Vertex Pharmaceuticals Incorporated

Vertex Pharmaceuticals Incorporated - Special Call - Vertex Pharmaceuticals Incorporated

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Operator Operator

Good day, and welcome to the Vertex Pharmaceuticals review of VX-548 Phase 2 Results in Diabetic Peripheral Neuropathy Conference Call. [Operator Instructions] I would now like to turn the conference over to Ms. Susie Lisa. Please go ahead.

Susie Lisa Executive

Thanks, Chuck. Good morning, everyone. I'm Susie Lisa, and as the Senior Vice President of Investor Relations, it is my pleasure to welcome you to this conference call to discuss results from Vertex's Phase 2 study of VX-548 in diabetic peripheral neuropathy, or DPN. Making prepared remarks on today's call, we have Dr. Reshma Kewalramani, Vertex's CEO and President.

Joining her for the question-and-answer portion of the call are Stuart Arbuckle, Chief Operating Officer; and Charlie Wagner, Chief Financial Officer. We recommend that you access the webcast live as you listen to this call. The call is being recorded, and a replay will be available on our website. We will make forward-looking statements on this call that are subject to the risks and uncertainties discussed in detail in today's press release and in our filings with the Securities and Exchange Commission. These statements, including, without limitation, those regarding Vertex's plans to advance VX-548 into pivotal development in peripheral neuropathic pain and into Phase 2 in lumbosacral radiculopathy, including the anticipated timing of these studies, our expectations for our VX-548 programs in acute and peripheral neuropathic pain, including next steps and other programs in our pipeline, are based on management's current assumptions.

Actual outcomes and events could differ materially. I will now turn the call over to Reshma.

Reshma Kewalramani Executive

Thanks, Susie. Good morning, all, and thank you for joining us on short notice. Vertex's differentiated R&D strategy continues to deliver, and we're excited to announce positive results this morning with our selective NaV1.8 inhibitor, VX-548, in a Phase 2 proof-of-concept study in patients with painful diabetic peripheral neuropathy or DPN. Let me first share some brief updates to provide perspective on the 548 program as a whole, and then I'll walk through the DPN Phase 2 results. We divide pain into 3 distinct categories: acute, neuropathic and musculoskeletal.

We've previously discussed the opportunity in acute pain, with over 80 million patients and a multibillion-dollar market today despite being almost entirely generic, including many generic opioids used in this setting. We recently completed dosing in our acute pain Phase 3 program with VX-548. And as previously discussed, we will unblind and analyze all 3 acute pain trials together and share results in early 2024. Moving to peripheral neuropathic pain or PNP, a collection of painful conditions unified by the same underlying pathophysiology of nerve impairment. There are approximately 10 million patients treated for PNP each year in the U.S.

representing another multibillion-dollar market today in the U.S. despite the fact that Tier 2, essentially all prescriptions, are generics. Nearly 20% of these patients have DPN and over 40% have lumbosacral radiculopathy or LSR. There's a large unmet need in PNP, given in LSR, there are no approved treatments.

And in DPN, currently available treatment options are associated with high rates of discontinuation, inconsistent dosing, polypharmacy and off-label use. Given the clear challenges of current treatments, including most commonly, the gabapentinoid class, we believe this creates substantial opportunity for a medicine that could offer a superior profile to currently used medicines. Our overarching goal in the PNP segment is to gain a broad neuropathic pain label, and we see the opportunity to do so with clinical studies in DPN and LSR which, when combined, represent approximately 2/3 of the PNP patient population in the U.S. We initiated a Phase 2 study in painful lumbosacral radiculopathy earlier this week. And next, I'll review the results of our recently completed DPN Phase 2 trial.

