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EDITED TRANSCRIPT

PFE.N - Pfizer Inc Analyst and Investor Call to Discuss Etrasimod Data Presentation at Digestive Disease Week Call

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OVERVIEW:

PFE discussed Etrasimod ELEVATE UC 12 and 52 results.

REFINITIV

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PRESENTATION

Operator

Good day, everyone, and welcome to Pfizer's analyst and investor call to review etrasimod's data presentation at Digestive Disease Week 2022. Today's call is being recorded. At this time, I would like to turn the call over to Mr. Chris Stevo, Senior Vice President and Chief Investor Relations Officer. Please go ahead, sir.

Christopher J. Stevo - *Pfizer Inc. - Senior VP & Chief IR Officer*

Thanks very much, Erica, and thank you to all of you for joining us on such short notice today. We're very happy to be presenting the etrasimod ELEVATE UC 12 and 52 results to you.

Today, we'll be making forward-looking statements, and I'd just like to remind you that these forward-looking statements are only applicable as of today, and we undertake no obligation to update them in the future. And if you have further questions on our forward-looking statements, you can find them in our SEC filings, including Forms 10-Q and 10-K under the section labeled Risk Factors and forward-looking information, et cetera.

Next slide, please. Now allow me to introduce you to today's speakers. We have Mike Vincent, the Chief Scientific Officer of our I&I Group; Mike Gladstone, the Global President and Commercial Lead of I&I; Mike Corbo, the Chief Development Officer of I&I; and our new colleague, Sheldon Sloan, the Arena VP for the etrasimod UC team.

And with that, let me turn it over to Mike Gladstone to begin. Thank you.

Mike Gladstone - *Pfizer Inc. - Global President, Inflammation & Immunology*

Thanks, Chris. Good afternoon, everybody. We are more than pleased to have the opportunity to talk about the etrasimod Phase 3 results, and thank you all for being here today. The results you're going to see today not only show potential best-in-class efficacy, but they show a clinical profile that's unlike any current available treatment. We believe that we have the potential efficacy and safety profile that health care providers and patients have been waiting for. These Phase III results support the positioning of etrasimod as a first-in-line oral therapy after conventional treatments fail. We're looking forward to bringing etrasimod to the patients that desperately need new options.

And now I'll turn it over to Mike Vincent to walk us through the mechanism of action and the disease state. Mike?

Michael S. Vincent - *Pfizer Inc. - Senior VP and Chief Scientific Officer, Inflammation & Immunology*

Thanks, Mike. So as most of you know, ulcerative colitis is a chronic and devastating inflammatory disease that affects nearly 1 million people in the U.S. The symptoms include chronic diarrhea with blood and mucus, abdominal pain, weight loss. And as you can imagine, these are symptoms and signs that interfere with social functioning and one's quality of life. Newly diagnosed patients often have frequent flares. Given the high rate of treatment failure for UC patients, they may cycle from one treatment to the next to seek relief from often debilitating symptoms. This underscores the need for new therapies with greater efficacy.

Next slide. The treatment paradigm in UC is really one of failing first. Often, patients will be started on less effective or older medicines with poor side effect profiles. And then they are increasingly advanced to more aggressive therapies, with surgery as a potential last resort treatment option for UC patients. In the middle here is really the unmet need where physicians are looking for treatments that they can advance patients to before getting into the more advanced biologic and potentially more toxic therapies with worse benefit/risk profiles.

Next slide. So coming now to etrasimod. The molecule really was designed to be a selective S1P inhibitor, and it's selective for 3 of the subtypes of the S1P receptors. The first, S1P1, controls lymphocyte trafficking and it has a domino effect pharmacologically. It also has an effect of modestly lowering a heart rate on the first dose. And it is designed such that the etrasimod molecule most resembles the natural ligand, sphingosine-1-phosphate. This results in an optimal balance between the heart rate effect and the immunomodulatory effect. Etrasimod also inhibits S1P4 and S1P5, both of which have modulatory functions on the immune system that benefit ulcerative colitis.

Next slide. The end result of treatment with the S1P modulator, etrasimod, is a new steady state of lymphocytes where they are sequestered in the lymph node and are less available in the intestine where they can drive inflammation. Indeed, our clinical data supports that we can treat patients without the need for a dose titration or in-clinic monitoring due to the first dose related to heart rate. And we think our clinical data show an excellent safety and efficacy profile.

And now Mike Corbo is going to share the Phase 2 data with you.

Michael Corbo - *Pfizer Inc. - Chief Development Officer, Inflammation & Immunology*

All right. Thank you, Mike. I appreciate it, and good afternoon or good evening, everyone. I'm going to really talk to you a little bit about the transition from the Phase 2 and then we'll hand off to Sheldon on the Phase 3. But based upon all of the initial work at Arena on this molecule, they designed a Phase 2 trial, the OASIS trial that I think you're all quite familiar with. And looking at both 1 and 2 milligrams of etrasimod, this really determined the ultimate dose for Phase III for etrasimod being 2 milligrams, if you think about just clinical remission looking at around 30% in the Phase 2, which obviously was quite impressive and also in the 40s for endoscopic improvement. And again, this was the basis of the end of Phase 2 discussion. And based on these data, they did design a Phase 3 program, which Sheldon is going to take you through. But those 2 studies form the basis of the entire dossier.

