Vertex Pharmaceuticals Incorporated

Vertex Pharmaceuticals Incorporated - Q3 2024 Earnings Call

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Operator Operator

Good day, and welcome to the Vertex Pharmaceuticals Third Quarter 2024 Earnings Call. [Operator Instructions] Please note this event is being recorded. I would now like to turn the conference over to Ms. Susie Lisa. Please go ahead, ma'am.

Susie Lisa Executive

Good evening, everyone. My name is Susie Lisa and as the Senior Vice President of Investor Relations. It is my pleasure to welcome you to our third quarter 2024 financial results conference call. On tonight's call, making prepared remarks, we have Dr. Reshma Kewalramani, Vertex's CEO and President; Stuart Arbuckle, Chief Operating Officer; and Charlie Wagner, Chief Financial Officer.

We recommend that you access the webcast slides 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 marketed medicines for cystic fibrosis, sickle cell disease and beta thalassemia; our pipeline, including the potential near-term launches of the vanzacaftor triple-NCF and suzetrigine in moderate-to-severe acute pain; and Vertex's future financial performance are based on management's current assumptions. Actual outcomes and events could differ materially.

I would also note that select financial results and guidance that we will review on the call this evening are presented on a non-GAAP basis. I will now turn the call over to Reshma.

Reshma Kewalramani Executive

Thanks, Susie. Good evening all, and thank you for joining us on the call today. Third quarter performance extended our strong momentum for the year with continued outstanding commercial execution in both CF and the early launch of CASGEVY as well as launch preparedness for two potential near-term approvals in early 2025. We also continue to rapidly progress programs in our clinical pipeline and achieved a significant milestone with three new programs advancing into Phase III clinical trials in just the last quarter. In CF, we are reaching more patients and delivered $2.77 billion in revenue, representing 12% growth this quarter versus Q3 2023.

Based on the strong growth year-to-date and our Q4 outlook, we are increasing our full year product revenue guidance to $10.8 billion to $10.9 billion while maintaining our previous operating expense guidance. With CASGEVY, the early launch is going very well. The enthusiasm from patients and physicians remains high, and we are pleased with the ATC and patient cell collection metrics. I'm particularly pleased to share that in Q3, the first patient received commercial CASGEVY, resulting in the first revenue recognition for this medicine. With respect to the overall pipeline, we remain on track to deliver our January 2023 [5 and 5] ambition with 5 new product launches over 5 years as we advance into this new era of revenue diversification.

Specifically, in addition to the CASGEVY launches in sickle cell disease and beta thalassemia, we are preparing for potential third and fourth product launches in early 2025, the vanzacaftor triple in CF globally and suzetrigine in moderate to severe acute pain in the U.S. Beyond that, the programs in Phase III development inaxaplin in APOL1-mediated kidney disease, suzetrigine in diabetic peripheral neuropathy, povetacicept in IgA nephropathy and VX-880 in type 1 diabetes are all progressing nicely. And we're also making strong progress in our mid-stage clinical pipeline with potentially transformative medicines, VX-993 in acute and peripheral neuropathic pain, VX-670 in myotonic dystrophy type 1, or DM1, and povetacicept in indications beyond IgA nephropathy. Tonight, I'll focus my R&D comments on CF, and four additional programs that have made notable advancements this quarter. First, in CF, our four marketed medicines are treating the underlying cause of disease in more than 68,000 patients around the world.

This includes children as young as 1 month with KALYDECO, as young as 1 year with ORKAMBI and as young as 2 years with TRIKAFTA. We are poised for the potential approval of the vanzacaftor triple, our fifth medicine for people with cystic fibrosis, 6 years of age and older. We have a PDUFA date of January 2 in the U.S., and we have also completed submissions in the EU, the U.K., Canada, Australia, New Zealand and Switzerland. Reviews in these jurisdictions are underway. We have also already initiated the clinical trial in children with CF ages 2 to 5.

Finally, in CF VX-522, our CFTR mRNA therapy in development with our partners at Moderna has completed the single ascending dose portion of the Phase I/II study, and continues in the multiple ascending dose or MAD portion. This therapy seeks to provide treatment for the more than 5,000 people with CF who do not make any CFTR protein, and we expect to share both safety and efficacy results from the MAD in the first half of 2025. Next, in type 1

diabetes, VX-880 is the stem cell-derived fully differentiated islet cell investigational therapy for people with type 1 diabetes and impaired hypoglycemic awareness, who experienced severe hypoglycemic events or SHEs despite optimal medical care. I am very pleased to share that we have completed our end of Phase II meetings with FDA, EMA and MHRA and following the successful regulatory interactions, we have reached agreement with regulators to advance the current Phase I/II VX-880 study to pivotal development and convert the trial into a Phase I/II/III study. This trial will include a total of 50 patients with difficult to control diabetes and severe hypoglycemic events despite optimal medical management.

In this Phase I/II/III study, the primary endpoint is the proportion of patients achieving insulin independence with the absence of severe hypoglycemic events. We are excited to be in pivotal development for this groundbreaking, potentially curative therapy for patients suffering from the most severe form of type 1 diabetes. It is particularly noteworthy that the first-ever pivotal trial of an allogeneic regenerative cell therapy for type 1 diabetes is beginning less than a year after we received the first-ever approval for CRISPR/Cas9 gene-edited cell therapy with CASGEVY. We are proud of the progress represented by these advancements in the cell and gene therapy space. To close out on the VX-880 program, I'll provide a quick recap on the data presented at EASD this September.

