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## PRESENTATION

**Operator**

Ladies and gentlemen, thank you for standing by. Welcome to the poziotinib update conference call. (Operator Instructions) I would now like to hand the conference to your speaker today, Joe Turgeon, President and CEO of Spectrum Pharmaceuticals. Please go ahead, sir.

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**Joseph W. Turgeon** - *Spectrum Pharmaceuticals, Inc. - President, CEO & Director*

Thank you very much, operator, and good afternoon, everybody. Happy holidays. Thank you for joining us on this call, and we're going to review the recent progress we've made in our poziotinib clinical development program.

And you probably saw earlier today, we issued a press release, which is posted on our website with the information we'll be discussing today. In addition, a slide deck is available on our website, and it can also be viewed in the event window for those of you who are on this live webcast right now.

And as shown in the disclaimer on Slide 2, I'd like to remind you all today that this call will include forward-looking statements. Please feel free to reference our filings with the SEC for additional information about the risk factors associated with our forward-looking statements.

And with that, let's now turn to the announcements. I'll tell you, I'm really pleased today. I've been in this drug development business for 37 years, and it's rare that you have the opportunity to have an NDA submission to the agency.

And today, I'm excited to announce that, yes, indeed, we did get with -- due to the recent meeting we had with the agency, we did get an approval to go ahead and file an NDA submission for pozi, and that's going to be in the previously treated non-small cell lung cancer patients with exon 20 HER2 and insertion mutations. And this is, of course, from the successful outcome of Cohort 2 of the ZENITH20 trial.

And we're excited about that. There's a large unmet medical need, and there are no other products indicated for this, and we'll be submitting in 2021. The second bullet we're going to go over today is about Cohort 3. And I'll remind you that's part of the ZENITH20 trial. And that was for frontline eGFR exon 20 insertion mutations. Now it did not meet its primary endpoint of ORR.

However, as you'll see as we walk you through the data, it missed by a very narrow margin and it did demonstrate meaningful data that could help to advance the pozi program overall.

And then thirdly, Cohort 5, I'll remind you, is geared to answer the question. Does twice daily dosing improve tolerability of pozi, which could maximize the impact of the drug? And as you'll see, the preliminary data we'll show you today shows a meaningful improvement in tolerability, which could prove to be important to the future development of poziotinib.

So with that, we're going to go into much more detail with everything. And Dr. Francois Lebel, our CMO, is going to walk you through all the deeper look at everything here and the data behind it. And when we're done, we'll have a Q&A that we can answer any questions or any comments you might have, and we look forward to that.

So with that, I want to turn it over to our CMO, Dr. Francois Lebel. Take it away, Dr. Francois.

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**Francois Lebel** - *Spectrum Pharmaceuticals, Inc. - Executive VP & Chief Medical Officer*

Thank you, Joe, and good afternoon, everybody. So let's look at the Slide 4. So this shows you an overview of the study design of ZENITH20. As you know, we have multiple cohorts. And today, on the left side, I'm going to be talking about Cohort 2, which will be the basis for our submission.

And also I'm going to provide you, for the first time, the results of Cohort 3. And I'm also going to get into Cohort 5, which you can see on the right side of the screen, which is an exploratory trial that we designed to examine various dosing level and frequency of dosing.

So with that, let's go to the next slide. And now this is simply to remind you that Cohort 2 has met its primary endpoint, the lower bound of the 95% confidence interval. We had to beat 17%, and we came out at 18.9%. So that made it a successful trial.

We had also a good disease control rate. And you can see here the PFS and the duration of response. So we met with the FDA. We had provided them this data, obviously, and a lot more.

And they agreed that we could go ahead and submit essentially under a pathway of accelerated approval under Subpart H this submission to seek an approval to the indication that Joe just mentioned. With that, I'm going to remind you next slide the safety profile that was in there. And obviously, we've discussed that as well with the FDA. So it's quite typical of tyrosine kinase inhibitor. And we are seeing the frequent rash and diarrhea as the most common adverse events related to drug.

However, we also add the permanently discontinued patients were only 20 -- 12%. So even though patients had more adverse events, the permanent discontinuation rate was reasonably low. So the -- so that's an important finding. And also what I should mention here that's not on the slide is that we had in the high 80 percent drug interruption rate. So this is a parameter that we want to keep in mind as we go through this presentation. Next slide.