If you want to just go to the next slide -- I'm just talking folks. So you'll hear the data from Sheldon. But I think a couple of things before we go into the Phase 3 data that really excite us in Pfizer and in I&I. I mean first of all, for patients, we think these data are incredibly important. We think that

the level of remission that we see at about 12 weeks and treat through 52 are going to be really important for patients, and we're bringing them something. Hopefully, that is a good new option for them.

The other thing that really came of this is we got new colleagues through this acquisition of Arena, people who think differently, people who have a different angle on things. And Sheldon is one of those folks. In fact, he's a gastroenterologist and really contributing across the board in I&I. This also represents really the evolution of our portfolio. So we've looked for new mechanisms that we feel are important. We've been looking in this area for quite a while. When we really saw etrasimod and its design, we really felt that this was potentially an important drug.

But when we made this deal, just as a reminder, we saw those Phase 2 data that I just showed you. Beyond that, everything else was just an ongoing Phase 3 program. We looked at some blinded data. We then trusted our scientists to do modeling and really understand the potential of where this molecule may land with efficacy. But at the same time, while we were doing that, the other thing we learned was the folks at Arena were very talented. They designed a good program. They knew what they were doing. And really, it was a foundation of trust that -- trust in our science, trusting the people we were working with that we then brought to our senior leaders and eventually our Board. The data bear out that, that was a prudent risk that did pay off. So we like this because it exemplifies how we've been taking an approach to deploying our capital aggressively but responsibly.

So I'll let you be the judge if we did that well, and I will now hand off to Sheldon, and he will share the Phase 3 data with you.

Sheldon Sloan - *Arena Pharmaceuticals Inc. - Vice President, Etrasimod UC Team Lead*

And thanks, Mike. Let me be the third person to say thanks Mike on the call. I'm going to take you through the Phase 3 data. And I first want to set up how we did the trials. It's really important to understand the approach we used for the ELEVATE program.

For the UC 52 program, we used a trial design that has been used for IBD trials in the past and is basically one of the recommended pathways forward for the FDA as well as a rerandomized trial. So UC 52 used a treat-through design, which means patients get randomized on day 1 to a placebo or an active arm, and they stay on this treatment assignment for the entirety of the study. Any patient that falls out anyway along the way becomes a non-responder. And we think this more closely reflects real-world treatment or how patients get treated. For the rerandomization trials, Basically, at the end of induction, any patients who didn't respond is removed from the analysis for the rest of the remainder of the trial, and only those patients that responded to active drug are rerandomized to active or placebo in the maintenance period, effectively enriching the maintenance period with responders only.

So why are we talking about these 2 different trial designs? I think it's intuitive or people automatically comparing trials across all agents on the market. And it's important to note that it's challenging to compare trials that use different study designs. There are some analyses that suggest that rerandomized trials can, in some cases, increase the rates of remission at the end by as much as 1.5x compared to treat-through.

Next slide. So this is the study designed for our 2 pivotal trials, ELEVATE UC 52 and ELEVATE UC 12. ELEVATE UC 52 was a treat-through design trial, 433 subjects, a 12-week induction period followed by a 40-week treatment. Over this trial, we had co-primary end points of clinical remission at week 12 and week 52. Essentially, patients -- the study had to meet those end points or this would have been a negative study.

What is clinical remission is comprised of 3 parts of what's called a Mayo score -- a modified Mayo score. And this is comprised of an endoscopic assessment, so that's the scope, basically a colonoscope or flexible sigmoidoscope and what does it look like essentially through the colonoscope. And then it's 2 symptoms that patients report. It's stool frequency and rectal bleeding. In order to be clinical remission, these subscores have to come down to 1 or 0 in order for patients to be considered in clinical remission.

We also had key secondary end points. Endoscopic improvement was basically what does it look like through the scope and how did that improve over time in weeks 12 and 52. Symptomatic remission, what did the patient reports, stool frequency and rectal bleeding at weeks 12 and 52, and mucosal healing, which was a composite of both endoscopic and the microscopic or histologic, as we call, the biopsy appearance of the intestine. And this was done at weeks 12 and 52, and this is a marker really for patient outcomes. Two unique end points we also used at week 52 corticosteroid-free remission and clinical remissions at both week 12 and week 52.

For UC 12, we enrolled 324 subjects and for -- 354 subjects. And for this trial, it was 12-week induction and patients were randomized basically at week 1 and treated for 12 weeks with the same primary end points that we use, the primary end point of clinical remission and the same key secondary end points we use for UC 52.

