. This is a compound that blocks LPA1 receptor, and this is a compound by BMS. It was put in a double-blind placebo-controlled trial, which was a reasonable size, about 50 per group, so 150 patients total treated for about 6 months. And you can see very nicely on the graph on the right-hand side, a dose-dependent effect in reduction in FVC decline over the time, reaching statistically significant at the top dose.

Now unfortunately, this drug had off-target activity that led to liver toxicity in humans, and the study was stopped. But BMS has published that they were able to find another molecule earlier in development with the same method of action that does not suffer from these toxicities in animals, and they are continuing now its development as far as I know.

So what does our ISABELA program look like? So this program is made of 2 identical trials, each comprising 750 patients that will be randomized in a 1:1 ratio to placebo or 2 doses of '1690 to 200 or 600 milligram once daily. But the patients will be virtually all comers. So essentially, patients who are on standard of care are welcome, whether that includes antifibrotic therapy as an pirfenidone or nintedanib or on neither of them, but they are on some supportive care or for whatever reason, they're not on this medication, they're allowed to come in. We expect in the end, and that's what we target to have about 1/3 of the patients on pirfenidone about 1/3 on nintedanib and 1/3 on neither of them because that is how the situation is in the western world, the U.S. and

(technical difficulty)

Because we're going on top of center of care, we can afford to keep the patients on their randomized treatment even after the primary endpoint at week 52 until the last patient crosses the 52-week line, which means everybody else would have gone much longer than that. And if you think about be 1.5 to 2 years in life parts of the study, so some patients would have been on this up to even 3 years. And this will allow us actually to capture in a randomized placebo-controlled way, these events that are rare, that often do not happen in a very short trial. Things that are very important, hard endpoints such as death or hospitalization due to respiratory failure.

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And here, you can see it also very clearly that this program is quite innovative. It's the largest that we have that has been done so far in IPF. It's the closest to real-world setting, which is very helpful for the clinicians later so that they know how the drug will perform in as closed setting as what they will see in the clinic, but also will generate not only data on the primary endpoint, which is FVC, which is a regulatory accepted endpoint, but also generate data on this important endpoint, such as death and respiratory hospitalization.

On top of that, we will have large safety data that -- of -- in 1,500 patients, but not only for a year, but also for much longer period of time.

So where are we in the program? This is a very large program. It's the first for us at Galapagos, we're very proud of it. We're going to be in approximately 250 sites worldwide. Here you can see the distribution spanning from North America to Latin America to Europe, of course, even Africa, and Southeast Asia, including Japan. Japan has been the recent addition, I should say, to our sites. After having discussed the plan and agreed to it with the PMDA, we're very happy now to start in Japan, and we'll be able to recruit the required number of patients, so that in the end, we will do a global submission in Japan, U.S. and Europe around the same time. And we don't have to do something specific for Japan.

We are -- virtually finished activating more than 90% of the sites. And the study is progressing very, very nicely. This gives you a little bit of the time line that we have. We're very happy to say that we are 1/3 of the period so far. So we have 500 patients on trial of the 1,500. This is ahead of plan that we have put together very carefully with our partner CRO. And I think the feedback that we get from the sites and from the various patient organizations, and I think maybe afterwards, you can ask Toby some questions himself as well has been very, very favorable.

We have also talked about the need to do futility analysis because, again, we jumped from a small study to a much larger program. We want to make sure that if the results in FLORA were completely a fluke and the drug doesn't do anything that we stop the program without -- before we go all the way out. In order to do that, we did a robust analysis statistically to be able to see what are the operating characteristics of the program such that we can identify what is the number of patients we would need in order to make the right decision. What you don't want to do is stop the program when the drug still has efficacy and could be meaningful in the end or let the program continue if you have nothing. And in doing so, we reached the conclusion that we need about 1/3 of the patients or about maybe 30% of the patients to clear week 52. And with that totality of the data, we will have enough information to make that decision in a wise way.