Today's results add to the body of evidence that selective NaV1.8 inhibitors represent the first potential new class of pain medicines in over 2 decades. These data in DPN establish proof-of-concept for VX-548 in peripheral neuropathic pain and represent the first data from VX-548 in the chronic setting. The study met its primary endpoint with statistically significant and clinically meaningful reduction from baseline in the weekly average pain scores measured on the numeric pain rating scale, or NPRS at week 12 of treatment, with favorable safety and tolerability. Significantly, between VX-548 and its predecessor molecule, VX-150, this is the sixth positive Phase 2 proof-of-concept study of a Vertex NaV1.8 inhibitor, in pain conditions including bunionectomy and abdominoplasty as examples of acute pain and small fiber neuropathy and diabetic peripheral neuropathy as examples of peripheral neuropathic pain.

Turning to the details of the Phase 2 study of VX-548 in DPN. The goals of our Phase 2 study

in DPN were threefold: one, assess the magnitude of the treatment effect of VX-548; 2, assess the safety and tolerability of VX-548 in the setting of chronic treatment; and 3, assess the magnitude of the treatment effect and safety tolerability of pregabalin in the same study to provide context so that we could appropriately design the Phase 3 VX-548 studies. Slide 6 shows the study design. We evaluated 3 doses of VX-548, and the study also included a pregabalin reference arm. Patients were randomized to receive either high dose, mid-dose or low dose of VX-548 or pregabalin, at the maximum recommended daily dose in DPN for pregabalin of 100 milligrams 3 times a day, following a 14-day washout and a 7-day run-in period to establish the patient's baseline on the NPRS.

The primary endpoint was changed from baseline in the weekly average daily pain intensity on the NPRS at week 12. We also assessed other endpoints, including the following secondary endpoints: a responder analysis of the percentage of patients who showed reductions in pain scores greater than 30%, 50% and 70%; assessment of sleep; the patient's global impression of change in overall status; and the safety and tolerability of VX-548. A couple more points before discussing the efficacy results. Approximately 65 patients of those who enrolled in the study had used medicines for peripheral neuropathic pain in the year prior to enrollment, and about 35% were naive to PNP medications in the prior year. Baseline characteristics were generally balanced across the treatment groups.

However, the VX-548 high-dose arm had both a numerically lower baseline creatinine clearance, and a higher number of patients with impaired renal function with creatinine clearance less than 90 compared to the other arms of the study. Pregabalin is primarily renally excreted and per the pregabalin label, dose is adjusted lower if creatinine clearance falls below 60. In our Phase 2 study, in order to maintain the blind we made a simplifying protocol specification to discontinue patients across all arms of the trial if the creatinine clearance falls below 60. To be clear, pregabalin does not alter renal function, and the emerging profile for VX-548 does not suggest any impact on the kidney. The trial specification to discontinue patients from study drug was put in place to accommodate the renal excretion of pregabalin.

Lastly, the study was structured with a reference arm. No direct comparison was planned and the study was not designed or powered for statistical comparison. The results are on Slide 7. I'm going to focus my comments on the VX-548 groups, and will start with the primary endpoint of the change from baseline in the NPRS at week 12. For the high dose, the mean change from baseline was minus 2.26; for the mid-dose, minus 2.11; and for the low dose, minus 2.18.

These changes represent 35% to 39% reductions in NPRS from baseline. Regarding statistical significance, all VX-548 groups had reductions in pain scores from baseline with p-values of 0.0001. On clinical meaningfulness the minimally clinically important difference, or MCID, is NPRS change from baseline of minus 1. And the clinical meaningful difference is NPRS change from baseline of minus 2. All 3 doses of VX-548 showed improvement of greater than 2 points on the primary endpoint.

The pregabalin reference arm showed a mean change from baseline of minus 2.09 at 12 weeks, and was studied to provide context for the magnitude of the treatment effect and the

overall profile of VX-548. Moving on to Slide 8. Overall, the results of the secondary and other endpoints were consistent with the positive results for the primary end point. Here, we showed 2 of the prespecified endpoints of particular interest. The left panel is important because it shows the time course of pain relief and the results by week.