Now this slide is constructive because this is how we did the trial sequentially. We started our study essentially the second quarter of 2019 and was enrolling throughout the pre-COVID period and throughout the entire -- the rest of the trial enrolled throughout the COVID period. This trial was sequential. We did -- we opened up sites basically once we finished enrollment in UC 52 for UC 12. So UC 12 essentially was enrolled entirely during the COVID pandemic. This may play a role, but essentially, we need to make sure we understand the sequential appearance of this or conduct of this trial.

The subject disposition for this trial, most patients got to week 12. So 90% of patients in all arms made it to week 12, and in UC 52 (inaudible) treat-through design, only about (inaudible) the beauty of the treatment (inaudible) UC 52 met all its key secondary end points at both week 12 and week 52 robustly (inaudible) stool frequency and rectal bleeding and mucosal healing, which is a very high bar, basically one of the endoscopy combined with the histology improved to the point of healing looked like at weeks 12 and 52. In addition, clinical response was met at both weeks 12 and 52.

There are 2 end points that we looked at uniquely at week 52, sustained clinical remission, which is essentially subject to remission of (inaudible) patients as well (inaudible) enrolled into the trial. And looking at a more stringent end point of 12-week corticosteroid-free remission amongst subjects who are on baseline corticosteroids, we saw a similar percentage

(technical difficulty)

Okay. So I understand I was cutting out. I apologize. Okay. So let me just reiterate. Okay. Go to Slide 12. I'm sorry. Let me just reiterate what I was highlighting. So UC 52, as I mentioned before (inaudible) was a 52-week treatment, which was a (inaudible) means we had to meet both to be a positive trial. The key secondary end points were endoscopic improvement, symptomatic remission, mucosal healing, corticosteroid-free remission only at weeks 12 and clinical remission both at weeks 12 and 52.

Just to reiterate, and I don't know where I cut out, the clinical remission consists of a (inaudible) modified Mayo Score (inaudible) stool frequency and rectal bleeding. For endoscopic improvement, it's entirely dependent on what that looks like through the scope, did that improve. And the symptomatic remission is dependent on the stool frequency and rectal bleeding. Mucosal healing is comprised of what does it look like through the scope as well as how does the tissue improve microscopically. And then finally, corticosteroid-free remission and clinical remission

(technical difficulty)

Michael Corbo - *Pfizer Inc. - Chief Development Officer, Inflammation & Immunology*

Okay. Sorry. We're going to do a real quick switch for him to connect -- find a phone and then kill his microphone -- his computer, okay?

Sheldon Sloan - *Arena Pharmaceuticals Inc. - Vice President, Etrasimod UC Team Lead*

Okay. I'm on, I think. There we go.

Michael Corbo - *Pfizer Inc. - Chief Development Officer, Inflammation & Immunology*

All right. That's good. Thank you.

Sheldon Sloan - *Arena Pharmaceuticals Inc. - Vice President, Etrasimod UC Team Lead*

Okay. Should I just reiterate this slide, Mike, and then move forward?

Michael Corbo - *Pfizer Inc. - Chief Development Officer, Inflammation & Immunology*

No, that's okay. I think most people got most of it. You can just roll now. We think we can hear you now.

Sheldon Sloan - *Arena Pharmaceuticals Inc. - Vice President, Etrasimod UC Team Lead*

Okay. Great. Okay. So apologies for that. Let's go to the next slide. Okay. So what you're looking at is our results from our UC 52 trial. We met our co-primary end points of clinical remission at both week 12 and week 52, essentially hitting a remission rate of 27% and increasing to 32%. So 32% of patients who started the trial on etrasimod were in remission by week 52, which is a very remarkable result for a treat-through trial.

If you go to the next slide, these are our key secondary end points. And again, etrasimod met its key secondary end points robustly for endoscopic improvement, again what does it look like through the endoscope, symptomatic remission, what do the patients report for stool frequency, rectal bleeding and mucosal healing, what does it look like through the colonoscope as well as -- and combined with the microscopic or histologic appearance. We also met the secondary end point of clinical response.

Next slide. Okay. We had 2 unique end points at week 52, as I mentioned before, sustained clinical remission, subjects in remission at both week 12 and week 52, which were highly significant, as well as a very important key secondary end point of corticosteroid-free remission. This is something critical to get patients off of steroids because of very common drug use in patients with IBD. What we found was we had a 12-week corticosteroid-free remission amongst all subjects and about 1/3 of the population. And if we look at a more stringent end point of looking at all those subjects on corticosteroid at baseline, we reached basically about the same percentage of a third of those patients were able to be weaned off of steroids, again a very highly significant end point and significant for the patients.

Next slide. Now I want to talk about our week 12 -- our UC 12 results. Again, we met our primary all key secondary end points. For clinical remission, we hit our remission rate at 25%, which is very similar to UC 52, which is 27%. And for all key secondary end points, again, we're robustly positive for endoscopic improvement, symptomatic remission and mucosal healing. In addition, clinical response was also met.