So it's really a robust futility analysis that we plan to conduct.

So we have reached the target, we think of it -- of the patient recruited now. Now we need to get them through the trial. So we expect by this time next year, should have enough of the information that we need. Then we need to bring the data in, analyze it, have it go through the Independent Data Monitoring Committee. So we expect that we'll be able to communicate on this in the first quarter of 2021 or early in that quarter as well.

And as I said, the recruitment is going very well. We're very excited. I can say with confidence that around this time next year, we should be done with the recruitment. And then you can imagine it's going to take a year to get through -- the patients to get through the treatment, and then the follow-up visits and getting the data in. So I expect that we should be able to communicate top line results in the early part of 2022.

And with that, I think I have covered all that I wanted to cover around IPF and filgotinib earlier, and I'll turn it over to Bart to tell us a little bit about how we're going to be growing and going forward from here?

Bart Filius ***Galapagos NV - CFO & COO***

Thank you, Walid. Let me say a few words in conclusion on how we're going to build out our company towards a fully integrated biopharma company and also take a quick second to reflect on the transaction that we signed earlier this year with our partner, Gilead. Now this slide is familiar to most of you, I would say, but I think given the size as well as the complexity of this transaction, I think it's

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worthwhile to highlight a couple of aspects here.

So first of all, our transaction that we have signed with Gilead is lasting 10 years. And as a result, it provides Galapagos a very important time period of independence and ability to invest in our own R&D platform with all the strengths that Piet and Walid have been showing earlier on this morning and allowing to build that forward on a stand-alone basis. It's also important from a financial point of view. We've received $4 billion of upfront for the transaction that we've signed in July, received this in August. And I remind you that there is further opt-in fees and milestones connected to the various programs. There is a license built in already on '1690, our program in IPF. But there is an opt-in moment for '1972, our osteoarthritis program, and that probably is going to take place somewhere in the course of next year, that type decision. And then there is further opt-in options when programs achieve the end of Phase II in our pipeline.

So significantly, also in terms of cash. Also an equity investment, this number has gone up since the previous slide that you've seen because Gilead has had also the rights to increase their stake to a level of 25% by the exercise of a specific warrant. That warrant has been exercised, meanwhile. And last week, they've increased their stake to 25.1%. I think we've issued a press release on this as well. And the total amounts received for the equity investment is now $1.5 billion.

And then finally, and that's obviously a key, key component of the economics of our collaboration with Gilead that we are receiving royalties on all our products, start at 20%, they go up to 24%. And that's where we see a very meaningful percentage. So in case you're wondering, is there future exposure economically to the U.S. at Galapagos? The answer is definitely, yes. We receive royalties on all of Gilead sales outside of Europe, and we retain 100% of the European economics. This is slightly different than the filgotinib transaction, whereas royalties and a profit share in Europe. And here, we retain all of Europe for Galapagos during the collaboration for all our programs.

And that's important because it allows us to make the next step also operationally and build the next leg to our company, which is also the commercial leg and make sure that we become a commercial powerhouse. First in Europe, and then you never know, down the line, when we'll make the shift also to the U.S. but first, we're focusing clearly as part of this transaction on Europe. And we do this with our first opportunity around filgotinib where we have a joint co-commercialization agreement in place, and we have extended the operational rights as part of the Gilead collaboration to be the launching company of filgotinib in rheumatoid arthritis in 3 out of the 5 EU5 countries. So Spain, France and Italy will be launched in RA by Galapagos, whereas Gilead will launch in Germany and the U.K. in RA. And we've swapped our territories for our subsequent launches. So when we go to IBD, first in line will be UC. We'll be launching in Germany and the U.K., and Gilead will launch in Spain, France and Italy. And not on this chart, but the Benelux has always been part of the exclusive territory for Galapagos. So we'll be launching all indications in Galapagos.