These remarkable data form the basis of our recent regulatory discussions and included more patients with longer duration of follow-up compared to the ADA presentation. These data showed 4 patients had 12 months of follow-up and all 4 achieved the primary and secondary end points. Specifically, they had elimination of severe hypoglycemic events, achieved insulin independence and achieved the ADA recommended hemoglobin A1c levels of less than 7%. Also at EASD, we shared that an additional 5 patients were off exogenous insulin as they progressed towards the 12-month primary endpoint evaluation. Safety and tolerability with this latest data cut were consistent with the June ADA presentation.

Beyond VX-880, our cells plus device or VX-264 program encapsulates the same VX-880 cells in a proprietary device designed to eliminate the need for immunosuppressants. We are currently enrolling and dosing patients in Part B, which is at the full target dose with the stagger between patients. The next stage, Part C of the trial, is at the full target dose without a stagger. We expect to share data from Parts A and B of the VX-264 study in 2025. Moving now to the povetacicept program.

Pove is a dual antagonist of the BAFF and APRIL cytokines, which play key roles in the pathogenesis of B cell-mediated autoimmune diseases. This dual inhibition mechanism of action, the preclinical and clinical data to date plus pove's once-monthly dosing frequency with small volume subcutaneous route of administration, give us high confidence in the promise of povetacicept as a transformative medicine for patients with IgA nephropathy and potentially additional B-cell-mediated diseases. Pove recently hit multiple milestones. First, I'm very pleased to share that we began the global Phase II RAINIER study of pove in patients with IgA nephropathy. This study is a randomized double-blind trial of pove 80 milligrams versus placebo on top of standard of care.

The trial is underway with screening, enrollment and dosing ongoing across multiple clinical sites globally. Importantly, the trial is designed with a preplanned interim analysis to evaluate

proteinuria when a certain number of patients reach the 36-week time point. This preplanned interim analysis could support a potential accelerated approval in the U.S. For full approval, the study will continue through week 104 and assess GFR. Second, the recently initiated RAINIER Phase III study was supported by positive data that we shared at the recent American Society of Nephrology Meeting.

In IgA nephropathy, updated Phase II data on patients with IgA nephropathy who received 80 milligrams of povetacicept continue to demonstrate Pove's best-in-class potential, with a mean 66% reduction from baseline in UPCR at 48 weeks with stable renal function. These results were accompanied by a 63% achievement or 5 out of the 8 study participants of clinical remission, defined as UPCR of less than 0.5 grams per gram, negative hematuria and stable renal function. We are very excited about these results and the potential they represent for IgAN patients globally, including the approximately 130,000 patients diagnosed in the U.S. Third, at ASN, we shared emerging pove data from another renal B-cell mediated disease, primary membranous nephropathy, a disease that affects 60,000 patients in the U.S. with no approved targeted therapies.

These data are from 3 patients who received pove at 80 milligrams subcutaneously every 4 weeks. On proteinuria, at 24 weeks, treatment with pove resulted in a mean 62% reduction from baseline in UPCR. And 2 of the 3 patients achieved partial clinical remission, defined as UPCR of less than 3.5 grams per gram and greater than 50% reduction in UPCR from baseline. In addition, anti-PLA2R1 antibodies, a biomarker of disease activity declined by a mean of 87% at week 20 in these patients. Across the renal studies, pove was well tolerated and most adverse events were mild or moderate.

We look forward to updating you as the pove programs progress. Shifting gears now from pove to the pain portfolio and starting with acute pain. The FDA review of suzetrigine in moderate-to-severe acute pain is well underway with a PDUFA date of January 30, 2025. The Phase III data from the 2 RCTs and the single-arm safety and effectiveness trial that form the basis of the acute pain regulatory submission were presented for the first time at the recent American Society of Anesthesiology Annual Meeting. There was very strong physician interest and positive feedback to the presentation of this data set.

And we now look forward to the completion of the regulatory review, potential approval and launch of suzetrigine. Stuart will provide more detail on the acute pain launch readiness. As suzetrigine progresses through its regulatory review, additional assets in the pain portfolio are also advancing through clinical development. Our next-generation NaV1.8 inhibitor VX-993 is being studied in 2 acute pain studies, a Phase II study post bunionectomy with the oral formulation and a Phase I study with the IV formulation. We also continue to make strong preclinical progress with our NaV1.7 pain signal inhibitor program that may be used alone or in combination with NaV1.8 inhibitors.

In peripheral neuropathic pain, or PNP. In diabetic peripheral neuropathic pain, which is one type of PNP, for which an estimated 2 million Americans seek a prescription pain medicine annually. I'm very pleased to share 2 updates. First, we have initiated the Phase III pivotal program for suzetrigine. Second, we have also initiated a Phase II study with the oral formulation of VX-993.

And in lumbosacral radiculopathy or LSR, another type of PNP that impacts more than 4 million Americans each year and for which there are no specifically approved medicines in the U.S., we have completed the Phase II trial. We remain on track to share Phase II results from this study by the end of this year. As a reminder, this is a 12-week trial of about 200 patients randomized to either suzetrigine 69 milligrams or placebo. The primary endpoint is the within group change in the NPRS score from baseline to the end of the 12-week study. The design allows for an efficient evaluation of the magnitude of the treatment effect for suzetrigine as well as the placebo group, so that we may appropriately size a potential Phase III trial if the Phase II data support advancement.