All VX-548 groups showed clinically meaningful and sustained change from baseline in NPRS to week 12. The right panel shows the responder analysis, which is important because it is one of the analyses that regulators have historically accepted and reflected in labeling. The 30%, 50% and 70% responses showed depth of pain relief. In all VX-548 dose groups, more [Technical Difficulty] than 30% of patients achieved a 50% reduction or more and more than 20% of patients in the mid- and high-dose groups achieved a reduction of 70% or more in pain scores. The pregabalin depth of response in the same categories is provided on the slide for reference.

Before moving on to safety, a quick comment on dose response. While our goal was to select doses that would result in a broad range of exposures, that did not happen. The actual exposures in the 23, 46 and 69-milligram dose groups were overlapping and in the high end of the expected therapeutic range. Given all the exposures were in the expected therapeutic range, it is actually reassuring to see robust and consistent change from baseline in the NPRS score in all VX-548 dose groups, as well as consistency in the secondary and other endpoints out to 12 weeks of treatment. Transitioning now to safety, Slide 9 summarizes safety and tolerability.

Similar to the efficacy section, I'll focus my comments on the safety and tolerability profile of VX-548, which was generally well tolerated at all doses studied for 12 weeks of treatment. The majority of AEs were mild to moderate, and there were no SAEs related to VX-548. One death in the mid-dose VX-548 group was due to atherosclerotic cardiovascular disease and was not related to VX-548. Focusing on treatment-related AEs. The rate of VX-548-related AEs across all 3 study arms was 14.5%.

For context, the rate of pregabalin-related AEs was 27.8%. Slide 10 lists all the treatment-emergent AEs; that is to say whether related or not, that occurred in 2 or more patients in any treatment arm, so you have a view of the comprehensive emerging safety and tolerability profile, which is quite favorable. Most AEs occurred in 1 to 2 patients. A few points regarding creatine clearance. We see no evidence of VX-548, or pregabalin for that matter, impacting renal function.

However, as mentioned earlier, there was a numeric imbalance in baseline renal function in the 4 arms of the study. The high-dose arm had both a numerically lower mean baseline creatinine clearance as well as a higher proportion of patients with impaired renal function defined as creatinine clearance less than 90.

And lastly, with regard to relatedness, there was one related AE of creatinine clearance decrease each in the pregabalin arm, in the mid-dose 548 arm, and in the VX-548 high-dose arm.

Slide 11 is the final slide on safety. Given the importance of assessing the emerging safety profile of VX-548, here we provide the related TEAEs in 2 or more patients in any treatment

arm. Again, we see a favorable profile for VX-548. As before, the pregabalin related TEAEs from this study are presented here for context. The related AEs seen in the pregabalin arm are consistent with the labeled safety profile of the drug.

Slide 12 provides a high-level overview of our pain development program. We believe the greatest value we can create for patients and shareholders is by discovering and developing transformative medicines. And once we crack a disease area with a transformative treatment, we believe in serial innovation and out-innovating ourselves. You've seen us do this in CF, and we aim to do the same in pain and every other disease in our sandbox. As evidence to this commitment to serial innovation, our broad and deep portfolio of potential pain medicines is depicted here, including NaV1.8 inhibitors and NaV1.7 inhibitors, which could be used alone or in combination.

To put a fine point on it, our novel non-opioid selective NaV1.8 and 1.7 inhibition approach is attractive for multiple reasons. It targets the underlying causal human biology of pain transmission. It works in the peripheral nervous system. And because of its mechanism of action, it holds the promise to work broadly in acute pain and in peripheral neuropathic pain. To conclude, we are very excited about these Phase 2 results because they clearly demonstrate the potential of VX-548 and the NaV1.8 inhibitor class to offer effective pain relief and a superior profile compared to available therapies for patients suffering from DPN, the starting point for a broad PNP indication.