Here, we're now talking about Cohort 3. This, as Joe has indicated to you, we did not meet the primary endpoint. The lower bound was 18.4%. That's what was observed, and we needed 20% ORR. However, if you look attentively on this slide here, you will see that we have a PFS of 7.2 months median and duration of response of 6.5 months with a disease control rate of 86%.

So this is actually very good numbers, especially as you compare it to our other cohorts. And we are quite pleased with that. Obviously, we wanted to see and meet or exceed the primary endpoint. But if we go to the next slide, you will see -- now I'm on Slide 8. And here, we're showing you the waterfall plot and as you can see visually, 91% of the patient had tumor regression to the tune of reduction of 25.5%.

So if you -- we advance 1 slide, and you will see that I circled a number of bars, each bar represents a patient. And as you can see here, there's a number of patients who were very close to the reduction of 30%.

And it would have not taken much to get them over the line, if you want, and that would have been a positive outcome. Actually, I can mention to you that if 3 patients would have crossed this line, we would have had a positive study with primary endpoints. So that brings us to really think about is there, what is it that we can do to slightly -- just slightly improve. Obviously, we want to do that for a patient.

And next slide, and here now we're going to talk about what kind of adverse events were seen in Cohort 3. And again, it's quite typical of what we saw before and certainly with the class. And the permanently discontinued rate here is a little lower than Cohort 2, 8%. And the Grade 3, you can see at the bottom, so diarrhea, rash, stomatitis, again, the common or the more common adverse event or a drug-related and keep that in mind because I'm going to show you some data on BID a little later that will make this even more interesting.

Now again, we are seeing pneumonitis rate to be very low, which is good. As you know, there are a number of other drugs in class or in different class who may have a problem with pneumonitis, but we have not seen this across our cohorts. So that's important.

Next slide. I'm on Slide 10. Here, this is a modeling that we had done some time ago when we -- Cohort 1 -- we got the results of Cohort 1, and we said, look, the half life is 7.9 hours. So maybe we should look into dosing differently than once a day. I'll remind you that Cohort 3 has been fully enrolled by the time that we decided to explore BID dosing. So you may say, well, why are you doing BID dosing?

So in black -- if you look at the black line here, the high peaks that you see here is when you give 16-milligram QD, once a day, and you get these high peak above 60-nanogram per ml and then you -- every day, you got a peak. And then we model what happens if you do BID. And we're showing you here in red what happens, at least during -- with modeling.

And you can see that we could substantially reduce the Cmax here. So obviously, this is modeling. It's a theory. And then the next thing that people get concerned about is, okay, but what happened at trough, meaning just before the next dose, where are you?

And if you look at the bottom of the red lines, you can see that we're significantly above what's called the IC50. The IC50 is a black line, straight line, just above the baseline here. And that's the minimum -- the inhibitory concentration of 50% that we need to stay above to make sure that we retain anti-tumor effect.

And you can see from the red line, the modeling that BID should afford that. In other words, now we're postulating that if we were to give BID dosing, we should reduce adverse events and we should retain anti-tumor activity. So now let's look at some real data in Slide 11. And the good news is that -- and this is preliminary data. The Cohort 5 is still enrolling.

And we are presenting to you data before the study is completed here. But nonetheless, there's a clear message here or trend where Grade 3 treatment-related AE, and here, we've included rash, diarrhea and stomatitis in Cycle 1. And you can see that we are able with BID dosing to reduce the incidence of AE of those serious AE -- not serious SAE, but Grade 3 or higher by 32%.

So that's quite a finding, at least we believe so. And then if you look at -- does that translate in decreased number of interruptions. When a patient gets an adverse event that is severe or moderately severe, then the doctor often will say, well, interrupt the dosing. So we look at the interruption rate. And you can see here, 16-milligram QD, we got 69%. And that 8-milligram BID, we brought it down to 43% for a reduction of 38%.

So obviously, we're quite excited about this. We believe that not only is this good in terms of improving tolerability but also could impact our ability of patient to stay on drug longer and gain the benefit of the anti-tumor activity.

Next slide, please. And so now let's conclude. So the news basically is that we had a good meeting with the FDA, and they've agreed that we can file on the basis of the data on Cohort 2. I should say, submit on the basis of the data from Cohort 2. And we're showing you the indication here, which is what the Joe has described to you.

And Cohort 3, we did not meet the primary endpoint. However, as I reviewed with you, we certainly see evidence of good, solid clinical activity. And to finish, we -- the data in Cohort 5, the preliminary data that we have, certainly supports our hypothesis that BID dosing may be the way to go.

So with that, I will conclude here and pass the microphone, I guess, back to Joe. You there, Joe? Are you muted?