Next slide. Okay. Now looking at cross-trial comparisons within class, these are not head-to-head and you can't draw conclusions but it can be informative. For clinical remission, the point estimate for UC 12 was 25% and UC 52 was 27%, which is highly competitive with ozanimod, which had an induction remission rate of 18%.

We go -- if we go to the next slide and look across the therapeutic approved therapies for UC, starting with the biologics, the induction rates for ELEVATE are very competitive with adalimumab, vedolizumab and ustekinumab. And if you look at the right-hand side of the slide, there are 2 JAK inhibitors which are label-restricted to be used after TNF, so potentially a different population than you might use or consider an S1P. But even with that caveat, etrasimod is competitive.

Let's go to the next slide. This is a summary of our safety. The safety was well-balanced, adverse events between both trials. And just to point out, this was not exposure-adjusted, so you'll see there are more patients that were exposed in UC 52 in the treatment arm. No deaths occurred in either trial. The overall infection rates were balanced between both arms in both studies. As you can see, the serious adverse events were low. And if you look at it in just greater than 1 subject, only 2 were reported. That would be ulcerative colitis and anemia.

Next slide. Looking at the most frequent adverse events, those included headache, worsening of UC, dizziness and COVID. I just want to point out that was very balanced across all arms.

Next slide, so just to look at the pharmacologic differences or potential differences between etrasimod and ozanimod. If we first look at the onset of action, we see marked lymphocyte reduction occurring within several days for etrasimod. Ozanimod is actually titrated over a week, and the

lymphocyte reduction actually lags. There's no dose titration expected or to be required for etrasimod. So we get the full therapeutic dose on day 1. Ozanimod does require 3 doses over a week to get the full therapeutic dose. And this strategy is used to minimize the first dose heart rate lowering.

Because etrasimod is very effective the first day and we've had data to suggest that we have an effect on the heart rate, which is within the single digits, we were able to give the full therapeutic dose on the first day. Having said that, not only in the Phase II trial did we have a mean heart rate change from baseline in less than 10 beats per minute, but we basically are confirming that in our Phase III trial within the 5% to 7% range of heartbeat -- beats per minute drop after the first steps.

If we look in the case of the need to discontinue the drug. So for etrasimod, recovery is rapid. The half-life is 30 hours. And within a week, it returns -- the patients return to normal range in their lymphocyte count. Ozanimod, because of the long-acting metabolite, it takes longer for lymphocytes to recover after sensation. And finally, there are no major metabolites for etrasimod. And so it does not affect metabolism of other drugs. And because of the multiple P450 pathways involved in metabolism, there's a low potential for drug-drug interactions. Ozanimod has a major metabolite that inhibits the enzyme, monoamine oxidase. And that drug affects the clearance of many other classes of drugs. And so that would be one of the areas that's already labeled for ozanimod.

So with that, that's a summary of the etrasimod Phase 3 data. And with that, I will hand it over to Mike.

Mike Gladstone - *Pfizer Inc. - Global President, Inflammation & Immunology*

Okay. Thanks, Sheldon. I appreciate it. If you can go to the next slide. This is the next slide. This is a compelling marketplace because patients are in need of new therapies. There are about 1 million U.S. patients today living with the effects of ulcerative colitis. Now we expect this market to double by 2030. In addition to that, not all patients respond in the same way. More than 85% of patients don't achieve or maintain remission with most of the medicines even over time. So patients suffering from ulcerative colitis need more safe and efficacious options. S1Ps can help fill that gap, and etrasimod has the potential to be the best in the class. Now based on the data we've seen so far, we are more confident than ever that if approved, etrasimod can compare favorably amongst all UC drugs given what we see as a very attractive clinical profile.

If you can go to the next slide, please. Etrasimod has the potential to fill a gap in the UC treatment paradigm. The area of unmet need is in the green in the prebiologic space. That's after 5-ASAs and steroids and before TNFs. Etrasimod has a potential to have a best-in-class efficacy with a favorable safety profile. When you combine that with once-daily administration, it has the potential to be a very attractive first-line option post 5-ASAs or steroids.

If you can go to the next slide, please. The reason we get out of bed in the morning is to serve immunoinflammatory patients. Now that's whether they're new to therapy or whether they cycle through options, as these patients so often do. Now we plan on filing the UC indication with the FDA a little bit later in the year, but we're not going to stop there. We have ongoing studies in additional GI indications like Crohn's disease and EOE, and that can help bring etrasimod to more immunoinflammatory patients in the future. We've got a talented team in place here at Pfizer, along with the talented Arena that can help us make this a reality for patients. And at that point, we're going to use our reach and experience with GIs to get it in the hands of patients who need it the most as fast as we possibly can.

If you could go to the next slide. We're going to be bold in our core focus areas, including medical dermatology, gastroenterology and rheumatology. And this is underpinned by an unmet patient need. Now we recognize that fibrotic manifestations of the disease encompass these 3 areas.

