Vertex Pharmaceuticals Incorporated

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Philip Nadeau Analyst

Good afternoon, and welcome once again to TD Cowen's 45th Annual Healthcare Conference. I'm Philip Nadeau, one of the biotech analysts here at Cowen. It's my pleasure to moderate a fireside chat with Vertex Pharmaceuticals. We have with us today David Altshuler, the Executive Vice President of Global Research and CSO; as well as Stuart Arbuckle, the EVP and Chief Operating Officer.

Maybe gentlemen, to kick us off, can you give us a brief state of the company overview? When we meet at Cowen next year, what will we look on -- look back on a success? Please help us understand your top priorities for the next 1 to 2 years.

Stuart Arbuckle Executive

Okay. Well, thanks for having us firstly, Phil. State of the nation. Well, we finished 2024 in great shape. We had a terrific year in 2024, particularly with our CF franchise treating more patients around the world and delivered really great revenue growth for the year, and we ended up 2024 getting approval for ALYFTREK, which is our fifth medicine now approved for patients with cystic fibrosis.

And obviously, we are well underway with the launch of that medicine as we -- moving to 2025, we're focused on that launch, obviously, the continuing global launch of CASGEVY for sickle cell disease and TDT patients, where we expect that program to gather momentum in 2025.

And then most recently, January 30, we had JOURNAVX approved our non-opioid pain signal

inhibitor for moderate to severe acute pain, and we're a month into that launch and the excitement around that program is enormous.

So we are in this, as we like to say, a new era of commercial diversification, building on our leadership in CF, expanding now into sickle cell disease, TDT and then obviously, most recently, moderate severe acute pain.

From a development point of view, we have a great late-stage pipeline. We have four programs in pivotal development. We have inaxaplin, povetacicept, JOURNAVX in neuropathic pain and also [zumila-cel] in type 1 diabetes, so four programs in Phase III development.

And then a really good looking early clinical pipeline behind that, which we can talk more about. And we are strong from a financial perspective. So I'd say the company is really firing on all cylinders, diversifying commercially, a great late-stage pipeline, a research engine, which has proven to be incredibly productive and great financial flexibility as well.

Philip Nadeau Analyst

Before we dive into the pipeline programs, I think one of the most common questions we get, Stuart, is actually on you. Congratulations on your upcoming retirement. It's well earned, well deserved. And investors don't [indiscernible] you a retirement certainly, but they do wonder why it's coming right now in the early stages of the JOURNAVX launch. Can you talk a little bit about -- why is this....

Stuart Arbuckle Executive

Yes. Firstly, let me be 100% transparent. This has got nothing to do with Vertex. This company has never been in a better place, scientifically, clinically, commercially, financially, so it's got nothing to do with the company or where we are. I've never been more excited about the future of this company has.

It just so happens that it's the right time for me from a personal perspective. I have a milestone birthday coming up in July. I'd always promise myself that I'd like to be not working this hard by the time I got to that age. And so it's just the right time for me personally to move the next chapter.

In addition to all the things I said about the strength of the company, it is incredibly strong from a people perspective. And so we have a great successor for me as Chief Commercial Officer, Duncan, who's been by my side for the best part of a decade at Vertex. I've known Duncan for 30 years. We were at Glaxo together in the dim and distant past. So he is an amazing commercial leader.

And then the rest of my responsibilities are going to go to Charlie Wagner, our CFO, who's going to be a great next COO for this company. And so the company is in great hands.

Philip Nadeau Analyst

Congratulations again. Now diving into the programs.

Stuart Arbuckle Executive

That's the end of the niceties.

Philip Nadeau Analyst

Now we get down to real business. JOURNAVX, it was supposed to be in the channel by the end of February and available soon after. Can you give us an update on the launch? Have the first prescription has been written and filled?

Stuart Arbuckle Executive

Yes. So the product was in the full line wholesalers in February. It is now making its way into the retail channel. It's going to be available nationwide, I'm delighted to say in pharmacies across America, somewhere around 30,000 retail pharmacies will have JOURNAVX and in addition, it will be in hospitals as well. So that's fantastic.