This study also adds to the body of evidence for the safety and tolerability for VX-548 with 12 weeks of dosing, in support of our acute pain program. These results drive our urgency to advance VX-548 into pivotal development in patients with DPN, and into Phase 2 in patients with LSR. In the near term, the next steps include engaging with the FDA in our end of Phase 2 meeting, advancing VX-548 into pivotal development in DPN, and enrolling and dosing the LSR study which recently initiated. In the mid and longer term, we look forward to advancing the next wave of NaV1.8 and 1.7 inhibitors and securing a broad PNP label, which would be a first in the U.S. With that, we'll be happy to take your questions.

Operator Operator

[Operator Instructions] And the first question will come from David Risinger with Link (sic) [Leerink] Partners.

David Risinger Analyst

Yes. And congrats on the results. So Reshma, you provided color on kidney function. But I was hoping that you could discuss the 36-patient Phase 1 trial that was recently completed to evaluate PK and safety in patients with renal impairment. And then I noticed in your slides that you're also highlighting follow-on candidates 973 and 993.

Can you discuss how their profiles differ from 548 and how you're weighing commercialized [Technical Difficulty] acute pain than neuropathic pain since the 2 indications need to be priced differently per dose?

Reshma Kewalramani Executive

Thanks very much for the kind words, Dave. Let me tackle the question on the Phase 1 study. And then I'll turn it over to Stuart to talk about commercializing VX-548, which is obviously first in line and will be commercialized first, pending our Phase 3 program. So the studies that we're doing in Phase 1 are all of the typical studies that you would do for any small molecule, including studies in liver impairment and kidney impairment. To be clear, we see no evidence for 548 impairing kidney function.

This is about figuring out how to dose VX-548 in the event we have patients who have decreases in liver or kidney function. Those results will be available in the near term. Stuart, do you want to take the question about commercializing VX-548.

Stuart Arbuckle Executive

Yes, Dave. So obviously, we're very excited about these results because they continue to demonstrate the potential of the NaV1.8 class to create a new paradigm in pain management, including in neuropathic pain. To answer your question, we do see a path forward to be able to take forward VX-548 data willing, both in acute pain and in neuropathic pain, and successfully commercialize the same asset for both of those 2 indications. Clearly, those indications are often treated in different settings of care and things like that. So obviously, there will be pricing and contracting issues to work through, but we certainly see a path of being able to commercialize 548 in both settings.

And as Reshma said in her prepared remarks, both of them have significant unmet need. Both of them have very poor treatment options available today and we are more confident than ever with these data in hand, that VX-548 has the potential to be a multibillion-dollar product, if it's successful in its studies and gets regulatory approval.

Reshma Kewalramani Executive

Charlie just reminded me, Dave, that you also had a question on 993 and 973. These are next in the series of NaV1.8 inhibitors and behind those, we have NaV1.7 inhibitors. This is part and parcel of our portfolio approach. And for example, these are, 993, 973 have greater potency and 993 has the opportunity to also be dosed IV. Obviously, now that we believe [Technical Difficulty] this disease with this class of assets, we want to make sure we can help patients across the spectrum of acute pain as well as neuropathic pain.

Operator Operator

The next question will come from Mohit Bansal with Wells Fargo.

Mohit Bansal Analyst

Congrats on my side as well. So a couple of questions. One is on -- so given the success in DPN, how much can you read into this success? And how much can it -- how much confidence does it give you in the broader peripheral neuropathy pain program? Is there a correlation there?

And secondly, on the Phase 3 trial design, how similar or different it could be from the DPN Phase 2 trial? I know FDA typically likes multiple doses exploration, just to make sure that patients can actually have a lower dose as well in case they need it. But how are you thinking

about that?

Reshma Kewalramani Executive

Mohit, you cut out there. I think the second part of your question is about dose selection for Phase 3 DPN. Was the first part of your question, the read-through of these results to the Phase 3 acute pain program?

Mohit Bansal Analyst

No. I mean -- so the first part of the question was regarding how much you can read into the broader peripheral neuropathy program that you are running?

Reshma Kewalramani Executive

Okay. Got it. So Mohit's question refers to what do we see in this Phase 2 result in DPN? And what can we read through to LSR, lumbosacral radiculopathy, which falls in the same broader category as PNP. So obviously, as Stuart said, we have more confidence today than ever before because we now have the Phase 2 results in hand, safety and efficacy.