To wrap up the discussion on the pipeline today, a brief update on the myotonic dystrophy type 1 or DM1 program. DM1 is the most prevalent type of muscular dystrophy, impacting 110,000 patients in the U.S. and Europe and for which there are no approved therapies. Our Phase I/II clinical study of VX-670 initiated late last year, and I am pleased to share that the program has accelerated. The SAD portion of the Phase I/II clinical trial has completed dosing, and we have initiated the MAD portion of the study.

In the MAD, we will be collecting both safety and efficacy data. The primary endpoint of safety and the secondary endpoint is the change from baseline in the splicing index on muscle biopsy. We are excited about the progress and potential for VX-670 and look forward to providing updates on this program as it advances. With that review of the R&D highlights, I'll now turn it over to Stuart for a commercial update.

Stuart Arbuckle Executive

Thanks, Reshma. I'll begin by discussing CF and then provide some highlights of the ongoing CASGEVY launch and the outlook for suzetrigine in acute pain. Once again, we delivered strong results in CF as we further grew the number of eligible patients taking our CFTR modulators in both the U.S. and outside the U.S. We have made rapid regulatory and reimbursement progress with our CF therapies.

Notably, KAFTRIO now has regulatory approval and reimbursed access in every single country in the EU. We expect sustained revenue growth in CF over the short, medium- and long term. In the near term, we remain focused on reaching more eligible patients around the globe with our currently approved medicines. We anticipate the launch of our vanzacaftor triple combination therapy will drive further growth in CF. We expect this new treatment option, if approved, will be of interest both to those patients on a CFTR modulator and the more than 6,000 patients who have discontinued one of our current CFTR modulators.

And longer term, the potential successful development of VX-522 for the more than 5,000 people with CF who do not respond to CFTR modulators would drive additional growth in CF. Now turning to CASGEVY, our transformative onetime therapy for patients with sickle cell disease and beta thalassemia. CASGEVY has been enthusiastically received by patients, physicians and policymakers and the launch is gathering momentum across all regions. Two important markers of our launch progress are ATC activations and patient cell collections. On ATC activation, we now have 45 authorized treatment centers, up from just over 35 in Q2 and are well on our way to our goal to activate approximately 75 total ATCs globally.

On patient cell collections, approximately 40 patients have already had at least 1 cell collection, up from approximately 20 as noted on our Q2 call. We've also now had the first commercial patients receive their infusions of CASGEVY. On the payer landscape, we continue to work to secure access for patients. Coverage has not been a significant obstacle to patient access for this life-changing therapy in the U.S. And we were very pleased that in the U.K., a positive coverage agreement for TDT was reached in September with NHS England less than 6 months after regulatory approval.

Furthermore, we have now also entered into commercial discussions with the NHS to secure access for sickle cell disease patients. We also continue to make exciting progress on the regulatory front with approvals in the quarter for both sickle cell disease and TDT in Switzerland and Canada. And in the Middle East, we anticipate CASGEVY regulatory submissions in Kuwait and the United Arab Emirates by the end of this year. Given our confidence in the growing patient demand we are seeing for CASGEVY, we are investing in additional manufacturing capacity. And in September, we were pleased to attain approval for a third manufacturing facility for CASGEVY with our partner, Lonza.

We are focused on a strong finish to the year for CASGEVY. We continue to see high interest levels and recognition of the value of CASGEVY among patients, physicians, governments and other stakeholders, and we remain confident in our view that CASGEVY represents a multibillion-dollar opportunity as it helps more and more patients around the world. We have built a strong foundation for this transformational therapy and we look forward to the momentum it will carry into 2025. Shifting now to suzetrigine in acute pain as we are approximately 3 months from our U.S. PDUFA date and potential launch.

Our field teams are fully hired and trained, and we are launch ready. Suzetrigine has the potential to provide a transformative treatment option for the 80 million people who seek a prescription therapy for moderate-to-severe acute pain each year in the U.S. And in doing so, we believe we will have the opportunity to build another multibillion-dollar franchise for Vertex. Despite existing therapies, patients and providers across the U.S. recognize the high unmet need for effective and well-tolerated pain management options.

This was underscored by a recent nationwide survey we commissioned. The State of Pain survey included responses for more than 500 providers and 1,000 patients and highlighted the significant challenges with current moderate-to-severe acute pain treatment. Among many notable survey findings, I'd note that in contrast to the view held by some that opioid use disorder is only a risk of long-term opioid use for chronic conditions, 78% of the health care providers surveyed expressed concerns over the side effects of opioids and potential for developing addiction when treating patients for acute pain. Additionally, nearly 90% of providers reported that the risk of side effects of existing therapies limits their ability to treat acute pain adequately. And 2/3 of patients indicated they would request a non-opioid option if they experience acute pain again.