We're a month into the launch, I would say, the level of awareness and excitement around JOURNAVX is as high as I've ever seen for any product that we have launched. We are beginning to embark on our discussions with physicians. They're incredibly excited about the profile. We're continuing to advance our discussions with payers, PBMs, GPOs, formulary decision-makers, P&T committees, the level of excitement, I'd say, is absolutely amazing for JOURNAVX. And yes, we're really excited about the future it has in moderate to severe acute pain.

Philip Nadeau Analyst

Maybe to drill down on the payer part of the equation. What has been the feedback about their willingness to pay $15.50 per pill for a branded drug in the pain space. What utilization management techniques do you think could be applied?

Stuart Arbuckle Executive

Yes. So obviously, we were having discussions with payers in a compliant way, pre-approval about the unmet need and the clinical profile of JOURNAVX and really nobody has any doubt -- in any doubt about the enormous unmet need for new non-opioid pain meds and everyone is super impressed with the profile of JOURNAVX.

Obviously, now we have the two other important bits of information that they need. One is the actual indication, which is very broad for moderate to severe acute pain, regardless of the etiology of that pain. And of course, they now know what the price is. I'd say the discussions continue to be very positive. We are looking to try and accelerate their coverage of JOURNAVX versus the kind of normal time lines.

We are advocating for as little in the way, not surprisingly, of prior authorizations and utilization management as we possibly can for a couple of reasons.

One, prior auths can be both burdensome and delay patients actually getting access to a medicine that may not be a problem as much for a chronic condition, which is slowly progressing, let's say, but these patients are in acute pain. They need treatment now.

And the other thing, which I think is a lot of people have brought up around utilization management is, obviously, we are launching into a market which is 100% genericized. So do we think there's going to be step outs. I don't see medically or ethically how people can think about putting in place step edits that make people go through a generic opioid given everything we know about opioids and their broad range of adverse events, including addictive potential. So we are advocating for as little as we can in the way of utilization management and prior auth so that patients get access to JOURNAVX when they need it.

Philip Nadeau Analyst

And on the legislative front, NOPAIN Act went to effect on January 1. Can you summarize what that does for you and for JOURNAVX and then the other legislative efforts that are underway to help with reimbursement?

Stuart Arbuckle Executive

So NOPAIN, just in case people aren't aware of it was an Act which went into law on the first of January of this year. It essentially enacts an add-on payment for Medicare patients treated in the outpatient setting or the ambulatory surgical center setting. It provides an add-on to the institutions for the cost of a non-opioid pain medicine. So over and above what they would get from their standard DRG, it provides them an add-on payment for the non-opioid pain medicine. .

JOURNAVX was not included on the list of products eligible for an add-on payment on the first of January because they don't want to put things on that list, which aren't yet approved and we weren't approved until January 30. We are now going through the administrative steps to have JOURNAVX added to the NOPAIN Act list of approved medicines because it's just gone into effect. There is no typical time line. This is the first time a product has ever been added to this list. And obviously, we also have a new administration.

So we're not entirely sure how fast it's going to be or how quickly we're going to get JOURNAVX added, but I have no doubt we will get added and I'm no doubt it's been a relatively short term. But because we are the first product ever to go through the process, it's hard to tell you exactly how long that's going to take. So that's for Medicare in the outpatient and ACS settings.

There are a number of other policy activities ongoing. So seven states last year enacted legislation around the use of non-opioid pain meds, either saying that you couldn't disadvantage the non-opioid pain med versus generic opioids or mandating that physicians counsel patients on their non-opioid options. 24 additional states this year already, since the beginning of the year, have put legislation on the books and it's making their way through their various houses to do similar things.

And then we also have other federal bills, which are also progressing. The Alternatives to PAIN Act is probably the most well known. The Alternative to PAIN Act has very broad bipartisan support was just reintroduced. It essentially is looking at Medicare Part D coverage and again, really importantly mandates two things: firstly, no utilization management control, so no step edits and things like that. and additionally, equal co-pays for the patient between a generic opioid and branded non-opioids.

So there isn't a financial disincentive to patients to take a generic opioid when there's a better alternative. So that could be a really important act. Again, that's for Medicare Part D coverage.