Now we're building on our strength to deliver an innovative, diversified portfolio, but we will pursue investments in high-potential assets that help complement our pipeline, and I think you've seen that. We're going to lead by augmenting our presence within the areas of focus through combination of life cycle management and medical derm and targeting white space and adjacent indications, things like specialty derm diseases such as alopecia, vitiligo; specialty GI diseases such as EOE; specialty rheum diseases like idiopathic inflammatory myopathy and ankylosing spondylitis.

We're looking and we aim to deliver diverse mechanisms of actions and diverse modalities to the portfolio. We're going to apply our scientific expertise in immunoinflammatory diseases, and we'll bring the power of the commercial organization to make this a transformative impact for patients. We're not going to stop until our patients find relief.

And with that, I'll turn it back to Chris to lead us in the Q&A.

Christopher J. Stevo - *Pfizer Inc. - Senior VP & Chief IR Officer*

Mike, thank you very much. And with that, as Mike said, let's start the Q&A session. Erica, would you please poll for questions?

QUESTIONS AND ANSWERS

Operator

(Operator Instructions) Your first question comes from the line of Evan Seigerman with BMO Capital.

Evan David Seigerman - *BMO Capital Markets Equity Research - MD & Senior BioPharma Research Analyst*

Congrats on the data. I had 2 for you. One, just kind of looking at the commercial potential. I know you outlined this asset versus other ones in the class, JAKs and biologics. Do you -- how does this kind of resonate with physicians that you spoke with at the meeting? Do they view the differentiated profile as you do? And then how do you expect that this could potentially help set up for a strong commercial launch?

Mike Gladstone - *Pfizer Inc. - Global President, Inflammation & Immunology*

Yes. I can tell you that while we don't have a firm number, what I -- to answer your question, we get really encouraging feedback from our key opinion leaders and our prescribers. They see this as the potential to really meet an unmet need. And when we discuss with them what our profile looks like, the prescribers in research are telling us that they believe that there'll be a preference for etrasimod as a potential best-in-class product in S1P. And with that, we believe that we're going to be able to take a larger share of the class than expected and we'll be able to continue to grow that over time. So the feedback we're getting back so far from the prescribers and the key opinion leaders is excellent. So thank you for the question.

Operator

Your next question comes from the line of Terence Flynn with Morgan Stanley.

Terence C. Flynn - *Morgan Stanley, Research Division - Equity Analyst*

Maybe 2 from me. You highlighted that UC market doubling by 2030. Just wondering if you could give us a little bit more color on what's driving that. Is it incidence, diagnosis, patients on therapy, total dollars? Just digging a little bit deeper there.

And then I was wondering on the -- if there are any factors that you thought contributed to the differential placebo response in the 2 induction phases of the data you presented today?

Christopher J. Stevo - *Pfizer Inc. - Senior VP & Chief IR Officer*

Thanks, Terence. So I think the first question is for Mike Gladstone. And the second question would be for Mike Corbo. And Sheldon, if you have anything to add to that.

Mike Gladstone - *Pfizer Inc. - Global President, Inflammation & Immunology*

Yes. Thank you. With regard to doubling the marketplace, all those factors will contribute. You'll have some increased patients moving to new therapies. But the larger piece is in terms of dollars and the additional products in the marketplace. So we think the overall value is going to double over time. It's driven partially by patients and then partially by -- and then to a greater extent by the more therapies in the marketplace.

Michael Corbo - *Pfizer Inc. - Chief Development Officer, Inflammation & Immunology*

All right. And then Terence, it's Mike. From -- with respect to the difference in the placebo rates, it is something that we are investigating. Despite a higher placebo rate in ELEVATE 12, it was a highly successful study though, primary and all key secondaries.

We are doing covariate analyses right now to try to get an understanding of where there any factors that potentially could have contributed versus what we saw in ELEVATE 52. Geographies are not super different or anything like that, but there's certainly a time factor that we're trying to investigate a little bit better in understanding could that have potentially played a role as well as -- obviously, we'll do the normal things like baseline clinical characteristics, nothing like immediately jumps out. But one of the factors we are looking at probably most closely is the time that the study was actually conducted. And more to come on that when we complete the analysis. Obviously, data are so relatively fresh and we're putting all that together into the dossier. So as I said, highly successful though despite that higher placebo rate in the one study.

Operator

Your next question comes from the line of Tim Anderson with Wolfe Research.

Brian Tsang - *Wolfe Research, LLC - Research Analyst*

This is Brian on for Tim. One of the benefits you talk about with etrasimod is no need for dose titration, which we see as a competitive advantage. Bristol's product titrates because like all their S1Ps, there's an effect on bradycardia and AV block and -- but it's less than something like with Gilenya, but we still see that. We saw a few cases with etrasimod in the maintenance portion. Have you had any discussions with FDA so far? And how confident are you that FDA will allow this in the label?

Christopher J. Stevo - *Pfizer Inc. - Senior VP & Chief IR Officer*

It sounds like a question for Mike Corbo. Sorry. Go ahead.