But each of these programs needs to go through their own exploration and so we're excited to advance this into LSR. The study has already initiated. As I've said previously, the safety is very much applicable across the board to all of our VX-548 programs. And on efficacy, we have to look at each of these programs individually. We should be able to do so in the near term with LSR, given the study has already begun.

With regard to dose selection on the DPN study, that is something that we're going to be talking to the regulators about at our end of Phase 2 meeting. So stay tuned, and we'll have more to share with you after we have those discussions.

Operator Operator

The next question will come from Colin Bristow with UBS.

Colin Bristow Analyst

Congrats on the data. Perhaps a commercial question. Just given the similar efficacy for Lyrica, from a commercial perspective, would you expect the use to be reserved to Lyrica-intolerant patients, at least in the sort of initial phase of use, just given that this is obviously a genericized market. And then as we think through to the acute pain program, assuming positive data, what is your appetite to use the priority review voucher for the filing there?

Reshma Kewalramani Executive

Colin, on the use of priority use vouchers and all that, we are fortunate that we have several of them, and I'll reserve commentary on our exact filing strategy as we get through Phase 3. Let me turn it over to Stuart to talk about the commercial opportunity, which I do think is large and significant.

Stuart Arbuckle Executive

Yes. So Colin, thanks for the question. In terms of the commercial opportunity, as Reshma

said, we think it's very significant. If 548 has a superior benefit risk profile to pregabalin, as we expect it will based on these data, then we certainly think that is going to be a very significant product, and we will be looking for a broad label in diabetic peripheral neuropathy, not a label which [neeses] us for more kind of severe patients. Just on that topic, I mean, the unmet need here is very, very substantial for new therapies in DPN.

If you look at the current treatments that are used, there are very high discontinuation rates, very high rates of dose adjustments. There's significant switching between different classes and different types of medicines. 40% of patients in 1 year will try 3 or more different medicines. That's the level of switching and polypharmacy there is for patients with diabetic peripheral neuropathy. That's the level of unmet need here.

So as we've said, we think the need is very, very substantial. And as I've said, if we have a superior benefit risk profile, we think 548 is going to have great uptake in DPN. In addition, just to reinforce something that Reshma said as well, DPN isn't where we're going to stop. We have initiated our study in lumbosacral radiculopathy. And the reason we've done that is, what we are seeking finally is a broad label for the treatment of peripheral neuropathic pain writ large, which impacts about 10 million people here in the United States alone.

Colin Bristow Analyst

That's great. Congrats again.

Operator Operator

The next question will come from Salveen Richter with Goldman Sachs.

Salveen Richter Analyst

Congratulations on the data here. 2 questions for me. One is, can you explain how the 3 doses ended up at the high end of the therapeutic index, and what this means for dose selection on the forward. And then 2, what can you tell us on the thoughts of the Phase 3 trial design for this program? And what profile payers want to see in order to reimburse the drug?

Reshma Kewalramani Executive

Thanks very much, Salveen. On the dose response, as I said in my prepared remarks, we wanted to select 3 doses that would span the exposure range. That is to say, having at least one dose that would be below the therapeutic effective levels. Because this is the first time we've dosed VX-548 in the chronic setting, we've also learned about PK/PD and exposures, and it's a learning process. The one thing that I take away from this though, and it's a silver lining, if you will, is the consistency of the response given that all 3 doses were in the therapeutic range.

But that's what it is. It's our first time dosing VX-548 over a 13-week period. With regard to the trial design, I'll cover that, and then I'll turn it over to Stuart for a couple of words on payers. We have to go through our end of Phase 2 meeting to talk about the patient population that we want to study, about the endpoints, both primary and secondary. NPRS is very standard, but the depth of response is also very important, and so we're going to talk about that.