Philip Nadeau Analyst

Talk a bit about the pain market, the acute pain market specifically, how big is it? And how would you segment it in terms of channels or patient groups?

Stuart Arbuckle Executive

So moderate, severe to acute pain, 80 million Americans roughly per year get a prescription for moderate, severe acute pain, of which 40 million even today get an opioid. Despite everything we know about them and their adverse events and addictive potential, which I think talks to the fact that there really are no or were until a month ago, really no good treatment alternatives to kind of standard NSAIDs and/or opioids.

In terms of how the market breaks down, about 2/3 of those patients are seen within the institutional setting. So I think hospitals, ambulatory surgical centers, things like that. And they are either given a prescription and that prescription is filled in the institution if they're staying in patient for 2 or 3 days, let's say, after some procedure or a fall or whatever it might be. So they can get a prescription, and it's given inpatient or they're given a prescription once they're discharged for their ongoing pain management.

So those 2/3 of patients treated in institutional setting account for about 50% of all prescriptions. That's less than the 2/3 of patients largely because the prescriptions in the institutional setting are only for 2 or 3 days. The institutional prescriptions, that's about 15% of the 50%, the discharge is 35% of the 50%. And then the rest is largely office-based prescribing, which is all filled in retail through somebody's standard pharmacy benefit.

Philip Nadeau Analyst

And which segments is -- are you going to target? Or which ones are you going to prioritize?

Stuart Arbuckle Executive

Well, I think JOURNAVX is going to get used across all of them, to be perfectly candid with you. From a field force, from our sort of face-to-face promotional efforts, we're targeting the institutional setting because that's around about 2,000 institutions, which generates, as I say, 50% of all the prescriptions. Our other targets such as the high-volume prescribing offices, but as you can imagine, with something like moderate to severe acute pain, there is a very long tail when you get into the lower deciles, where there's tens and tens of thousands of physicians producing relatively less volume. We are certainly not targeting those folks.

Philip Nadeau Analyst

Investors are debating how quickly JOURNAVX is going to launch. Street consensus is about $90 million for this year. How does Vertex feel about its ability to hit consensus and the trajectory that's necessary to get there?

Stuart Arbuckle Executive

Yes. So we don't give individual product guidance. We give total product revenue guidance for the company. What I can tell you is what our priorities are for JOURNAVX. They are really twofold.

One is to get broad payer access for JOURNAVX through 2025. That's going to be a big area of focus because obviously, that's going to be setting us up for the long-term future. The other one is to get a broad base of prescribers prescribing it so that we've got large volumes of prescription. . Because payer coverage can take some time to come through, we are going to be solving for patients who don't yet have payer coverage, but get a prescription we will be solving for that at the pharmacy, so that the physicians aren't getting callbacks from the pharmacy saying this product isn't covered by this patient's plan and the patient isn't left with the choice of either paying cash or abandoning that prescription or asking for something else.

So we'll be solving that.

So what we have said is that we expect volume to run ahead of revenues in 2025 whilst we work our way through to getting robust and broad coverage of JOURNAVX during the course of 2025.

Philip Nadeau Analyst

Maybe two more questions on JOURNAVX before moving on to the rest of Vertex. And both on the pipeline. The DPN pivotal trial is underway. Can you talk about Vertex's confidence and success in DPN. I think one thing investors are now debating is we've seen Phase II data for DPN and LSR, magnitude of benefit across placebo for Pregabalin and JOURNAVX is basically the same across both studies.

So how confident can we be that we know whether it works in chronic pain?

Stuart Arbuckle Executive

So we feel very confident in DPN. And that's because DPN is a well-established indication where there's lots of Phase II studies and Phase III studies. We did a Phase II study originally VX-150. We did a Phase II study with the VX-548. We're in Phase III, and we feel very good about all that.

With regard to chronic pain, as you said, we divide that into -- for ourselves, we always go after the underlying cause of the disease. And so we divide that into peripheral neuropathic pain where the nerve itself is the problem and other kinds of chronic pain where, let's say, it's a tissue damages like that. We're focused on peripheral neuropathic pain. Whereas DPN is very well established, and we feel very good about where we are. As we've looked at that's about 2 million out of 10 million people with PNP, there's 4 million people or so who have LSR.