These survey findings were similar to sentiments relayed in our conversations with anesthesiologists and pain specialists at the recent ASA Annual Meeting, where our Phase III results were well received, confirming our belief that physicians are eager for a new therapeutic option to fill the gap between NSAIDs and opioids. The views expressed in the

State of Pain survey and at ASA are not surprising given the tragic statistics surrounding opioid use. For instance, approximately 10% of acute pain patients treated initially with an opioid will go on to have prolonged opioid use, and 85,000 will develop opioid use disorder within the first year. Overall, the cost of the opioid crisis remains stubbornly high at $180 billion per year. $60 billion of this spend is on health care costs, including an estimated $10 billion to $20 billion for the health care costs of opioid use disorder that are attributable to opioids initially prescribed for acute pain.

We are hearing these same survey sentiments directly in our pre-approval information exchange conversations with payers as well as targeted IDN and hospital formulary decision-makers. These conversations are going well, and we are working to accelerate both formulary and payer coverage decisions by engaging early to quantify the unmet need and highlight suzetrigine's benefit risk profile. Ultimately, our goal is to fundamentally change the way pain is treated. Our key commercial focus for suzetrigine in 2025 is securing broad access and investing to ensure a seamless experience for patients and physicians. Therefore, we have made the strategic decision to invest in initiatives that enable smooth, rapid access for patients prescribed suzetrigine.

This is critical given the time-bound nature of treating acute pain. One key initiative is our work to secure national retail distribution. Another initiative is the creation of financial and co-pay assistance programs for patients that will support patient access, given expected strong demand from physicians and patients ahead of the typical payer coverage time lines. This will enable patients who are prescribed suzetrigine to receive the medicine that they and their physician think is right for them. Together, these elements of the launch plan will enable us to build a strong base of prescribers that will benefit the acute pain program for the long term.

Our goal is to maximize the long-term value of the significant innovations in our pain pipeline, including suzetrigine in peripheral neuropathic pain, IV and oral formulations, VX-993, NaV1.7s, and potential combination therapies. We look forward to beginning to deliver on this transformational vision, starting with patients with moderate-to-severe acute pain post the potential approval of suzetrigine in early 2025. Finally, we continue to see momentum on the policy front. The NOPAIN Act, which goes into effect on the first of January 2025 includes an add-on payment for novel oral non-opioids when used in the hospital outpatient and ambulatory surgery center settings. Furthermore, the proposed alternatives to PAIN Act is now cosponsored by 64 members of Congress from both parties, given its logical appeal to equalize branded and generic co-pays as well as prohibit requirements to step through opioids before a branded non-opioid can be used for Medicare Part D patients.

Additionally, all 50 states have guidelines limiting opioid use and approximately 1/3 of all states require or encourage prescribers to consider non-opioid alternatives. Furthermore, there is good momentum. Over 1/3 of states are considering legislation to ensure that patients have equal access to non-opioid options in Medicaid and/or state-regulated plans. To conclude, there has never been a more exciting time to be at Vertex. We continue to drive sustained growth in CF with the anticipated launch of the vanzacaftor triple early next year.

And we are in a new and exciting era of commercial diversification with the ongoing launch of CASGEVY in the U.S., Europe and the Middle East. We are executing on our launch

preparations for suzetrigine in acute pain while looking forward to multiple programs in Phase III development and even more in the early and mid-stage pipeline. I'll now turn the call over to Charlie to review the financials.

Charles Wagner Executive

Thanks, Stuart. Vertex's excellent Q3 results demonstrate once again our consistent, strong performance and attractive growth profile. Third quarter 2024 revenue grew 12% year-over-year to $2.77 billion, with strong growth of 10% in the U.S. and 14% outside the U.S. Year-to-date revenue of $8.1 billion represents 10% growth over the comparable 9-month period in 2023, including 9% growth in the U.S.

and 13% growth outside the U.S. Reported third quarter revenue included $2 million from the first patient dosed with CASGEVY. On the expense front, Q3 2024 combined non-GAAP R&D acquired IPR&D and SG&A expenses were $1.08 billion compared to $993 million in the third quarter of 2023. Q3 operating expenses include $15 million in AIPR&D charges compared to $52 million in Q3 '23. Q3 2024 non-GAAP R&D expenses of $764 million increased 5% year-over-year reflecting ongoing investment in the advancement of our broad R&D portfolio, including multiple clinical trials and the absorption of Alpine Immune Sciences' expenses, partially offset by the transition of certain costs from R&D to COGS and inventory following Phase III clinical successes.

Within R&D specifically, the Q3 sequential step-up in non-GAAP R&D expenses reflects the advancement of multiple studies, including suzetrigine, pove and inaxaplin in Phase III programs, VX-993 in Phase II acute and peripheral neuropathic pain studies and our ongoing work in T1D. Q3 '24 non-GAAP SG&A expenses of $300 million increased 39% versus prior year, primarily as a result of investments in the commercial organization, including launch activities for CASGEVY and onboarding of the full field force for suzetrigine in acute pain. We reported third quarter 2024 non-GAAP operating income of $1.31 billion compared to $1.17 billion in Q3 '23. Our non-GAAP tax rate for the quarter was 19.8%, in line with the 19.4% reported in Q3 '23. We ended the quarter with $11.2 billion in cash and investments.

We deployed over $300 million of cash in the third quarter to repurchase 640,000 shares. And year-to-date, we have deployed over $750 million to repurchase over 1.7 million shares. Now switching to guidance. We are raising our 2024 total product revenue guidance. With one quarter remaining in the year, we have a strong line of sight to a revenue range of $10.8 billion to $10.9 billion, representing 10% revenue growth at the midpoint at current exchange rates.