And then, of course, it's a matter of how do we get to the broad PNP label. It's certainly going to be a combination of VPN and LSR, but what types of trial, what patients, how long and how many of each are all conversations we're going to have with the regulators at the end of Phase 2 meeting. Stuart, some comments on the payer view.

Stuart Arbuckle Executive

Yes, Salveen, on payers, I would say they are well aware of the unmet need in the treatment of neuropathic pain. They're well aware that the existing agents have variable efficacy, that there are high rates of discontinuations and switches and that sort of thing, as I've described earlier. So they are very well aware of that. They're very interested in new treatment options coming forward which have a superior benefit-risk profile. As you referenced, everything else that's currently used is generic.

And so they are going to be looking for something that has a strong benefit-risk profile. And based on the data we've got with 548 in Phase 2, we're super excited to take it forward into Phase 3, where we're going to be able to more fully elucidate the full profile of 548, and we're excited to see what that shows and then take that to payers.

Operator Operator

The next question will come from Robyn Karnauskas with Truist Securities.

Robyn Karnauskas Analyst

I think my question is more for Stuart, about the commercial side for neuropathic pain. Obviously, patients are on this drug longer. Can you talk a little bit about how long patients are typically on drug for neuropathic pain, and the magnitude of that market versus acute? And the second question is more about, you talked about discontinuation for the other drugs. Is it mainly from side effects?

Do you expect that to be the same for yourselves? Like why do people discontinue the current drugs? Is it not -- is it for efficacy or more for safety?

Reshma Kewalramani Executive

Robyn, let me turn it over to Stuart in 1 minute. I'll just make a couple of comments from the medical perspective. So as we use existing therapies, even the class of therapy sort of gives you an impression of how these drugs work in a pain condition. We are using anticonvulsants. So the gabapentinoids fall into the class of anticonvulsants.

Or we use antidepressives. And for example, because of some of the somnolent effects of the anticonvulsants, people alter the dosing pattern, don't take it at all or only take it at night. So these are some of the foundational challenges we're dealing with in medicine. Over to you, Stuart.

Stuart Arbuckle Executive

Yes. So Robyn, just to again paint the market sizes with a couple of numbers. Acute pain, as we've said, affects about 80 million Americans per year. Neuropathic pain -- chronic neuropathic pain affects about 10 million patients a year. But by definition, those patients are

in chronic pain.

Those people are in pain every single day of their lives and therefore, looking for relief every day of their lives. The markets in terms of revenue are approximately the same size today, despite both of them being 90-plus percent genericized. The chronic neuropathic pain market is also around about $4 billion in revenue today. In terms of the high rates of discontinuations, why does that happen? It really is happening for both sides of the coin.

Either lack of and/or variable efficacy, or people having to down titrate the dose or discontinue, because they can't manage with the side effects that you get. And the side effects that are some of the ones that we saw in our own study, where people have somnolence, dizziness, blurred vision, things like that, which interfere with their daily lives.

And so that's why you see these high levels of discontinuation rates. You see them either trying other classes of medicine or down titrating doses, adding other classes of medicines in to try and get that balance of effective pain relief but with manageable tolerability. That's why we're so excited about the profile of 548. It seems to us it's got that combination of really effective pain relief but with a great tolerability profile.

Robyn Karnauskas Analyst

And just to push you a little further on that, though, you're saying that markets are somewhat similar, but I would assume that if your drug is more safe and tolerable, they'd be on drug longer. So can I assume that neuropathic pain could be a much bigger opportunity than acute, if you're on drug more than 3 months? [I think it] sounds like that's what you're saying.

Stuart Arbuckle Executive

Yes. No, I agree with you, Robyn. I think there is an opportunity to increase the volume of medicine that is used because they exist in both classes, actually in both segments, acute and chronic neuropathic, because the existing medicines do not have the same sort of efficacy and tolerability profile. So I do agree with you. Our hope would be that 548 would be something which, as I say, combines great pain relief with great tolerability profile and maybe something that patients can start with and stay with.

Operator Operator

The next question will come from Brian Abrahams with RBC Capital Markets.