There's another 4 million have a variety of other things.

In LSR, it turns out, and this was interesting to learn. We couldn't find any Phase III studies. There are no approved medicines. We only found two Phase II studies that were like more than a couple of dozen people and that were longer than 28 days. And so it turns out, this is an area where there's very little precedent, there's very little -- and little precedent means

there's also very little information and trained individuals and sites to figure out how to do those studies.

And so it's actually very different than DPN. DPN remember is diabetics and they see one group of doctors and LSR is like a back pain problem. They see a different set of doctors.

And so we feel that in trying to bring JOURNAVX to a broad PNP label, just as we brought it -- have been able to get a broad moderate to severe acute pain label that we will work with the regulators now that we have these two Phase II studies, we can go have the end of Phase II meeting and talk about what would it take to get a broad PNP label. And as we've said and Reshma said on the call, once we've finished our own studies and thinking about how to do that have met with the agency probably midyear, we'll share what the plan is.

But the key thing is to innovate, we always do serial innovation. I think naturally, that's seen as like the medicines themselves. And we do have VX-548, we have the VX-993, and we have other 1.8 inhibitors and we're working on -- we've cracked Nav1.7 are nearing the clinic, but that also means how you do clinical trials, right? And if it's a case like DPN or acute pain, where there's a well-established practice where everything works well when people have done it, you may not need to innovate in that.

But when it comes to LSR where no one us to become the best experts in how to do that. And if that works with JOURNAVX, fantastic, it could lead to a broad PNP label. That's quite a good return on investment. If you add 4 million people, but actually, if it doesn't, we'll still be better at doing LSR, we'll learn more. And so when 993 comes along or the next medicine comes along, it will be that much faster and better because our goal is to transform the treatment of pain with these sodium channel-specific peripheral nerve blocking agents.

And I'm very confident that will happen. And that requires not just think about one indication at a time or one molecule at a time, but a plan of how we get there in the future.

Philip Nadeau Analyst

Turning to the CF franchise. Your guidance for this year's growth is 7% to 9% year-over-year, which is solid growth, although a bit of a deceleration from prior years. What are the pushes and pulls in that guidance? What could drive revenue growth better than that? Are there risks that could fall short?

And where do you think the CF franchise is in terms of saturating the market?

Stuart Arbuckle Executive

Yes. So as you said, the CF growth has been spectacular over the last few years, and we had a very strong 2024. We do see continued growth from patients who could respond to CFTR modulators and ALYFTREK is going to be a big part of that as it may encourage patients who previously discontinued to come back on to a CFTR modulator and because the ALYFTREK label, certainly the approved label here in the U.S. is broader than even TRIKAFTA has an additional mutations on it, which aren't on the TRIKAFTA label.

So ALYFTREK itself has the potential to provide incremental growth as does continuing to get to younger groups of patients as we continue to kind of march down the age ranges,

TRIKAFTA is now down to 2 to 5. KALYDECO's down to patients as young as 1 month. So we continue to look at going down in terms of ages that's so important because we believe that if you can treat patients early enough in life and get to high enough levels of control, high enough returning CFTR function to where it would be in a patient who didn't have CF, then we'll be able to sort of prevent the manifestations of CF developing as we know them today. So that's been the goal, and we are continuing to pursue that goal of getting to younger patients.

Then I would say the third element of growth is actually the increased number of patients living with cystic fibrosis, some of which is due to better data capture and better registries in countries, but some of which is also due to the fact that patients with CF are now living longer largely as a result of CFTR modulators and improvements in the quality of care for CF patients. So those are really the growth drivers of CF going forward.

The last growth driver for CF would be the ability to treat patients who don't respond to CFTR modulators. So about 93-ish percent of patients produce some protein and our CFTR modulators need some protein to work on. But there are patients who have genotypes where they produce no CFTR protein at all. For them, we need a different approach, and that's where the 522 program, as we call it, which is our partnership with Moderna and our mRNA program is intended to try and develop a medicine to serve those. As I say, that's about 7%, north of 5,000 patients in the world who, as I say, today, don't have anything to treat the underlying cause of disease.