For Vertex operating expenses, our non-GAAP guidance continues to be a range of $4.2 billion to $4.3 billion in combined R&D and SG&A expenses, which is unchanged from the guidance provided on our last earnings call. For acquired IPR&D, we continue to expect approximately $4.6 billion for the year, including the Alpine asset acquisition charge recorded in the second quarter. Given that the Q2 2024 Alpine AIPR&D charge was not deductible for tax purposes, we expect the non-GAAP full year 2024 tax rate of approximately 90%. Aside from the impact of the nondeductible Alpine AIPR&D charge, our underlying full year 2024 non-GAAP effective tax rate would have remained in the range of 20% to 21%. As a result, the fourth quarter non-GAAP tax rate is also expected to be 20% to 21%.

In closing, Vertex posted excellent results yet again as we delivered double-digit revenue growth, advanced our CASGEVY launch, prepared for important anticipated regulatory approvals in early 2025, progressed our pipeline to be in four Phase III studies and continued to develop our mid- and earlier-stage pipeline. These and other anticipated milestones of continued progress in multiple disease areas are detailed on Slide 19. We look forward to updating you on our progress on future calls, and I'll now ask Susie to begin the Q&A period.

Operator Operator

[Operator Instructions] And the first question will come from Jessica Fye with JPMorgan.

Jessica Fye Analyst

Congrats on the povetacicept sub data at ASN.

I believe you're targeting an at-home monthly dosing profile for that product, but we noticed the Phase III RAINIER trial involves post-dose monitoring. Can you talk about the work you would need to do in order to get this approved for at home delivery? Do you need to run like a human factor trial, some bridging study? And could all of that be accomplished maybe during an open-label extension portion of the trial so that the product could launch with at home dosing?

Reshma Kewalramani Executive

Jess, let me take that question. This is Reshma. Thanks very much for the kind words. Yes, we were very excited about the results that we showed at ASN not only on proteinuria, but the emerging GFR results as well as the results on hematuria, and then, of course, the results in a related but separate B-cell-mediated condition called membranous nephropathy. You're right, in the current protocol, there is an injection that's administered by a health care professional in the office, and as would be expected and is conventional in biologics development, we fully expect and are planning for and have had all of our regulatory interactions to have povetacicept ready to be delivered at home monthly for commercial approval.

So yes, all those plans are in place, and we fully expect that for commercialization. It will be at home, monthly, small volume, subcutaneous administration.

Operator Operator

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

Salveen Richter Analyst

It's nice to see the progress here. For the upcoming Phase II suzetrigine data and LSR, could you help frame what Vertex is looking for in the delta and the NPRS score, for the drug versus baseline? But also versus placebo, recognizing that you're not powered on this front, just in order to kind of decide to move forward into this Phase III. And Separately, if you could just help us understand the confidence in defining this patient population for your trial?

Reshma Kewalramani Executive

Yes. Sure thing. Salveen, we are very close to having the results. So I'll let the results speak for

themselves. And as I said in the prepared remarks, I do fully expect for us to be able to share them before the end of the year.

In terms of framing the study and what do we want to gain from the study? I would say three things. Obviously, we're looking for a good safety profile. So we're looking at the safety. But I think your question really pertains to efficacy.

So on efficacy, it's a measurement within group of the VX-548 NPRS score baseline to 12 weeks. We're looking for that number to be statistically significant. We're also looking for the magnitude, the sheer number of that NPRS score, the magnitude of that treatment effect. Same thing for the placebo arm. We're looking for the magnitude of that treatment effect.

And as you rightfully pointed out, we did not power the study to be able to measure the change from baseline, 548 versus placebo because that's what we intend to do in the Phase III study. We need the magnitude of these treatment effects so that we can appropriately size the Phase III trial, assuming Phase II is positive. With regard to the confidence in the trial, as I said before, the results were available for the acute Phase II and then Phase III, the DPN Phase II. And now as we await the LSR data, I have high confidence and that comes from three places. One is the mechanism of action.

Two is the building body of clinical evidence, not only in acute pain, and DPN from 548, but the predecessor molecule VX-150. And one thing that you asked directly about, which is the selection of patients. The LSR study was designed to think through what the placebo effect might be to make sure that sites were appropriately trained, to make sure that we selected patients who really had LSR, lumbosacral radiculopathy. And we've done that carefully through patient selection on physical exam, which is really the best way to identify these patients. So I have high confidence based on all three of those factors, including the patient selection.

Operator Operator

The next question will come from Terence Flynn with Morgan Stanley.

Chun Yu Analyst

This is Chris on for Terence. Just one question on suze. We know that you won't comment directly on its pricing, but can you provide some of the inputs that you are considering as you make decisions on how to price the drug?

Reshma Kewalramani Executive

Absolutely. Stuart?

Stuart Arbuckle Executive

Yes, Chris, we're going to be taking into account the same considerations we always do for all of our medicines, and that's driven by the level of clinical benefit that we believe suzetrigine delivers. And also the unmet need that it is solving both at an individual patient level, but as importantly, at a societal level, and we'll be taking all of those inputs into account and making our pricing decision much closer to the approval time.