**Joseph W. Turgeon** - *Spectrum Pharmaceuticals, Inc. - President, CEO & Director*

Yes, I was on mute. And I'd say, operator, could you open up the line for questions? I really appreciate you going through the data, Dr. Francois.

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## QUESTIONS AND ANSWERS

**Operator**

(Operator Instructions) And our first question will come from the line of Ed White from H.C. Wainwright.

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**Edward Patrick White** - *H.C. Wainwright & Co, LLC, Research Division - MD of Equity Research & Senior Healthcare Analyst*

So just on the Cohort 5 data. It looked good on the twice daily dosing. If the efficacy improves over what we saw in Cohort 1, could you expand this trial to become a registration-enabling study? Or would you need to run a completely new trial to address that patient population? And maybe if you can just give us an idea of the patient population that's in Cohort 5, the number that have EGFR or HER2, that would be helpful.

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**Francois Lebel** - *Spectrum Pharmaceuticals, Inc. - Executive VP & Chief Medical Officer*

Sure. Good question. So we have a Cohort 2 that -- we have an agreement with the FDA here that they thought the data was good enough for us to submit. So that's obviously our priority. However, it's clear that we're going to present and discuss the additional data that we have here, especially as it relates to dosing.

I don't know the answer to your question as to whether or not the FDA would consider this additional data as part of the -- let's hope, the first approval eventually, or they would ask us to do some additional work. I don't know the answer to that question. But it's clear that the patient makeup, if you want Cohort 5, you may recall that whenever we had a cohort that was fully enrolled, and that would include Cohort 1, 2, 3 now, then those patients, if they were a candidate to be in those cohorts, because they were fully enrolled, they would automatically go to Cohort 5.

So we have a mixed population, I would say. It's -- and I'm giving you a rough estimate, it's probably at this point 2/3 of the patients that are EGFR in there. And -- but over time, it fluctuates and it changes as cohorts fill up in the 1 to 3. So I hope this answers your question.

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**Edward Patrick White** - *H.C. Wainwright & Co, LLC, Research Division - MD of Equity Research & Senior Healthcare Analyst*

I think you misunderstood, Francois. I was thinking more looking towards Cohort 1. And so if the efficacy in Cohort 5 is more impressive and hits the parameters that you were hoping for in Cohort 1, could you turn Cohort 5 into a registrational study for those EGFR patients?

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**Francois Lebel** - *Spectrum Pharmaceuticals, Inc. - Executive VP & Chief Medical Officer*

Yes. Well, so that's what I was trying -- I guess I wasn't very clear.

So we believe that the findings that we have here of better tolerance and decreased dose interruption is applicable to both HER2 and EGFR patient. And so we will have to discuss this with the FDA.

When you say, can you turn it into -- the question is, do we really have to provide additional data or additional study? It may be that we could actually get it approved. Obviously, it's subject to discussion with the FDA. They saw the data. They saw close we came, especially in Cohort 3 to a positive trial. And if they are convinced that when you give BID dosing, you improve tolerability, and later on, if we -- once we get results for efficacy, then maybe we'll have to see what -- where they go with that. We may not have to do an additional trial. We'll see.

**Joseph W. Turgeon** - *Spectrum Pharmaceuticals, Inc. - President, CEO & Director*

So obviously, Ed, that means we would discuss all this with the FDA when the time is right.

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**Edward Patrick White** - *H.C. Wainwright & Co, LLC, Research Division - MD of Equity Research & Senior Healthcare Analyst*

Right. Okay, Joe. And just on the Cohort 3 patient population, 94% had drug interruptions. What were the -- do you have any data on what the adverse events that caused the interruptions? Was it the diarrhea? Was it the rash? Just trying to figure out what's going on there. And you said the efficacy was very close. You missed by 3 patients. Is this something that you're -- I'm just trying to get an idea of maybe in Cohort 5, how many patients -- well, I guess you already said that.

But how many patients are addressing this Cohort 3 again to see if you can get more data and get closer to the number. And then lastly, just wanted to ask a question on Cohort 4. What number -- what percentage of those patients are being enrolled are BID.

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**Francois Lebel** - *Spectrum Pharmaceuticals, Inc. - Executive VP & Chief Medical Officer*

Okay. So the type -- sure. So 2 -- I think 2 questions. So the first one is what kind of adverse event are we seeing in Cohort 3. So just like the other cohort, we're seeing -- like the ones who lead to a temporary discontinuation or dose reduction, they're the same, the rash, the diarrhea, the stomatitis. Those are the main ones and -- across the cohorts.