Brian Abrahams Analyst

Congratulations on the data. I was wondering if you could talk a little bit about the site that enrolled about 10% of patients, but looks like it was excluded from the efficacy analysis due to patient noncompliance. Can you talk a little bit about what happened there? What the data might look like if you were to have included that site and whether or not this site is also included in the acute pain Phase 3s?

Reshma Kewalramani Executive

Yes. The data that we're talking about is, there was one site with a total of 19 patients enrolled and those 19 patients were spread across all of the 4 arms, the 3 VX-548 arms and the 1

pregabalin arm. They were not -- the patients were not compliant with their medicine, and we know that because we're measuring concentrations. Therefore, that site was excluded from the efficacy analysis. It was included in the safety analysis as was mentioned, I think, on Slide 6.

We've done sensitivity analyses using the data from those patients, and it doesn't change the results of the study. With regard to whether the site was included in the acute pain studies or not, I really don't know, but I'm sure we will be able to look at that and we can certainly let you know. Remember, the acute pain trials are 1,000 patients each.

Operator Operator

The next question will come from Michael Yee with Jefferies.

Michael Yee Analyst

Congrats on the great data. We had a 2-part safety question. Going back to creatinine clearance. I think you made a couple of comments about above or lower than 90. Can you just describe a little bit more what you were seeing on the creatinine clearance, because there was, I think, 11% at the higher dose.

But how do you define the creatinine clearance and what do you think the ramifications of that are?

And then the follow-up question is on QT. I noticed, obviously, the QT study had completed on clinicaltrials.gov. I just wanted to confirm that, that was a successful result and comment on that.

Reshma Kewalramani Executive

Yes. The creatinine clearance, we've looked at the creatinine clearance GFR, any measure of kidney function and there is no impact of honestly, pregabalin nor of the VX-548 on renal function. We took some time to explain that creatinine clearance element, because we had this rule in the study, that if the creatinine clearance dips below 60, we automatically terminated those patients. So that's why we made a special point to make sure that, that was clear. On QT, yes, the study is complete.

No, nothing to report. All good there.

Operator Operator

The next question will come from Paul Matteis with Stifel.

Paul Matteis Analyst

I wanted to just ask one follow-up on the 19 patients from that site. How did you define noncompliance? Like is it not taking drug at all? Or was it just numerically lower than some of the other sites, understanding that in all these kind of neurology indications, compliance is never 100%. And then just on the drug development path forward, it's not uncommon in CNS to run extra studies.

If you just look at depression or schizophrenia or other areas with high intrinsic clinical risk, how do you think about going forward in running just 1 Phase 3 in each of these individual indications versus running multiple to diversify your risk?

Reshma Kewalramani Executive

Paul, on the one site with 19 patients, because this was a Phase 2 study where we did frequent PK monitoring, we can tell very clearly that one site is different than all the other sites, and this only happened with one site. So that's how we can tell because we actually measure concentrations. On the Phase III trial, you raise a very good point about study design and number of studies, and these are all part and parcel of what we're going to talk to the agency about. First, we need to understand what the agency needs for a Phase 3 program with the kind of label that we desire, which is broad peripheral neuropathic pain. And then we can go about designing the studies not only for regulatory approval, but additional studies that we may think are necessary.

So stay tuned. We'll certainly share the outcomes from our end of Phase 2 meeting with the regulators.

Operator Operator

The next question will come from Geoff Meacham with Bank of America.

Geoffrey Meacham Analyst

I also wanted to offer my congrats on the data. A couple of questions. The first one is that you guys previously have talked about not going after sort of the chronic pain market -- chronic non-neuropathic pain. I wonder whether today's data make you reconsider that. I'm thinking in terms of like with respect to chronic back pain or markets like that, that traditionally require a bunch of Phase 3s.