Operator Operator

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

Mohit Bansal Analyst

I would ask another question on LSR. So if you look at -- so the question is two parts. One, when you look at Lyrica's mechanism of action, can you just compare in contrast versus VX-548 and how direct VX-548 versus Lyrica? And Lyrica also, if you look at some of the subgroup analysis where people looked at neuropathic pain specifically, it does seem to have some impact in neuropathic pain. Can you confirm that?

Even in LSR-related neuropathic pain. Can you confirm that?

Reshma Kewalramani Executive

Sure. So Mohit, you asked some really good questions about gabapentin or gabapentinoids. So Lyrica is an example of that versus suzetrigine. Let's tackle mechanism of action first. The mechanisms of action are completely different.

So the gabapentinoids work because they are -- they were discovered and developed originally as antiepileptic medicines, and what they do is depress the central nervous system. That's how those medicines work. It doesn't really have anything to do with pain, neuropathic pain or otherwise. The way that the suzetrigine molecule or VX-548 works, is it specifically acts on NaV1.8 channels that are specifically found in [c-fibers] that are only in the peripheral nervous system. And the reason for the confidence based on mechanism of action.

Again, when we were waiting for the acute pain results and the DPN results in the same confidence frankly, here as we wait for LSR results is because of that very specific mechanism of action. Pain signal, the way we feel pain is by way of the action potential being propagated by what are called these NaV channels. So that's on the mechanism of action. On Lyrica and where did they have positive results. I can speak to the high level of gabapentinoids, and the gabapentinoids have had positive results.

And as you know, they are indicated for diabetic peripheral neuropathy. However, they did not have positive results for LSR. Now it is entirely possible that in some studies or in some subgroups there could have been some signal, but I won't comment on that. I will tell you that it is not approved in the U.S. for LSR.

Operator Operator

The next question will come from Tazeen Ahmad with Bank of America.

Tazeen Ahmad Analyst

As we think about LSR and read-throughs to the other indications that you're pursuing, regardless of whatever the data shows for LSR, should we try to have a read-through as to what the results could mean DPN for example, which I think is reading out next year? And then secondly, I did want to ask about news from a competitor. Orion Corporation, I believe, recently announced that it's NaV1.8 ODM-111 was discontinued in both acute as well as

chronic pain studies. They said in the press release due to a narrow therapeutic window. I was curious if there was any kind of interpretation to make from that molecule not moving forward given the similarity and mechanism of action?

Reshma Kewalramani Executive

Sure thing. Tazeen, let's take on the question you asked about the molecule that was discontinued. It doesn't surprise me, and I won't comment directly on that molecule. But the reason I say it doesn't surprise me is that many, many companies have worked for many, many years, if not decades, to try and tackle NaV1.7 and NaV1.8, including ourselves. And the challenge has long been -- well, let me start with the reason people have been targeting Nav1.7, 1.8.

Many people call it the holy grail of potential targets in pain conditions because it is so specific to the transmission of pain. The challenge has been that the NaV1.1 through NaV1.9 channels are similar, and as people have tried to discover drugs that target NaV1.7 or 1.8, they've run into serious challenges in coming up with molecules with specificity, which is why I say I'm not surprised at all. Our molecule is 40,000-fold more specific. It is very, very specific for the NaV1.8 channel versus anything else. I'll tackle your second question about how should we think about LSR versus DPN.

Well, the commonality is that there are both types of peripheral neuropathic pain. But no, I wouldn't see any reason to relate the LSR data to the DPN data. The 548 same molecule that's already in DPN is in Phase III development. We've already had regulatory interactions. We've completed our end of Phase II meetings.

We -- as I said in my prepared remarks, we are well on our way in terms of the Phase III trial, screening, enrollment and dosing and I don't expect any changes.

Operator Operator

The next question will come from Michael Yee with Jefferies.

Michael Yee Analyst

We had two pipeline questions. We are excited about the idea you have 993 as well, which is the second compound for NaV1.8. I just wanted to understand if there is a significant benefit other than potency. Because I don't recall the 548 which PK are exposure limited. So I think that you're getting plenty of drug on board, and you've already had some pretty good results.

So I just wanted to understand if 993 despite being more potent -- significant other properties that would hit better on the NaV1.8 channel in the clinic. Our second question is actually a simple one on APOL1, which I know is -- hasn't been talked about too much here, but given the positive regulatory environment that we are seeing in IgAN, I was just wondering if you believe that on the 1-year interim you could probably file on UPCR? Just remind us what you've said and what you think you could do on the 1-year data?

Reshma Kewalramani Executive

Yes. Sure thing. Let me tackle 993 first. Michael, as you know, across our entire portfolio,

every single lead asset has a follow-on asset, and that is because if it is humanly possible to do better, just like we did in CF, we are committed to be the ones who do so. So one purpose of 993 is in that vein of serial innovation.

And if we can do better, we're going to be the ones who do it. The second reason specifically is we seek to really be broad in the pain space. VX-548 cannot be formulated into an IV formulation, 993 can. So that's the second reason for 993. And the third reason is we're making good progress with our NaV1.7 program.

That's still in preclinical development. But as that program progresses, we'd like to identify the best potential NaV1.8 to be used with NaV1.7, whether that's 548, whether it's 993 and/or other molecules is a third reason that we're developing 993. So we have the most optionality for the best pairing of the NaV1.7 program, which could be used alone or in combination with NaV1.8. And then moving to the question on inaxaplin, this is a program in APOL1-mediated kidney disease. This program is in Phase III development, and we are continuing with the enrollment in this program.