So in case you're wondering why is this the choice that we've made. Obviously, in any type of co-commercialization agreement, you need to make sure that you organize something as efficiently as possible in the best interest of the molecule. And we've came to the conclusion that a split by indication is the most efficient and appropriate manner to organize ourselves in this co-commercialization. And at the same time, it allows both companies also to book revenues in all of these territories. So we will be the revenue booking entity for Spain, France, Italy and the Benelux, whereas Germany and the U.K. for all indication sales revenue will be booked by Gilead.

It will also really allow us to build our infrastructure in a phased manner. So the focus clearly now is on those first countries, and we have a little bit more time -- even though not that much, a little bit more time to build out our own infrastructure also in Germany and the U.K. And as we are a lead company in those countries, we will be also responsible for the physical distribution, and we will also be the party who will negotiate and execute on access negotiations with governments.

So we are really in full launch mode with filgotinib as we speak. And that's important because obviously, time is short until actual launch. We hope to have an approval in Europe in the second half of 2020. So a little less than a year from now. And we will be launching very shortly thereafter in our countries. We anticipate that probably the Benelux countries or Holland will be one of the first, but France will follow very shortly thereafter, while Gilead will ensure that the launch in Germany, which is most likely going to be the first country in RA launch, will be executed perfectly.

And by doing so, we're establishing Galapagos in all of those countries, we are engaging with the key opinion leaders. We were already

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doing this for a while, obviously, we are bringing this forwards. We're working on the access. We have all the access teams in place, and we're building things like the physical supply chain and all the support functions as well. And then as I said, UC will give us a bit of extra time for Germany and the U.K., but not even that much. Earlier, you've seen that we expect the data in UC in the first half of 2020. If you then roll forward with a filing in Europe, we should be in a position perhaps by the end of '21 to be launching in UC. And this is the second indication when then the reimbursement process will be relatively smoother. We'll be probably launching towards the end of that year already, which is 2 years from now.

So this is a big feat for the company and a big opportunity as well. So in those next 2 years, you'll see us in France, Spain, Italy, Germany and the U.K., as I mentioned. But clearly, the objective is also then to grow in the rest of Europe, for all our other programs. And as I said before, for all our other programs, Europe is exclusive to Galapagos, and we will be then also launching '1690, hopefully, later on, in all of those other countries in Europe. So we're building our geographic footprint as expeditiously as possible.

So with that, let me conclude with 2 or 3 more slides on what I would call the outlook for Galapagos as a company and give you a bit of perspective also on the news flow for 2020 before we take the opportunity to take questions on all of the topics that we've had so far today in the presentations.

So first of all, let's remind ourselves, we're doing this to bring innovation to patients and innovations that work that I'd like to focus on and emphasize as much as possible.

2019 has been a transformative year for us with the Gilead collaboration and where we will also still apply for approval in the U.S. in RA later on in this year. So it's been an amazing year already. 2020, and I'll get back into a bit more detail in a second, we'll provide news flow on all of our key pipeline assets. So it's a very, very news flow rich year next year that's coming to us.

And then clearly, what's our ambition beyond, let me stress that one more time. It's a continued focus on innovation. I think today was a fantastic example of how we are innovating from the very early works in target discovery up until the very late works in late developments. And that is and will remain the focus of Galapagos.

We hope to be doing additional product launches, obviously, and build a European commercial powerhouse while doing so.

In 2020, more specifically, what can you expect from us in 2020? A lot. First of all, we'll have filgotinib -- the Phase III start in ankylosing spondylitis. Very importantly, obviously, for our filgotinib program as well is going to be the data readouts on ulcerative colitis in the first half of 2020. And then the launch of filgotinib, probably in the U.S. and Europe and Japan in 1 year as well. So it's going to be a big transformative year again for Galapagos there because of all the events around filgotinib.

Then very interestingly, we haven't spoken about that a lot today. We are waiting for the data, obviously, to come in the course of, again, the first half of next year is going to be our osteoarthritis compound, '1972. And that is going to be a very interesting data set. Phase 2 B, 850 patients that are going to be unblinding in the course of 2020. Then there is 2 earlier PoCs, one in -- with '1205 in IPF. And that's the PINTA trial. And then also we have a trial with our autotaxin inhibitor '1690 in systemic sclerosis, and we'll hope to see data with those 2 compounds in those 2 indications in the course of 2020 as well.