Michael Corbo - *Pfizer Inc. - Chief Development Officer, Inflammation & Immunology*

I'll start out. Sure. Okay. Thanks, Brian. I think the titration has never really been -- actually, the design of the molecule, as Mike Vincent was saying, was actually to try to minimize the first-dose bradycardia. So when we looked at the clinical development of etrasimod, none of the regulators felt that was necessary to titrate. So have we had a discussion with them since the Phase 3 data? No. Obviously, the data has just come out.

But when you look at the first dose -- and again, we only really see this in the first dose, the heart rate reduction that we actually see in etrasimod is pretty much along the same lines as you see with ozanimod after their final titration. So from our perspective, we don't really see this as a factor.

It's never been requested. And again, it will all be subject to regulatory discussion and approval. But at this time, we don't feel that it's going to be necessary.

Operator

Your next question comes from the line of Louise Chen with Cantor.

Louise Alesandra Chen - *Cantor Fitzgerald & Co., Research Division - Senior Research Analyst & MD*

So first question I have for you is, is there an opportunity for the first-line treatment for UC using etrasimod?

And then secondly, how does etrasimod complement your IBD portfolio, which also includes the TL1A asset and ritlecitinib?

Christopher J. Stevo - *Pfizer Inc. - Senior VP & Chief IR Officer*

I think the first question is for Mike Gladstone. And for the second question, I don't know, Mike?

Michael Corbo - *Pfizer Inc. - Chief Development Officer, Inflammation & Immunology*

I think we can tag team, Mike and Mike, about that, Mike Vincent and Mike Corbo, all right?

Mike Gladstone - *Pfizer Inc. - Global President, Inflammation & Immunology*

That's always a safe bet with a Mike and Mike tag team. First of all, we think this position -- thank you for the question. We think this is -- etrasimod is ideally placed for that first-line, post 5-ASA and steroid treatment before you get to TNF inhibitors. Given the clinical profile that we have, we think that, that is the sweet spot. And we do think that's the area of unmet need.

And I'll take a quick stab at how it fits in the portfolio. And then, Mike, please feel free to chime in. This also is a perfect complement to our portfolio. If you look at the area of unmet need, patients could potentially -- this would fit for patients before they get to TNF inhibitors or further down the treatment paradigm. And as you get a little bit further down the treatment paradigm, you have the opportunity to potentially get to a ritlecitinib, which could be one of, if not potentially, the most effective JAK for ulcerative colitis. And then when you look at TL1A, although it's very early in Phase II, that's a product that could help patients along every step of the continuum who could potentially fail. Mike, is there anything else you'd like to add there? Or did that cover most of it?

Michael Corbo - *Pfizer Inc. - Chief Development Officer, Inflammation & Immunology*

I mean, maybe let me just touch on it and then maybe Mike Vincent can talk also a little bit about kind of the continuum. Yes, definitely, etrasimod, we do feel in addition doing to -- in addition to the Phase III, obviously, we have the GLADIATOR study, which is a milder population. We hope that helps support that earlier line use. TL1A has some unique properties, and I'll let Mike talk about that, but we have the potential to being able to select patients based on a biomarker. So that would give another further differentiation, a different subset of patients.

If you think about further into the treatment paradigm, patients that are more experienced in their drug therapies, we already have Xeljanz. And ritlecitinib is a TEC inhibitor with some JAK3 activity that also potentially can benefit patients a little further on in their journey. Mike, do you want to add to that?

Michael S. Vincent - *Pfizer Inc. - Senior VP and Chief Scientific Officer, Inflammation & Immunology*

Maybe just to emphasize that these are 3 very distinct mechanisms of action. And in particular, ritlecitinib, as Mike Corbo just told you, has significant TEC inhibitory activity in addition to covering JAK3. So we think it's quite differentiated from the rest of the class. And between the 3 agents, so I think what we've been trying to get across here is that patients need different mechanistic options as well. So we think there's a nice complementarity in our pipeline as well with etrasimod.

Operator

Your next question comes from the line of Geoff Meacham with Bank of America.

Geoffrey Christopher Meacham - *BofA Securities, Research Division - Research Analyst*

I just had a couple of quick ones. The first one is looking at the data from induction to maintenance, I mean you guys saw improvement in some but not all the end points. So in the real world, what do you think the duration of therapy could be? And how long have you followed up patients for the whole program looking to some of the Phase 1 or Phase 2 studies?

And the second question is looking at other indications. Crohn's and EOE are obviously 2 ones that are on deck. Are there any differences with UC in terms of S1P receptor biology? I wasn't sure if there was a clear difference in pathophysiology among the different I&I indications.

Christopher J. Stevo - *Pfizer Inc. - Senior VP & Chief IR Officer*

So first question, I think, sounds like a Mike Corbo question and the second one maybe more of a Mike Vincent question.

Michael Corbo - *Pfizer Inc. - Chief Development Officer, Inflammation & Immunology*

Yes. How about if I start out with the maintenance and maybe Sheldon, a little bit of a follow-up, and then we hand off to Mike Vincent as far as expression potentially.