You asked a really interesting question about the regulatory environment. It does seem to be evolving right in front of our eyes here in renal medicine, particularly in homogeneous proteinuric kidney diseases. We had our end of Phase II meeting with the regulator some time ago, so before the more recent discussions in FSGS. And what we've said in our agreements pertain to a potential accelerated approval with a certain number of patients at the 1-year time point with endpoint read on GFR slope. But it's terrific to see the discussions continue on whether proteinuria in and of itself can be an endpoint for other proteinuric kidney diseases.

Operator Operator

Your next question will come from Evan Seigerman with BMO Capital Markets.

Evan Seigerman Analyst

So now that you had a patient go through the full CASGEVY commercial process, can you discuss what you learned about the administration? What went well? What do you hope to optimize further? And when do you expect to dose the next patient?

Reshma Kewalramani Executive

Yes. Sure thing. Let me turn that over to Stuart, Evan.

Stuart Arbuckle Executive

Yes, Evan. I think I covered much of this on our Q2 call actually, that we've learned an awful lot, as you always do when you were out there post approval, commercializing a medicine in the real world as it were. And I think we've learned or reinforced our learnings that we kind of went into, that we know that this is a very big decision for a patient and the physician, but particularly for the patient to make to embark on what is a lengthy treatment journey. But we know that there is significant enthusiasm for that because there is the potential for lifetime future benefit. So we've learned that it is a big decision and that is taking a lot of time for physicians and patients to have those discussions, to want to embark on that journey.

And that includes discussions at the beginning before the cell collection process begins, but also includes discussions at the end of the process when scheduling the actual CASGEVY infusion because obviously, that part of the process entails the patient being an inpatient for a number of weeks. And obviously, that is a significant disruption to anybody's life. And so that is something in which they need to think very carefully about. When they are, they're going to take time out from their normal life to go through the final step in the process. I guess a couple of the other things that we've learned is that authorized treatment centers are also very keen to sign up for the potential to be able to provide CASGEVY to their patients.

And I'd say the last thing that we've learned is that, the enthusiasm that payers and policymakers showed when the product was initially approved around the scientific advance that CASGEVY represents has really translated into excitement, to want to be able to provide this medicine to their patients. And we've seen that here in the U.S. where reimbursement is not an access barrier to patients initiating. And we've seen that we've been able to secure reimbursement agreements in, for instance, the U.K. for TDT.

We have early access programs, for instance, in Italy. And also, we have good access in Saudi Arabia, which is as we've said before, has a particularly high prevalence of disease. So I say we learn things on all elements, patients, physicians and payers and policymakers and we'll continue to learn as we move forward.

Operator Operator

Next question will come from Phil Nadeau with TD Cowen.

Philip Nadeau Analyst

Congrats on the progress. And a question for Stuart as well on suzetrigine's commercialization. Stuart, you mentioned in the prepared remarks that contracting discussions are underway. And then you also gave I think one example of strategic initiatives in the co-pay assistance programs. Could you further characterize the contracting discussions, how are those going?

Does insurance understand the need for new non-opioid options? And then in terms of the strategic initiatives, is it mainly on co-pay assistance? Or are there other strategic initiatives that are also underway?

Stuart Arbuckle Executive

Yes, Phil, thanks for the question. So I would say that the conversations with payers are going very well. There is a high degree of appreciation for the unmet need, not surprisingly. And there is a lot of enthusiasm for a new treatment option, which has the kind of benefit risk profile that suzetrigine has, the first novel, non-opioid medicine for literally decades. So high level of enthusiasm for it, not surprisingly.

Payers are aware of just how many patients suffer from acute pain in the United States. And so they are thinking their way through budget impact. So we're very early in those discussions. But our focus, and I would like to think theirs is, is to make sure that as close as possible to approval, we can make sure that we have reimbursed access so that physicians

and patients can get access to the medicine that they want to use. So I would say those discussions are going very well.

I pointed to a couple of initiatives that I think are really, really important, Evan. You picked up on one of them. Whilst the discussions are going very well, we know that there is often a lag between approval and having reimbursed access as payers have to work through their normal process. And obviously, we're trying to accelerate that. But we are anticipating there will be some lag for some patients groups.

And there, you really have two choices. You can kind of accept there's going to be a lag -- a gap, sorry, and some patients don't have reimbursed access and so therefore, won't get access. Or you can try and solve that problem whilst the plans are working on reimbursed access and coming up with their final policies. And we've chosen to solve it. We know there's going to be a lot of enthusiasm from physicians and patients who want to try suzetrigine.

We want to make sure that we are doing everything we can to make that a seamless experience, even if the plan hasn't yet made a final decision. The one other area I would share with you, which I pointed out is retail distribution. Obviously, patients in acute pain can't wait. And so when they turn up at a retail pharmacy with a prescription for suzetrigine, that suzetrigine needs to be there on the shelf so that the pharmacist can dispense it. And so one of the other areas that we are spending a lot of time focused on is ensuring there's national retail distribution of suzetrigine, again, as close as possible to approval as we can.

So that's a couple of areas that we are working on.

Operator Operator

Next question will come from Debjit Chatterjee with Guggenheim Partners.