And then obviously, finally, Toledo. Piet pointed out earlier, we're going to be doing a UC study with our pan-TOL '3312, and we're going to be expecting top line data in patients next year. And then at the same time, we'll be starting with our second Toledo compound '3970 in multiple proof-of-concept studies as well.

So a very news flow rich 2020. And I would invite you to share the joy of the ride with us also next year. Pioneering for patients. That's what we're doing here. We discover, we dare, we care. I thank you for your attention.

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Elizabeth Goodwin ***Galapagos NV - VP of IR***

Thanks very much to all of our speakers. We're going to go now to the Q&A part of the session. We've got about 25 minutes left for that. I'm very pleased. I'd like to invite our operator, Elaine, now to explain to the callers how they can pose a question, and we'll alternate between the room and the phone. Go ahead, Elaine.

QUESTIONS AND ANSWERS

Operator

(Operator Instructions)

Elizabeth Goodwin ***Galapagos NV - VP of IR***

Okay, we are going to start here in New York with Brian Abrahams from RBC.

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

Two questions for me. One on IPF and one on Toledo. On '1690, I'm wondering what changed to sort of guide this -- your evolution and what proportion of patients might be required for the futility analysis. I think before you had talked about maybe 1/4 of the patients, now it sounds like closer to 1/3. I'm just wondering if that reflects any evolution in your understanding of the natural history of the disease or anything you're seeing with respect to the standard deviation or variability around blinded treatment effect in the ongoing study. And then on Toledo, it sounds like a lot of enthusiasm for 3970, in its potential. How do you weigh pursuit of inflammatory indications versus fibrosis indications given the potential you're seeing from the preclinical studies? And what's your level of confidence that TOL 1 is what's responsible for the systemic toxicity and that '3970 can be safely given systemically?

Walid Abi-Saab ***Galapagos NV - Chief Medical Officer***

Brian, I'll take the first question. So I can tell you there's -- this is not influenced by any new data or any changes in deviation or anything like that. It's fundamentally by us actually doing these models take time to build. And you want to test them out and make assumptions and try to get to what we call operational characteristics to essentially know how you can protect yourself about -- from making bad decisions, stopping a program that is promising or continuing with a program that is not. But that's really what drove it. We're still not far from the quarter of number of patients. So we're maybe 28 -- to be honest with you, is the number is 28%. But those have to cross the finish line, right? And that's something that we probably initially talked about it without really thinking that, oh, no, this has to be when these people cross the finish line and how many more behind them are in various stages because we take all of these data and put them in our model to help us with the decision. So I can guarantee you, it is not based on any new information that changed our assumptions for the worst, not at all. It's just a matter of getting together, putting the program in place and looking at our recruitment rates and how we're doing and when we can deliver that.

Piet Wigerinck ***Galapagos NV - Chief Scientific Officer***

Okay. On a -- related to first question, inflammatory versus other indications. It's a new concept, and we really want to grab it, develop it, understand it. And the science is better understood in the inflammatory area. So that's where we're going to push first hard, and it's also an area where a number of designs of studies allow you to serve, typically, faster. That's why we're going to do them earlier. While if you look to osteoporosis of fibrosis, these are long term studies. So that's where we say, let's take the time so that we understand the signs as well, very good and that we designed it right. But probably for those diseases anyway, you're talking 6 month studies, 12 month studies anyway, so -- and then you need the chronic tox package. On Tol 1 and systemic toxicity, we only put compounds in the clinic, which are safe. So in that sense, and every compound is different. What I've told you as well is that with every compound, the fact that you're more selective, you do something differently. So we've been mixing Tol 2 selective and Tol 3 selectives. And we're always surprised because sometimes it works or doesn't work. So just being present there, sometimes it does something which we never calculate, we never measure. So it's not too much on the toxicity, I would say, but every compound is different. We test the compound, and then we move forward. '3312 really in the -- IBD model was the best we've ever seen. So while if you look to the other models, it's nicely active, but you need to push the dose and that we say, "Okay. Why not trying '3970, which has benefited there?". Thank you.