And the second one, I know Reshma, you're obviously talking to FDA end of Phase II meeting. But maybe just give us some consideration for having to use pregabalin or maybe another active comparator in your Phase 3 for neuropathic pain. A lot of questions here today on considerations with regard to payers and things like that. But wonder if you can capture maybe a novel differentiation or some metric using an active comparator or more than one?

Reshma Kewalramani Executive

Yes, sure thing. So Jeff on the question of, let's call it, musculoskeletal or osteoarthritic or sort of back pain. Those are important pain conditions and honestly, millions of Americans suffer from that. And the treatment there isn't great either. However, strategically, it doesn't fall in our area of -- our strategic area of pursuit.

In that, it requires a primary care sales force. That doesn't mean our drug won't work there. I bet you it will. And I say that because we actually studied musculoskeletal pain, i.e., osteoarthritis with the predecessor molecule VX-150, and it was positive there as well. So our focus here is on acute pain and neuropathic pain, which we're going to develop and commercialize ourselves as Vertex, because those are indeed specialty markets that work in our strategy.

For musculoskeletal pain, we'll get to those patients, but we won't be commercializing in that area ourselves, because it doesn't fit our strategy because it will need a primary care sales force. The other question about how could we design Phase 3 and what would that look like? I don't want to get ahead of our end of Phase 2 meetings, but a couple of comments to maybe give you some context. There used to be a regulatory guidance for drug development in neuropathic pain. It was withdrawn circa 2018 or so.

And basically, the fundamentals that are there that I think are important to keep in mind is, you don't have to study an active comparator. And there is openness about the endpoint, whether it's the NPRS over, for example, a 12-week period or if it's the NPRS at some other time periods. Or if it's the depth of pain response, like the 30%, 50%, 70% responder. And I think that, that old guidance document gives you at least a starting point of where we could begin. But I'll keep our thoughts about exactly what we're going to do and how we'll design it for after we have those meetings, so we can give you a clear path forward.

But I can tell you, I'm super excited about taking it to Phase 3.

Operator Operator

The next question will come from William Pickering with Bernstein.

William Pickering Analyst

Congrats on the data. For the creatinine clearance, how was the determination made that only one of the AEs that you saw in VX-548 was drug-related and implications for dose selection for Phase 3? And then I believe that one of your secondary endpoints on [cc.gov] was the, like a PRO patient global impression of change. So I was wondering what that data showed?

Reshma Kewalramani Executive

Yes. The AE determination will -- is by the investigator, and it's the same for all of the AE determinations. And with regard to the PRO, we'll share all the data in a manuscript that I'm sure will be out next year sometime. But it's very consistent, the PRO data, the sleep data, all the secondary endpoints are very consistent with the primary endpoint and with the data that we shared today.

Susie Lisa Executive

Chuck, we'll take one more question, please.

Operator Operator

Yes, ma'am. And the last question will come from Liisa Bayko with Evercore ISI.

Liisa Bayko Analyst

Congratulations on the data. Just 2 for me. First of all, can you just describe a little bit more about how VX-548 is metabolized, circulates and eventually leave the body? And then finally, just for the neuropathic pain, can you break down, I know you talked about the number of patients that have neuropathic pain -- and how many kind of fit into this peripheral form?

Reshma Kewalramani Executive

Yes. I'm going to ask Stuart to comment on the numbers of peripheral neuropathic pain and how they fall into DPN, LSR and other. On VX-548 metabolism, it's largely liver metabolized. Stuart?

Stuart Arbuckle Executive

Yes. Liisa, the 10 million people I was quoting in the U.S., they have peripheral neuropathic pain. Just under 2 million of them have diabetic peripheral neuropathy and then over 4 million have lumbosacral radiculopathy. So between those 2 specific indications within PNP, they account for over 60% of all patients with peripheral neuropathic pain.

Operator Operator

This concludes our question-and-answer session as well as our conference call for today. Thank you for attending today's presentation. A replay of today's event will be available shortly after the call concludes by dialing 1 (877) 344-7529 or 1 (412) 317-0088 using the replay access code 10184779. Thank you for your participation today, and have a great day.