And so that -- there's nothing really changed there. As to Cohort 4, I think we have said publicly that we were a little more than half enrolled at single daily dose of 16 milligrams a day, and we are currently enrolling at 8 BID. And we have not disclosed the number as to how progress is going.

We did see a little -- some impact from COVID on enrollment. And it fluctuates, but we are certainly enrolling. And for example, as of last week, I think we were enrolling 2 patients. So it's enrolling. And we will have to update you in the near future about how enrollment is going and provide you additional guidance as to what we see.

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**Edward Patrick White** - *H.C. Wainwright & Co, LLC, Research Division - MD of Equity Research & Senior Healthcare Analyst*

Okay. And maybe if I could just ask a last one on the submission to the FDA on the Cohort 2 data. Is there anything that you can tell us about manufacturing. Obviously, that's been the hold up for the approval of ROLONTIS. And just was wondering if there's any -- if you could shed some light about the manufacturing of pozi? And any thoughts that you have on how you can get this through the FDA?

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**Joseph W. Turgeon** - *Spectrum Pharmaceuticals, Inc. - President, CEO & Director*

Yes, Ed, fair question given today's world of -- with the pandemic. Now remember, when we put the file on next year, I'm hopeful that the pandemic could be behind us by then, and we'll be well into how -- back to inspections, et cetera. Now I can tell you the drug is a small molecule, so it's a pill.

It's not like making ROLONTIS, for example. So it's a small molecule process. And the manufacturer of it is a well known, well-established manufacturer, that I can tell you. But as far as inspections, I hope by the time this is inspected, this will all be behind us. Or they'll have a way to do it virtually on everybody because I can't just -- it can't go on like this forever, correct, right?

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**Edward Patrick White** - *H.C. Wainwright & Co, LLC, Research Division - MD of Equity Research & Senior Healthcare Analyst*

Right. I hope you're right, Joe.

**Operator**

Our next question will come from the line of Alethia Young from Cantor Fitzgerald.

**Alethia Rene Young** - *Cantor Fitzgerald & Co., Research Division - Director of Equity Research & Head of Healthcare Research*

Maybe a couple from me. Congrats on kind of working through this with the FDA. I would be interested to hear if there were any pressure points that you had to get the FDA in particular, comfortable with? That's my first question.

My second question is just looking at like the waterfall plot on the cohort data you showed today. Did you see like a relativity that people got partial responses who didn't have dose interruptions or have you done any sort of the analysis? And maybe my third question is just, is there any kind of color or commentary that you can provide around the ROLONTIS situation? It seems like we're kind of in the same boat that incidences rising again of COVID-19 around the world, so maybe there's no update, but just figured I would ask.

**Joseph W. Turgeon** - *Spectrum Pharmaceuticals, Inc. - President, CEO & Director*

Yes. Francois, why don't you take the first 2, and I'll take the ROLONTIS after.

**Francois Lebel** - *Spectrum Pharmaceuticals, Inc. - Executive VP & Chief Medical Officer*

Sure. So look, the meeting with the FDA was good. The main -- the first meeting, if you want, was to discuss the clinical data. We're in a dialogue with them. We're going to be discussing -- there's other issue whenever you have -- you're planning an NDA. You have to deal with the pharmacology, the toxicology, and the CMC. And so there is an ongoing or active dialogue that's happening now.

And so I'm not at liberty right now to give you any feedback. I think as that matures, we certainly will update you. There's no -- there's nothing though that stands out or there's no unusual request here. Everything that we're discussing is pretty standard for what you're concerned with when you are applying for an accelerated review. So that's the first question.

The second one, I think you talked about the analysis of the waterfall plot. So look, we're...

**Alethia Rene Young** - *Cantor Fitzgerald & Co., Research Division - Director of Equity Research & Head of Healthcare Research*

Is there any correlation with like if you were -- those people are to get full doses that you saw the PRs there or anything you can add?

**Francois Lebel** - *Spectrum Pharmaceuticals, Inc. - Executive VP & Chief Medical Officer*

Yes. Yes. No, we're at that kind of analysis. We're going to look at that, obviously, very carefully, and we're looking at -- we're going to look at mutational profile and new issue will suspect. And we plan to present, obviously, to a proper scientific venue in the near term these additional results. I can't -- I don't have them for you today. So that's kind of where we're going. We're looking to -- in the past, we always look to -- for meetings to go in-person.