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Elizabeth Goodwin ***Galapagos NV - VP of IR***

Before we go to the first question on the phone. I just want to remind everyone that we also have Dr. Maher here who could answer questions. He's agreed to stay, so that he can answer your questions if you have any. So you might want to take advantage of that opportunity.

Okay. Elaine, we can take the first question from the phone queue.

Operator

(Operator Instructions) We will take our first question from Mr. Peter Welford of Jefferies.

Peter James Welford ***Jefferies LLC, Research Division - Senior Equity Analyst***

Yes, sorry, I was on mute, I think. Apologies. So, firstly, just on IPF, actually a question for Professor Maher. I guess, I'm just curious, when you look at the treatment rate you're currently doing with the friendly dose and the internet. I guess I'm curious, what proportion of your patients you're currently treating with those drugs are equal -- sorry. And equally, have you gradually moved in from sort of severe to moderate to severe, to now more milder patients on these drugs? Or what sort of patients do you typically have to see before you put them on those therapies and why? And is there any, I guess, underlying effect as to your choice of the drug for those 2? And then, I guess, related to 1690 on that, given, obviously, that this was -- if you used, I guess, on -- in combination with existing therapy. I wonder if you could give us some sort of insights as to what the split of your patients would be if you were to enroll in ISABELA. As far as the 2 drugs and also naive patients who would be eligible to enroll in ISABELA, just so we can get the understanding from your perspective of also the patient that could be?

Toby Maher

The first part, and anyone that comes to see me, I will start them on treatment because I think the lung is a precious organ and we need to protect it. But my view is not shared by all pulmonologists and across Europe and the U.S., probably about 50% to 60% of patients with disease are currently getting access to treatment. That has steadily increased over the last 4 or 5 years, as people have gotten more comfortable with the idea of treating pulmonary fibrosis and the concept of trying to prevent progression. I think, as has been alluded to, there is a challenge around tolerability and in some institutions, about 30% of patients on both drugs for discontinuing within 12 months, which does speak to one of the unmet needs that we need drugs that are better tolerated for longer-term use.

The question about splits in a clinical trial. So in my practice, it's about 60% of patients from nintedanib, 40% pirfenidone. But I think we anticipated based on questions for sites in advance of the trial, that it would probably be a 50-50 split between the active treatment. But there would also be about 30% of patients who wouldn't be on treatment, either, because of reimbursement issues or because of intolerance.

Elizabeth Goodwin ***Galapagos NV - VP of IR***

We have a question in the back of the room from the Janney team.

Aaron Welch ***H.C. Wainwright & Co, LLC, Research Division - Analyst***

This is Aaron Welch from H.C. Wainwright. I have a question for Dr. Maher. So it looks like there is a significant variation in the rate of decline in the placebo groups from IPF trials. So I was wondering if you could give us any insight into any kind of baseline characteristics that may influence the different rates of decline. And also, if any of those baseline characteristics may be disclosed from the ongoing IPF trial?

Toby Maher

So one has to be a little bit cautious interpreting the different trials because a lot of the current difference in the placebo group is purely statistical. And it's dependent on how the analyses have been done. So we've now tended to move to mixed effects models, which get over the problem that you'll be missing about 20% of endpoint data at week 52. Historically, some of the studies would use last observation carried forward and they would impute to 0, the dead patients. And as soon as you impute to 0, you have a big impact on the apparent rates of decline in the placebo group, if you have a treatment advantage. And that's why the percentage trials look like the patients progressed at twice the rate to the mid-term mid-trials and it's purely statistical. And the enriched trial, we would love to be able

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to enrich a trial, we'd love to be able to pick rapid progressors, but we don't actually have any way of doing it at the moment. So essentially, purely by making a diagnosis of IPF, we are enriching as much as we can for the group of patients with the most aggressive form of fibrosis. But once we've done that, we haven't got any better way of then picking the even worse cases.