So from the maintenance study, I think -- Geoff, the one thing to really keep in mind is this is a treat-through design. So this is extremely stringent. We are not rerandomizing responders to further increase the numbers on the other side, although you can also say you're doing that for ethical reasons, too. So when we look at the maintenance, we feel across the board that it has consistently performed. We don't really see what we consider to be a reduction.

As far as the length of follow-up, I'll let Sheldon answer kind of how far we've gone out in treating patients. But our assumption is that patients are going to stay on this for an extended period of time. There won't be any limitation. But Sheldon, maybe if you can just give folks an idea for how -- our longest patients, how long they've been out there.

Sheldon Sloan - *Arena Pharmaceuticals Inc. - Vice President, Etrasimod UC Team Lead*

Sure, Mike. Yes. So we completed our enrollment for UC 52 approximately January 2021. And so if we look at that cohort, we were just starting to get data for -- through our OLE, or open-label extension, which is a 5-year trial. So we haven't done a data cut yet with that open-label extension other than for safety. And so we hope to probably, sometime this year, start beginning to think about when is the appropriate time to start assessing the data, whether it be from the last subject who is in or even sooner than that. So that's our plan of action for getting open -- long-term data.

I think just one other thing I want to mention and maybe it's pertinent that I think the -- again, this increase in remission from weeks 12 to 52 was something that even Bill Sandborn this morning at the Digestive Disease we commented on, which is remarkable. And even looking back historically,

looking at the infliximab, which is used at treat-through trial, even that was not accomplished. So one thing to think about for durability is small molecules do not develop antidrug antibodies. And I think that's another advantage of a small molecule versus a biologic over long term.

Michael S. Vincent - *Pfizer Inc. - Senior VP and Chief Scientific Officer, Inflammation & Immunology*

So a question on the S1P mechanism. Maybe I'll take that one. So in terms of how the system functions, we don't have any information that S1P is modulating lymphocyte trafficking or other immune cell trafficking differently across different indications. But as you would predict, each disease has its own unique pathophysiology. So at the end of the day, the steady-state distribution of inflammatory cells with etrasimod results in a lower inflammatory cell burden and organs that are inflamed. So we anticipate it to work well across a range of diseases. Obviously, we need to prove that is the case in a Crohn's disease trial and then the EOE trial, but the fundamental mechanism should be operative across different indications.

Operator

Your next question comes from the line of Carter Gould with Barclays.

Carter Lewis Gould - *Barclays Bank PLC, Research Division - Senior Analyst*

I know that it wasn't broken out in the presentation, but as you talk about frontline positioning, I was hoping you could comment even at a high level around the efficacy profile based on prior TNF exposure and if you saw anything even trend-wise that -- on that front.

And then on the Crohn's front, at the time of the acquisition, you had talked about potentially getting some of that -- seeing some data by the end of this year. I see in the slides now, that seems to be more 2023. I don't know if there's any changes there. I know you talked about being an adaptive design. I didn't know if you had committed to any changes there. Or maybe just broadly speaking, how these data have maybe changed your confidence as you think about development in Crohn's.

Christopher J. Stevo - *Pfizer Inc. - Senior VP & Chief IR Officer*

So the first question sounds like Mike Corbo and maybe Sheldon; and then on the Crohn's disease, also Mike Corbo.

Sheldon Sloan - *Arena Pharmaceuticals Inc. - Vice President, Etrasimod UC Team Lead*

So maybe I'll go first and then hand it off to Mike. You're looking at a subgroup of previous biologic exposure and if there's a difference between those who are exposed versus those naive. And what I could tell you is that we plan to present this data at a future congress. Bill Sandborn was asked that question this morning, and I can tell you what he said. It's that we know with at least at this point, patients exposed to at least one advanced therapy of biologic or JAK, they actually do very well on etrasimod. So we know that, and we're doing further analysis, but we're going to report that out at a future meeting. So I'll turn it over to Mike.

Michael Corbo - *Pfizer Inc. - Chief Development Officer, Inflammation & Immunology*

Okay. Thanks, Sheldon, especially as I was talking on mute. So I appreciate that. Carter, good to talk with you. With respect to the Crohn's study, yes, it is an adaptive study. There are various points in time that we look in on the study. So what I can tell you right now is we don't plan to adapt that study yet. It's still continuing as planned. Our next point in time that we will look at data to decide, do we change that study, do we focus it on one dose, et cetera, will be sometime next year.

So right now, it's still moving ahead as completely planned. In fact, everything that we have seen, that we looked at in the deal with Arena is all, like 100% on track. So we've not seen anything slip at all. So we're encouraged that it means that the integration means we're not breaking the new toy, okay? So it's encouraging for us that the integration has allowed business continuity and is allowing things to move along at pace.

Operator

Your next question comes from the line of Mohit Bansal with Wells Fargo.