Now it's standard, they're all virtual meeting. So we hope that we should be able to find one in the near term to present additional data to meet your curiosity there.

And I guess, Joe, I'll pass it back to you for ROLONTIS.

**Joseph W. Turgeon** - *Spectrum Pharmaceuticals, Inc. - President, CEO & Director*

Sure. Thanks, Dr. Francois. So Alethia, first thing, yes, there are -- there is some spiking of the virus around the world. I will say, as recently as last night, I was on with our Korean counterparts, they're still way ahead of where we are, but they have spiked up a little bit, not near the numbers we've had here because they've done very well.

But that being said, when you look at what's next? Number one is the FDA, I'll remind you. They have the authority to do virtual inspections, if they so choose.

And as this is backlogging, I think that, obviously, they're moving in the direction we hope of doing virtual, if they're not going to be able to do in -- on-site inspections. As a matter of fact, they did release their initial guidelines around virtual inspections. But I'll remind you all of this because it's a great question. I can't give you an exact date when it will be inspected. But I'm going to tell you, we're ready.

The facility has been through multiple mock inspections. It's kind of like the army now is what I say, we're still going through the drill on a weekly basis, still doing the mock inspections, getting ready for any questions we might get. We have Spectrum people on the ground at the plant. We have, of course, Hanmi people who are very well prepared, been working with us, and we have third-party experts there working for the readiness. So we really feel we're ready for this inspection. And the other thing I'll tell you, I won't go to any specifics of these discussions we're having.

But I promise you this, we're not just sitting here doing nothing. We are looking for any angle we can to try and generate some movement here because we're excited about this. We want to get out there and compete. We're in a great position to compete, as you know.

So we're not just sitting here. We're trying to make something happen behind the scenes. That I can tell you. Something has to go forward at some point because this backlog can't go on forever, and it's just going to get bigger, not smaller. Again, I'll remind everybody, just to remind everyone is we did not get a CRL. We got a deferral. There's been 1 or 2 others with deferrals only, not CRL. So we're pretty ready to go once we get this inspection going. And Alethia, I wish I can give you the exact date, but I can't. But I hope that helps.

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**Alethia Rene Young** - *Cantor Fitzgerald & Co., Research Division - Director of Equity Research & Head of Healthcare Research*

No, I get it. That's fair. I just figured I'd ask, but I appreciate it.

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**Joseph W. Turgeon** - *Spectrum Pharmaceuticals, Inc. - President, CEO & Director*

I'm glad you did.

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**Operator**

Our next question will come from the line of Ren Benjamin from JMP Securities.

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**Reni John Benjamin** - *JMP Securities LLC, Research Division - MD & Equity Research Analyst*

I guess, maybe just, I guess, the cadence of discussion and some color around that would be great.

So you went to the FDA, you talked about cohorts 1, 2. And did I hear you right, Francois, you talked about Cohort 3 as well. And then out of all the 3, the FDA kind of told you guys, great, Cohort 2 looks probably the best. Let's go -- move forward with that. Was there any feedback in terms of what you could do to potentially get approvals in the previously treated EGFR exon 20 or the first-line non-small cell EGFR exon 20.

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**Francois Lebel** - *Spectrum Pharmaceuticals, Inc. - Executive VP & Chief Medical Officer*

Yes, Ren, the order is little different than what you suggested there. So when you seek a meeting like this, you have to tell them -- if you're seeking a pre-NDA meeting, you want -- you have to tell them what data you want to use to support the submission. So the data we selected is Cohort 2 because that was the one that was positive. The FDA certainly was aware of our result in Cohort 1. And we did cover it in the discussion, but that was not the main basis of the discussion.

And Cohort 3 data, we did not have at the time of the meeting. They were certainly aware of what we were doing in Cohort 3 and 4. They were also aware of the maturity of the data, et cetera. But it's pretty clear that the FDA has confirmed that what they had told us before that these 4 cohorts are truly independent of one another, and a positive cohort does not impact the other.

So I think that in the discussion certainly was clear that they accepted that, and that they had not changed their mind as it relates to that.

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**Reni John Benjamin** - *JMP Securities LLC, Research Division - MD & Equity Research Analyst*

Got it. Terrific. I'm clear in my head now. And then I understand that you said you want to file in 2021. But it seems to me that you have the data unless you have to follow the patients longer or something along those lines, is it fair to say that it will be an early 2021 submission? Or is there anything more that you need to do that it could push it out further than kind of how I'm imagining the filing to take place?