Elizabeth Goodwin ***Galapagos NV - VP of IR***

We'll take another question from the phone line, operator.

Operator

And we have no further audio questions.

Elizabeth Goodwin ***Galapagos NV - VP of IR***

Okay, great. Let's -- we have a question here from Patrick Trucchio.

Patrick Ralph Trucchio ***Joh. Berenberg, Gossler & Co. KG, Research Division - Analyst***

Just first a follow-up question on filgotinib. Can you give us an update on the status of the MANTA and MANTA-RAy studies? And can you tell us how much, if any of the data, from these studies could make its way into the RA label in the U.S. at the time of potential approval? And to what extent would this data be available for the sales and marketing effort in the U.S.?

And then on IPF on '1690. Can you tell us what the efficacy hurdle is for the futility outcome, is the expectation in the -- for the top-line data, at least, the potential that we could see a stabilization in FVC. And then finally, I guess, can you discuss your level of confidence in the safety and tolerability of combining '1690 on top of standard of care?

Walid Abi-Saab ***Galapagos NV - Chief Medical Officer***

Thank you very much. Those were like 4 questions. But stack it up one at a time. So for the MANTA and MANTA-RAy, in discussion with our collaborators. Gilead. We're not really disclosing the numbers.

So what we are saying is that both studies actually MANTA and MANTA-RAy will be together. Both studies are progressing well. We're happy with the progress. But also, we want to say that neither of them are needed to be -- to gate filing. We will be doing everything we can to finish them as early as possible. And once they become available, then they will be used, whether it will be part of -- during the review process or afterwards will be made available. But I'm sorry, I cannot give you more information on it. I know it's very important. But this is something that we've been in discussions with Gilead on, and that's what we can say at this point.

Regarding IPF. So the study is powered, just to remind you, to detect an effect of 80 ml between placebo and drug. And that would be regardless of background treatment. So it could be -- it's for the totality of the patients. Those who are on no anti-fibrotic treatment or who are on the anti-fibrotic treatment totally. And the futility analysis essentially is done in such a way that if you have no effect at all on any of these doses, we will be given signal to stop. And that's how it's designed. But if there's an effect that could lead to a clinically significant number. And again, there are shades of gray. What we don't want to see is if we have good effects with 80, that this will give us a false signal to stop, and that's kind of the default false negative type of situation. That's kind of how we designed it, and that's what's giving us.

Lastly, regarding the safety, this is actually something that we've been monitoring very carefully because, and it was very important also as a way to convince the regulators and convince ourselves first and convince the ethics committees that we're very responsible the way we do this because we went from a very small study to a very large program. So the safety monitoring in the study is very robust. Both at our level, we review it very carefully on an ongoing basis. I tell you, I get a report every other week on this. But also we have regular meetings for the independent Data Monitoring Committee that they view the data first, when we are present, we present the data to them in a blinded manner, and then they have a closed session where they look at the data unblinded and they render their judgment, whether it's okay to continue or not. And so far, I can tell you that I've been very pleased with what we've seen so far. I have no concerns. And actually, the independent Data Monitoring Committee has been giving us the green light every time they met.

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Elizabeth Goodwin ***Galapagos NV - VP of IR***

We have another question here in the room. Go ahead.

Dane Leone ***Raymond James***

Just 2 questions for me. One, maybe starting with Dr. Maher. Since you're part of the FLORA study, obviously, this isn't going to be a statistical response, but could you give us any anecdotal feedback of what you perceived as clinical effect or patient condition with the patients that you did treat with '1690.