We have a Phase I/II program ongoing with that asset, which we will read out sometime this year, and we're optimistic that will put us on a path to deliver a medicine for those patients, which would be great for them and also be another potential driver of growth for our CF business.

Philip Nadeau Analyst

How rapidly do you expect the TRIKAFTA group of patients to switch to ALYFTREK?

Stuart Arbuckle Executive

Yes. We haven't given any guidance on that. And the fact that many of our CF medicines are indicated for the same patients and so may decide to be on one or switch to another that kind of those puts and takes. That's why we've -- for a number of years now, going back to even only when we only had KALYDECO, we've given total product guidance so that it really doesn't -- it's really hard to predict exactly how many patients will transition at which point in time over time. And that's why we've given total CF product guidance.

I expect the majority of patients will transition over time. Largely because certainly at a population level, and we showed this in the Phase III study, ALYFTREK is a better CFTR modulator than TRIKAFTA based on the fact that it restores CFTR function at a higher rate as measured by sweat chloride in patients with CF, and it has the benefits of being once a day, which actually for a CF patient, when you have to take a fat containing meal with every dose of your CFTR module is a bigger deal than I think a lot of people think it will be. So we do expect the majority of patients over time to transition from TRIKAFTA to ALYFTREK but we haven't kind of put some sort of artificial time line on how fast we think that will happen.

Philip Nadeau Analyst

Competition in CF seems to bubble to the surface every 2 to 3 years, and we're starting to see those bubbles again. Can you talk about what Vertex is doing to stay ahead of the competition? What are the next generation of Vertex's molecule is going to look like? How do you think you can improve on a lift?

David Altshuler Executive

Sure. So let me start just by saying our goal has been and remains to bring all people with CF who respond to CFTR modulator, which is like 93% or so to carrier levels of CFTR function because carriers are completely healthy with a safe once-a-day medicine early in life before tissue damage occurs. And we've gotten quite far in that journey. As you know, ALYFTREK for example, the 6 to 11 study, over 50% of the people in that study were already at carrier levels. And of the remainder, 95% in total were below the diagnostic thresholds.

And this is sort of a bell-shaped curve. It's not that it's like responders, nonresponders, it's just -- that gives you a sense of where things are. So the goal is to go -- shift that curve, if you will, to the left. So the mean has to be even lower so that like 90% of people are below that threshold. Is that possible?

Yes. Why do we say it's possible because we already have assets that are in the clinic, VX-118, which is a finished Phase I, VX-828, which is nearing the end of Phase I, will be in Phase II for combo therapy that in vitro has shown us in our predictive assays because remember, it's not just an HBE assay. It's how you run the HBE assay, It's knowing that you've calibrated it to the clinical outcome.

Our molecules, which we believe can bring us that will be in Phase II this year. And so we will always continue serially innovating because we want to do the best for patients and we feel very confident that those molecules not only fully restore function to CFTR as remember, ALYFTREK does as well, very close, but also have the clinical properties and the -- all the properties, not just working in a dish, but physical properties, no DDI, no auto induction, no safety problems to date, things like that bioavailability, cell penetration, all the things you need, not just to do it in the dish but to do it in a person in a combo therapy. And so we feel very good about that, but we'll never stop, right? We'll keep going until we've actually done that for all the patients.

Philip Nadeau Analyst

Turning to the kidney disease pipeline. Inaxaplin is obviously in a pivotal trial for APOL1-mediated kidney disease. Your guidance is to complete enrollment in the interim cohort this year, which we, at TD Cowen, think means the interim analysis is likely to happen in 2026, even though I don't believe there's formal guidance that says that. The language around that interim analysis is that, I believe it's UPCR based with supportive evidence in eGFR slope. Can you discuss how that interim analysis will be conducted and what is necessary to support a filing versus not?

David Altshuler Executive

Sure. Well, first of all, that study we worked with the agency, and so we prespecified what the interim analysis would be and what it would look like. We will complete, as you said, the enrollment of the interim analysis cohort this year. The patients need to be followed for 48 weeks because that's the threshold before we can do that analysis, you can sort of work that through and then we have to analyze the data. And it's actually eGFR slope and UPCR is what was agreed to.