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**Francois Lebel** - *Spectrum Pharmaceuticals, Inc. - Executive VP & Chief Medical Officer*

Yes, sure. So the -- we're not going -- today, we're not going to be able to give you any additional specificity as to when would we file. I mentioned that there is ongoing communication with the FDA and the original meeting that we had here was about the clinical results, but there are other factors that come into play that we have to discuss further like the CMC and the pharmacology, the toxicology. There's QT interval things, et cetera.

So these are part of normal process. So it's not -- there's nothing alarming in there, but those things have to happen. And once we have done this complete survey, if you want, with the FDA, then we would be able to provide you a little clearer picture as to when we think we can file.

But given what we know, we believe that this will happen in 2021.

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**Joseph W. Turgeon** - *Spectrum Pharmaceuticals, Inc. - President, CEO & Director*

And Ren, I'll tell you this -- Ren I'll just mention 1 other thing. Obviously, we're -- our team is starting to work on the file as we speak.

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**Reni John Benjamin** - *JMP Securities LLC, Research Division - MD & Equity Research Analyst*

Got you. Okay. Yes. No worries. I guess a final one for me. The Cohort 5 data looks really impressive for me, the fact that you can bring those dose interruptions down. And I guess I'm -- without, I guess, the corresponding sort of efficacy data, I'm left a little bit in the air just trying to figure out did you -- are you seeing -- does it seem like the efficacy is remaining on par, even if you don't have the exact numbers?

Or is it just kind of too early to tell? Any sort of color you can provide on the efficacy component to make sure that hasn't been impacted in anyway?

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**Francois Lebel** - *Spectrum Pharmaceuticals, Inc. - Executive VP & Chief Medical Officer*

Right. I don't have -- even if I would have it, I wouldn't be able to disclose that information to you today in terms of efficacy. It's somewhat preliminary here and getting the data announced with COVID has been a little bit of a challenge. I'll remind you, though, that if you look at the modeling, we -- certainly, it's suggestive that even BID dosing keeps us -- the trough is significantly above the trough that we add in single daily dosing. So that

might play in our favor. The -- so that's kind of all that I can say. We don't have the efficacy data. The only indirect marker that I could tell you is that overall, in Cohort 5, we continue to have pretty good enrollment in spite of COVID.

So -- and the level of interest of our investigators certainly has not dropped. So I think there is also, one would say, pretty good enthusiasm about the BID dosing approach here. And remember, Cohort 5 also had other dosing that we have looked at and continue to look at. So I can just say that, look, the investigators' certainly interest in this study has not dropped at all. So we're encouraged by that.

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**Reni John Benjamin** - *JMP Securities LLC, Research Division - MD & Equity Research Analyst*

Got it. Sorry, I put myself on mute here. If I can just sneak one last one. In terms of kind of upcoming data now for the remaining cohorts, could you just give us an update as to when we might be expecting further data announcements?

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**Francois Lebel** - *Spectrum Pharmaceuticals, Inc. - Executive VP & Chief Medical Officer*

So -- well, as I mentioned to you, we're going to present additional information about Cohort 3 in scientific venue that we have not -- we're putting the data and doing analysis as we speak. But we're looking to present that to you as soon as possible. Cohort 4, we need to -- it's a pivotal trial as opposed to -- it's not an exploratory trial. So we want to be cautious there that we don't do anything there that would compromise the integrity of that trial with the FDA.

So I don't think you're going to see data being released on Cohort 4. You'll see additional data on Cohort 3 and 5 first.

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**Reni John Benjamin** - *JMP Securities LLC, Research Division - MD & Equity Research Analyst*

Got it. Great. And good luck going forward with the FDA.

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**Operator**

And our next question will come from the line of Maury Raycroft from Jefferies.

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**Maurice Thomas Raycroft** - *Jefferies LLC, Research Division - Equity Analyst*

Congrats on the update today. I'd just have one. Just clarifying, for the clinical data, are you only including Cohort 2 in the NDA filing? Or will you include additional cohorts and/or more follow-up data? I guess are there any contingencies on the clinical data for your filing and eventual approval?

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**Francois Lebel** - *Spectrum Pharmaceuticals, Inc. - Executive VP & Chief Medical Officer*

Yes. Well, thank you for the question. The -- whenever you file an NDA or BLA, you have to identify and agree with the FDA as to what will be the pivotal trial and what data are you going to present.