And then the second question would be for Piet and Walid. You had a chart of the pathway of rebalancing the inflammatory -- the different ways of rebalancing the inflammatory, I guess, phenotype of different cells within the body. I'm just curious, you had one point up there for sphingocene 1 phosphate receptor as a target, and we know you're also interested in repolarization of different immuno-inflammatory cells like macrophages. I'm just curious, like, of the totality of the evidence that your teams are looking at. Do you think there's better evidence for modulating a phenotype in vivo or more on towards cell trafficking or like sequestering lymphocytes.

That was a lot, sorry.

Toby Maher

So I'll just give my very quick view. You're asking me an almost impossible question. Certainly, the drug was very well tolerated when we used it in the [FLORA] trial. One of the challenges of IPF studies is that we don't have a measure of individual response. SVC is very good for showing population change. But unlike cancer, where you might expect to see tumor regression with a successful treatment in IPF's success's stability and because of the variability of the disease, we will see in some patient stability. And I don't know if that's treatment success or just that patient's disease. So I don't think I can honestly answer you except to say it was well tolerated.

Piet Wigerinck ***Galapagos NV - Chief Scientific Officer***

And then the broader question on our approaches. If you look to the Toledo drug, that's where the interest comes from. So we see the repolarization across cell types. So does every cell type react as quickly? No. But if you see across the immune cells, you see that across all cell types sometimes -- some are a bit more sensitive and some are less sensitive. So it's not it for that program yet. We are at a similar choice there. We have the target, we see across those cells, fantastic data.

But not every cell is the same, that's clear. So -- and that's -- we're still there a bit in our old mode of working. We select the target we observe, we see good in vivo activity and we start to run.

So in the coming years, we'll get much more refined on that. And then select earlier on, what type of cells in one disease, do we really need to hit, zooming on those cells first, expect a better targets for those. So that's the plan we are moving towards but if you look into the current programs. In fact, it's with Toledo across cell types. That's what I can see -- what we see.

Elizabeth Goodwin ***Galapagos NV - VP of IR***

Okay. We have time for just a few more questions, and I'm going to go back to the phone and see if there's any question, one more chance. Operator?

Operator

We take our question from James Quigley of JPMorgan.

James Patrick Quigley ***JP Morgan Chase & Co, Research Division - Analyst***

So on the filgotinib program, so the psoriatic arthritis and ankylosing spondylitis trials. Given the black box warning for Rinvoq and the comments from the FDA around a class effect. Has this changed any of the recruitment or the feedback from investigators or monitoring required in the trial?

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Walid Abi-Saab ***Galapagos NV - Chief Medical Officer***

Thank you for the question. So the quick answer is no. I think the thromboembolic events have been essentially well-known for some time in this space. And all of the companies have been monitoring these very carefully. Fortunately, these are very rare events. And in the case of filgotinib they're even more rare. But no, we have not been having any difficulties or any concerns from investigators that I'm aware of. And I'm just assuming they're quite familiar with them.

Elizabeth Goodwin ***Galapagos NV - VP of IR***

Okay. A question from Graig. Go ahead.

Graig Suvannavejh ***Goldman Sachs Group Inc., Research Division - Executive Director & Senior Equity Research Analyst***

Thanks for the great presentation this morning. I've got 3 questions. Maybe the first 2 for Piet and one for Walid. On the Toledo program is very interested by the approaches of having a Toledo pan and a Tol 2, Tol 3 and a Tol selective molecule. Can you maybe walk us through what the incremental advantage would be of just going Tol 3 selective versus Tol 2 and Tol 3. So is there something about Tol 2 that might be potentially, I don't want to say problematic, but what is it about going after Tol 3 selective, that might be a better approach?

And then I was very interested about your interests going into the siRNA space. And I was wondering where the opportunities you see are in going after that mechanism? Are there -- is there something incremental that can be improved from the siRNA technology perspective? Or is it just an opportunity for the company to go into different diseases and have targets?