Debjit Chattopadhyay Analyst

My question, which is on inaxaplin. Given the recent traction, when should we expect enrollment completion? And additionally, given the historically low compliance rates for antihypertensives, how big could inaxaplin be in the growing Vertex renal franchise?

Reshma Kewalramani Executive

Debjit, this is Reshma. I'll turn it over to Stuart to give you a sense of the commercial opportunity here. With regard to enrollment completion, we haven't given guidance on that, and I'm going to leave it at that for now. I will just remind Debjit, that there's two enrollments to be aware of. One is enrollment to get us to the time point for accelerated approval.

And then second is the enrollment for the completion of the full study. Obviously, it's going to be faster to get to the enrollment number, which we also haven't shared, but it's a subset of the overall enrollment for the accelerated enrollment time point. Stuart, do you want to comment a little bit on commercial opportunity for inaxaplin? And Debjit points out, there is a large growing renal franchise here.

Stuart Arbuckle Executive

Yes. So in terms of commercial potential, we know that there is approximately 100,000 or so

patients living with AMKD between the U.S. and Europe. The vast majority of which are here in the United States. So there is a very, very significant commercial opportunity if we can deliver on the first product, which is actually treating the underlying cause of disease for these patients.

Now I say there are about 100,000 or estimated to be about 100,000 patients living with the disease. Many of them are undiagnosed and not genotyped at this point in time, given the fact that the gene was only discovered approximately 14 years or so ago. And so this is a very new disease. So obviously, this is going to require a large amount of disease awareness, increases in diagnosis and certainly genotyping, and we are already supporting initiatives like that. But in terms of total potential, as I say, over 100,000 patients, and therefore, we think inaxaplin has a multibillion-dollar opportunity ahead of it.

Operator Operator

The next question will come from Olivia Brayer with Cantor Fitzgerald.

Olivia Brayer Analyst

I wanted to follow up on LSR. What's the internal bar for actually moving VX-548 into a registrational program? Do you need to see a certain delta versus what the placebo arm shows at 12 weeks? Or would a faster separation in the initial first few weeks on treatment versus placebo actually be enough of a signal to take it forward? I guess what I'm asking, right, is if those 2 curves were to come together at the end of 12 weeks, what kind of signal would be enough to move it forward, if that makes sense?

Reshma Kewalramani Executive

Yes. Olivia, this is Reshma. I really do understand the question. What I said earlier, I think, is the best way to understand what we're looking for. We're looking for good safety.

And we're looking for the magnitude of the treatment effect in the 548 arm and the magnitude of the treatment effect in the placebo arm. You're very right to point out that there's going to be consideration that we give to when the curve separate. We're going to look at all of the details of the NPRS score, we're going to look at subgroups. We're going to do all of the things that you would expect us to do. The key point is we want to see the magnitude of the treatment effect, so we can appropriately size that Phase III trial, assuming that the data are supportive.

As I said before, it's not too much longer that we have to wait. And then once we have the data, we'll certainly be able to talk in a very fulsome manner about exactly what the basis of our decision making is and talk further about the potential Phase III study. Olivia, I'll just use this moment to correct on the question that -- I think it was Mohit who asked earlier, it could have been Tazeen. It is 30,000-fold more sensitive to NaV1.8 than anything else. I said 40,000.

And we can go on to the next question then.

Operator Operator

Our last question for today will come from Ms. Liisa Bayko with Evercore ISI.

Liisa Bayko Analyst

I was curious to follow up on something that Stuart had indicated earlier, and that was the anticipation of no prior authorization for suzetrigine? And kind of what are the factors that you can influence that can decide that? And how confident are you that will be the case? Because that seems that we did a doc call and it seems like the kind of no barriers to getting drug is really critical. And it seems like this would be a really key one, and you kind of honed in on it.

So curious how confident you are, what leverage you have there?

Reshma Kewalramani Executive

Stuart, maybe you could comment both on the policy front and the other work that you're doing on the commercial front.

Stuart Arbuckle Executive

Yes. So Lisa, thanks for the question. So on the policy side of things, we've already seen that there are a significant sensitivity to the fact that the sorts of utilization management controls that can get put in place, particularly for brands versus generics could be a barrier to suzetrigine being launched, which is why we referred to the alternatives to PAIN Act, which is looking to prohibit exactly that sort of thing for our Medicare Part D beneficiaries. In our discussions with the other plans that we are talking to through our preapproval information exchanges, that is one of the topics that we are talking about. Obviously, there is the level of unmet need.

Obviously, we are able to talk in a compliant way about the benefit risk profile of suzetrigine, but we are also talking about what are some of the conditions which people might seek to use to provide reimbursed access. Obviously, different providers and plans have different controls. Often prior authorizations are required, even if they aren't combined with other types of controls. So for instance, I could still imagine somebody needing to have a prior authorization for a suzetrigine prescription, certainly before a plan has made a definitive coverage decision. What I couldn't imagine is somebody having a prior [auth], which requires a patient to step through a generic opioid before getting to suzetrigine.

So I don't think there's really one answer to your question, Lisa, because prior [auths] are used in very, very different ways. But we are looking to make it as easy as possible for physicians and patients because we know there is going to be such broad enthusiasm for suzetrigine when it's approved, hopefully in the early part of 2025.

Operator Operator

This will conclude 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 replay access code 10187025. Thank you for your participation today. You may now disconnect.