And Cohort 2 -- is totally agree that, that is the data that we need to focus on. We will -- as I mentioned to you, we will, obviously -- they're aware of the other cohorts. And certainly, if they request additional information, we're going to provide it to them. The safety data set, I should mention this, we have a pretty good size of data set.

And certainly, the FDA recognized that. So we have dosed more than 1,100 patients here in various dosing, dose and schedule. So that's pretty good. And then as you may recall, we also had initially some very good data that came out in investigator-led study at MD Anderson.

So the FDA is aware of that as well. And that is what you call additional supportive data that we may present as well.

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**Maurice Thomas Raycroft** - *Jefferies LLC, Research Division - Equity Analyst*

Got it. Okay. That's helpful. So it seems like Cohort 2 is going to be the primary basis for approval. And if FDA requests some of the additional cohorts, you could include that in the filing as well?

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**Francois Lebel** - *Spectrum Pharmaceuticals, Inc. - Executive VP & Chief Medical Officer*

That's right. Depending on their status -- they're aware that Cohort 4 is enrolling still, right?

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**Operator**

Our next question will come from the line of Mayank Mamtani from B. Riley Securities.

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**Mayank Mamtani** - *B. Riley Securities, Inc., Research Division - Research Analyst*

Appreciate the update. Just piggybacking on some of the previously asked questions. If I may start with Cohort 5 and the 6 mg BID data specifically, is there anything -- any qualitative color you can give on what the progress because that would be the best way to think about dose response, and I'm not just thinking efficacy, I'm also thinking the tolerability profile ahead.

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**Francois Lebel** - *Spectrum Pharmaceuticals, Inc. - Executive VP & Chief Medical Officer*

So -- I'm sorry, I had a little difficulty getting your question. So you said -- can you repeat the question slowly?

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**Mayank Mamtani** - *B. Riley Securities, Inc., Research Division - Research Analyst*

Yes, happy to. The question is around Cohort 5, 6 mg BID. The data from that could be useful from a dose response standpoint, not just for efficacy, but obviously from tolerability profile?

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**Francois Lebel** - *Spectrum Pharmaceuticals, Inc. - Executive VP & Chief Medical Officer*

Yes. So well, thank you. You clearly pay attention here. So that -- yes, you're absolutely right. The 6-milligram BID we have not reported data yet, but I would say that anecdotally, we're seeing similar trends so to us, that's very good news as well. So you put your finger on something that is very good. And yes, it would provide us additional supportive evidence to discuss with the FDA.

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**Mayank Mamtani** - *B. Riley Securities, Inc., Research Division - Research Analyst*

Okay. Helpful. And then going back to Cohort 3, I might have missed that. Did you report the serious AE rate? I know you had that for Cohort 2. And just my broader question for you was, is there a message on safety profile between HER2 and EGFR that goes back to the biology of these patients?

Like -- or is it really just about the TKI profile that you have at pozi. It's a 2-part question.

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**Francois Lebel** - *Spectrum Pharmaceuticals, Inc. - Executive VP & Chief Medical Officer*

Yes, sure. Yes, the safety profile in the EGFR and HER2 has not been that different. It's not exactly the same, but it's really not that different. We have seen slightly higher rash rate and diarrhea. I mean those are the 2 more frequent adverse events that are seen across any of the cohorts.

So -- and that's why we were happy to see that BID dosing appears to be able to be reduced with BID dosing. So -- but those are the key AEs that we need to deal with. The -- in terms of your question about Cohort 2, 3., so the number I can give you is that the interruption rate in the early cohorts were in the 80%, meaning temporary interruption, the patient has some adverse event, the doctor stops the drug temporarily and then restarts it.

So that's not unusual for cancer studies, but the rate was quite high. And that's why we're reporting today in Cohort 5 that we have seen here in a preliminary fashion, but nonetheless, in 40 patients, basically an ability to drop the interruption substantially. So we're encouraged by that. Obviously, we need to confirm this with additional patients over time. But I think this is auger as well.

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**Mayank Mamtani** - *B. Riley Securities, Inc., Research Division - Research Analyst*

Great. Just my last question on the 70-patient cohort, the BID cohort for Cohort 4. Any qualitative color on how the enrollment that might be going. Is that in line with the excitement you saw with Cohort 5, for example?

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**Francois Lebel** - *Spectrum Pharmaceuticals, Inc. - Executive VP & Chief Medical Officer*

Yes. So my comment is, look, we see an impact on COVID. Everybody sees an impact on enrollment now with COVID, but Cohort 4 first-line HER2 is -- it's a little more difficult to recruit. But we're making progress. So I think we're in good shape here to update you sometime in 2021 as to how we progress. But Cohort 5, you've got to remember, allows patients with first-line EGFR, second-line EGFR or HER2. So it's a larger population that we can put in Cohort 5, and it's easier to recruit.