Mohit Bansal - *Wells Fargo Securities, LLC, Research Division - Senior Equity Analyst*

Congrats on the data. So just a quick question. I'm trying to understand the place of this drug. So KOLs we talk to, they all talk about using these drugs after the patients fail an anti-TNF. Do you get the same sense that they would use it after anti-TNF? And what would it take to move it into first line? Do you think pricing of Zeposia is a little bit prohibitive there? I mean how should we think about this drug moving into front line?

Christopher J. Stevo - *Pfizer Inc. - Senior VP & Chief IR Officer*

That goes across several areas. That's medical as well as commercial. So I guess we could go several ways there. Mike Gladstone, if you have any general thoughts on how you would position that, and maybe Mike or Sheldon have some ideas from the clinical side of things.

Mike Gladstone - *Pfizer Inc. - Global President, Inflammation & Immunology*

Sure. One of the things that we've heard when they look at the profile, the physicians we speak to, they do see this as a great opportunity to be used before TNFs. Now they do also acknowledge that some of the payers may push it to be potentially after TNFs depending on what the biosimilar world looks like in the future, but we think we have a real opportunity to reach patients before they get to TNFs.

Michael Corbo - *Pfizer Inc. - Chief Development Officer, Inflammation & Immunology*

And maybe I'll just add a little bit. Mohit, this is Mike Corbo. I think the data -- from a remission perspective, as Sheldon had pointed out, whether that be an induction or in treat-through in maintenance, the data are very impressive. We don't believe there should be any restrictions in the label. But as far as access goes, I mean I think hopefully, we can get it, to Mike's point, to a place where physicians have it as a choice because it does provide a lot of flexibility for a patient to be able to be on an oral therapy. If they have to interrupt, it's easy enough to interrupt and restart without antidrug antibodies forming. So it does give a lot more flexibility to patients and the physicians. So we would hope that our data are strong that it's a good option for patients, plus it potentially becomes a decent option across the board earlier in treatment.

Mike Gladstone - *Pfizer Inc. - Global President, Inflammation & Immunology*

And Mike, also to hit on the fact that as physicians get more experienced, they're going to feel comfortable putting it before. And the good news is in our trial, nearly 2/3 of the patients in ELEVATE 52 and ELEVATE 12 were naive to biologics and JAKs. So you put those 2 together, it spells an opportunity for prebiologic treatment.

Operator

Your next question comes from the line of Robyn Karnauskas with Truist Securities.

Nicole Germino - *Truist Securities, Inc., Research Division - Associate*

This is Nicole on for Robyn. Congrats on the progress in creating another oral option for ulcerative colitis patients. Can you provide more color on the reasons for discontinuation? It looks like it's a little higher in the etrasimod arm. And pending the regulatory decision on mirikizumab, beyond the oral drug convenience, what else are the other points of differentiation in your view?

Christopher J. Stevo - *Pfizer Inc. - Senior VP & Chief IR Officer*

Thanks for the question, Nicole. I think that sounds like a Sheldon and Mike Corbo question.

Michael Corbo - *Pfizer Inc. - Chief Development Officer, Inflammation & Immunology*

Yes. How about if Sheldon starts out with the reason for discontinuation? And I can address the second half.

Sheldon Sloan - *Arena Pharmaceuticals Inc. - Vice President, Etrasimod UC Team Lead*

Yes. So interestingly, we saw an imbalance in UC 12 in discontinuation primarily due to worsening of disease in 6 subjects and bradycardia in 3 subjects. None of those bradycardias were reported serious adverse events. We did not see the same imbalance in either arm for UC 52 or our Phase II trial. So again, the peculiarities of clinical trials, it just -- that's what we found.

And then your second question was differentiation against the IL-23s. Mike, is that the one you want to take?

Michael Corbo - *Pfizer Inc. - Chief Development Officer, Inflammation & Immunology*

I can. I mean if you want to chime in, that's fine too. But I'd just say at a high level, Nicole, I think from a differentiation perspective, yes, obviously, having an oral therapy that you can kind of come on and off obviously helps. We also think that the long-term remission with the treat-through data are extremely compelling and again offer a potential advantage over not only other small molecules, potentially other -- potentially biologics. So we do think the long-term data is differentiating as well as the flexibility of an oral. And Sheldon, I don't know if you wanted to add anything else.

Sheldon Sloan - *Arena Pharmaceuticals Inc. - Vice President, Etrasimod UC Team Lead*

No, Mike. I think that's fair.

Operator

And there are currently no further questions in queue at this time. I'll turn the call back over to management for closing remarks.

Christopher J. Stevo - *Pfizer Inc. - Senior VP & Chief IR Officer*

Great. Thank you very much, Erica. We are always available for your questions. If you have any follow-up questions, please reach out to us and we'll get you answers as soon as possible. Otherwise, we thank you very much for your time and interest and look forward to speaking to you again soon. Thanks very much.

Mike Gladstone - *Pfizer Inc. - Global President, Inflammation & Immunology*

Thank you.

Operator

This concludes today's conference call. Thank you for participating. You may now disconnect.