And the criteria will obviously be improvements in we're looking for improvements of the sort we saw in Phase I not only new UPCR but also the relationship of UPCR and eGFR slope across diseases of this sort is very clear. And so if that all holds, we're going to have a very potentially transformative medicine by those measures that we hope we could then get to patients even while we complete the study in terms of long-term outcomes.

Philip Nadeau Analyst

Is the bar statistical significance on those measures? Or is there a certain magnitude of improvement that has?

David Altshuler Executive

We'll see the data, and then we'll describe this.

Philip Nadeau Analyst

Okay. And povetacicept is also in a pivotal study where an interim analysis cohort is going to complete this year. Can you remind us of the endpoints for that interim?

David Altshuler Executive

Sure. So again, what it will complete this year is the enrollment of the interim analysis criteria -- interim analysis cohort, not the entire cohort, really you have to give a lot of credit, not just to Alpine, but also to our colleagues at Vertex because remember, they were completed Phase II. And in the year -- less than a year since then, we're able to have the end of Phase II meeting, start Phase III, and now we're at a global trial, as well as having made a deal to work in China. So we are really impressed by how our colleagues have accelerated that.

And the goal is obviously to get on the market as soon as possible. And the key metrics of proteinuria, which is a key metric in terms of all such diseases and has been shown as well to be predictive in this disease, but important to doctors, but obviously, we'll measure other things as well.

And we hope that profile as well as with safety and as well as actually some of the commercial aspects in terms of like the dosing regimen, the low volume, things like that, all will we think, have the potential to be a best-in-class drug for patients with IgAN. And then we also have the RUBY-3 and RUBY-4 studies ongoing looking at other conditions where we think there's potential for benefit. So we're really excited about Pove.

Philip Nadeau Analyst

Maybe a broader question on the pipeline. Can you talk a bit about how you think about assembling a pipeline in terms of stage of assets and a portfolio of risk in particular, I guess,

we're thinking you're throwing a lot of cash. Biotech valuations is very cheap. Would Vertex want to do a deal to come in and supplement what you already have?

David Altshuler Executive

I mean our BD strategy has not changed and remains the same. We have a corporate strategy in terms of not only the corporate strategy of investing in scientific innovation, transform medicine serious diseases and limited SG&A expense. So we keep doing that. . But we have an R&D strategy as well, as you know, validated targets that are the underlying causal biology, biomarkers, the clinical trials, et cetera, I'm going to run out of time, so I won't go through all those criteria we set.

And none of that has changed. We are agnostic to internal and external.

I think what's unusual about our company is it's not like there are two separate groups. The internal research and also external innovation, both report up to me. And then we look at what's the best opportunity inside or outside. And we don't allocate a specific amount of capital each year. We look for the best opportunities.

If we find those opportunities, and for example, there to advance diseases that are already in the sandbox where we find a technology or an asset that could do that, we'll do that. If it turns out as in the case of Alpine, we find a new disease area, a new asset, we've been looking at IgAN and put in our Sandbox for a while because of its underline biology, its nature, but we didn't have the asset. So then when we were able to see Alpine, we did that. And I think you could see all of those possibilities.

But one of the things we're careful about is not to say to spend this much money every year because you probably will. Instead, here's our strategy, have a very high level of rigor for high rates of success and have the resources so that when you find it, whatever it may be, you can move quickly and well.

Philip Nadeau Analyst

Great. We've covered a lot of topics in the last 10 seconds. Anything that we should have covered that we didn't?

David Altshuler Executive

No. All I would say is it's remarkable. It's, obviously, there's a near-term focus on the launches of ALYFTREK and JOURNAVX, CASGEVY. But what's remarkable, as Stuart said, is there's four Phase III programs on going with the Inaxaplin, Pove, JOURNAVX -- I'm sorry, JOURNAVX and DPN. And we didn't even talk about some [indiscernible], which is in pivotal development.

And then there's actually an early-stage pipeline that has great promise things like DM1 and ADPKD. So things are really exciting and just working to make sure we move them all forward effectively and well and help as many patients as we can.

Philip Nadeau Analyst

Thanks for a very interesting discussion.

Stuart Arbuckle Executive

Thank you so much.