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**Operator**

And our next question will come from the line of Michael Schmidt from Guggenheim.

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**Michael Werner Schmidt** - *Guggenheim Securities, LLC, Research Division - Senior Analyst & Senior MD*

Congrats on the update. Maybe just a couple follow-ups. On the FDA discussions around Cohort 2, obviously, the cohort did meet the response rate criterion. I was just wondering if you had any more discussions or any kind of clarity around the duration of response, whether there's a minimum that would need to be exceeded in that arm.

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**Francois Lebel** - *Spectrum Pharmaceuticals, Inc. - Executive VP & Chief Medical Officer*

Yes. There's no new information above that the -- at this time. But what I can tell you is the FDA obviously felt that it was -- probably will be a review issue, but certainly it was good enough for us to submit an application. So they could have -- you got to realize they could have said to us, no, don't bother submitting. That's not what they did. They said, yes, you can submit under Subpart H, which is good news. And we -- they certainly saw the numbers. So I think, as you know, there is no magic number that you have to meet.

It has to do with what is the medical need. As you probably know, there's no approved product here. So what we have here and have met the primary endpoint, it certainly warrants a review, and they confirmed that they're going to do that.

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**Michael Werner Schmidt** - *Guggenheim Securities, LLC, Research Division - Senior Analyst & Senior MD*

Makes sense. Great. And then in some cases, when companies submit filings for accelerated approval, a confirmatory Phase III trial is needed to be initiated at the time of filing. Did you have any conversations with the FDA around that as well?

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**Francois Lebel** - *Spectrum Pharmaceuticals, Inc. - Executive VP & Chief Medical Officer*

Yes, you're absolutely right. When you file under Subpart H, you have to do a confirmatory trial. We have proposed -- we had made a proposal and had good discussion with the FDA, and we will continue to discuss the proposal to arrive at the right place. They were aware, for example, that Cohort 4 and 5 are generating new data. And that's probably going to impact to some degree our proposal for the final confirmatory trial.

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**Michael Werner Schmidt** - *Guggenheim Securities, LLC, Research Division - Senior Analyst & Senior MD*

Okay. That makes sense. And then just on Cohort 4, which, as you said, is also a regulatory arm or a more -- a regulatory study. Just help me understand -- I believe this is a mixture of patients, some of them having received once a day and others the twice a day dosing schedule. Will the filing -- should that be successful will the filing be just from a twice daily dosing? Or will it be the entire cohort, which may be a mix of doses that were used? And what are the implications of that?

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**Francois Lebel** - *Spectrum Pharmaceuticals, Inc. - Executive VP & Chief Medical Officer*

Yes. So the original target enrollment at the 16-milligram once-a-day was 70 patients. We've indicated that we're more than half enrolled there. And the FDA likes to see often more than one dose level, even in pivotal trial. So we don't think that -- having some patient at single daily dose and other patient BID, we don't think that's going to get in the way of doing business, if you want.

Of course, you have to maintain the level of rigor, though, and making sure that we have independent central imaging and all the other parameters of pivotal trial. But we think we have a good number of patients on 16 QD with the data on BID is accumulating now in Cohort 4. But as you -- as 1 of your colleagues mentioned earlier, we're getting good data coming out of Cohort 5, and we certainly will put in front of the FDA whatever data we have.

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**Operator**

And I'm not showing any further questions in the queue. I'd like to turn the call back over to Joe Turgeon for any closing remarks.

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**Joseph W. Turgeon** - *Spectrum Pharmaceuticals, Inc. - President, CEO & Director*

Thank you, operator. And listen, I want to thank everybody who was on the call. Great questions. We appreciate it. And I'm glad we're able to report on everything here at the year-end. We're excited about having the okay to submit and -- here in 2021. And looking forward to in a not-too-distant future, we hope, getting this inspection done and starting the revenue trail here at -- again, here at Spectrum. So thank you for your interest. I hope everybody has a wonderful holiday season, and we look forward to talking to you in the coming year. Operator, thank you.

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**Francois Lebel** - *Spectrum Pharmaceuticals, Inc. - Executive VP & Chief Medical Officer*

Perfect. Thank you.

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**Operator**

Thank you. Ladies and gentlemen, this concludes today's conference call. Thank you for participating. You may now disconnect.