And then for Walid, just in terms of just coming back from ACR, I would love to get your impressions on what the feedback was from physicians on their initial thoughts around filgotinib. And maybe, if you felt that there were any takeaways from what their impressions are on the initial experience with upadacitinib in terms of the launch trajectory, what they're thinking about their excitement or not about that product?

Piet Wigerinck ***Galapagos NV - Chief Scientific Officer***

I'll kick off first. So the TOL program. Well, there are 3 targets. We learn as we go. And from the way I've been teached, I would by nature, go for a selective and say that every day, I see my scientists and they have designed a novel selective. It's not that easy to be the pan-Toledo, let's be clear. So it's more than -- there's one target, which is responsible for the activity and all the rest is baggage -- lost baggage. No, that's not what it is. They play in concert. And that's why going across the molecules and from 1 activity profile to the other, it is not a simple walk in the park, let's say like that. Each have their property, their strength, and we learn as we go.

Tol 3, indeed, if we look to the profile. It is from a scientific point of view, the least interesting because it does what an anti-TNF does currently, ah a bit more. So there are other mechanism of actions with similar profiles. On the other hand, if I can take the last patient of adalimumab, I'll be happy to do that as well because even oral does the same, we'll do that as well. So in that sense, a kind of a low base case scientifically. I believe I can do -- take that last patient of injection. I will do that. So no problem there that is -- we can play that game finally. We will do that as well. So let's be clear. But I hope scientifically and for patients long-term treatment is more in those others where we restore the balance in a better way. So let's be clear.

As siRNA , well 2 aspects. One, it's really a logic next step, if you look at the platform. That's why we want to do it that we believe will become much more efficient in selecting cellular assays, in vivo models because for every target because it's always a long walk in the dark, honestly, to find them. And it's always the question is the compound, good enough? Is the model good enough? So we believe we spend quite lot of time, iterations, making better compounds, other things. One is in siRNA sequence, if we would get good at that, normally, you should do it easier. Honestly, the limitations is how do to get it to the tissue? So it's quite -- I think we'll know that for liver, there is no problem, to get those into the liver. So and we are interested in NASH. This would be an obvious choice. In HBV, I have been impressed, I must say, with what those compounds do, a single injection every month, gives you a nice viral load drop with a once a month injection, okay. This is becoming competitive, I would say. I've worked in that area at early days and the field pushed on nicely. So it's clear that tissue by tissue, organ by organ, you will either need to rely on the [inaudible] properties or to targeting trick to get it there because [inaudible] they are going to be limited in terms of drug delivery. Walid, there was a question for you.

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Walid Abi-Saab ***Galapagos NV - Chief Medical Officer***

Yes. So I mean, I think what I can say, coming back from ACR. It's really a good time now for JAKs. I think the attention on JAKs and the amount of publications. And of course, the launch of UPA carries a lot of soundbites, so to speak, and presence in the meeting. But I think also, over time, people are getting -- the physicians are getting much more comfortable with the JAKs as a class, and they see the efficacy being really very strong and sustained. Unlike some of the concerns that you might have that you would lose effects over time with some of the biologics. Also, the safety profile, people are getting more aware and I don't know if you can say comfortable with it, but at least they're familiar with it, I guess, is the word that I'm looking for. And I would say that anything that's good for the JAKs class will be great for filgotinib. We -- with our efficacy, that's really right up there and a safety profile that is promising to be best-in-class gives you best risk benefit profile. And I think it's a great place to be. So we're very excited. Again, I'm looking forward to our next year's ACR, where we will be the center of attention, because by that time, we should be approved already, and I'm really excited to see this class really moving forward and bringing benefits to the patients because I do clearly see that they make a difference.

Elizabeth Goodwin ***Galapagos NV - VP of IR***

All right. Thank you. We're going to wrap up for now. And I just really appreciate everyone coming in person here to the Westin and dialing in and listening in to our webcast today.

If your questions are still burning, you can contact Sofie or myself. We'll try to get them answered for you today. And again, I thank you and I hope that you have a wonderful day today. Goodbye.

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