Vertex Pharmaceuticals Incorporated

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Philip Nadeau Analyst

Good morning, and welcome once again to TD Cowen's 44th Annual Healthcare Conference. I'm Phil Nadeau, one of the biotech analysts, and it's my pleasure to moderate a fireside chat with Vertex, one of the bellwethers of the industry. We have with us today, David Altshuler, the Executive Vice President of Research and CSO; as well as Charles Wagner, the EVP and CFO. I guess I'll hand it to you guys to give a state of the company overview, what are the challenges? What are the strengths?

And what does Vertex do over the next 12 to 24 months to create value?

David Altshuler Executive

Yes, Phil, thanks for hosting. Happy to be back at the conference. We will make some forward-looking statements, so I'd encourage people to take a look at our recent SEC filings. Phil, it's an incredibly exciting and dynamic time at Vertex right now. Just think back over the last 90 days or so.

We've had multiple approvals for CASGEVY. We've released positive data in our pain program, both in DPN and in acute, we've released positive data for our Avanza triple combo. We have done our earnings call, reported a great fourth quarter, given strong guidance for the year. It's been an incredible 90 days. And so where do we go from here as we get into 2024, we look forward to treating more patients with CF with TRIKAFTA, but also preparing for the launch of vanza.

We look forward to launching CASGEVY in multiple countries in the U.S., in Europe and in the

Middle East. We look forward to more data in the pain program and filing in acute pain in the middle of the year and filing for vanza in the middle of the year as well, also advancing our pipeline in a number of different programs, notably type 1 diabetes and AMKD.

So a really full slate for the year. I would note that with the CASGEVY launch, this will be the first time in more than 10 years that Vertex has revenues outside of CF. And so we really look at this as the first step in an era of commercial diversification for the company.

We see additional launches in pain and with Vanza and making significant progress towards our goal of 5 launches in 5 years. So all I can say is that we're all incredibly enthusiastic and busy right now. And it's really rewarding to see how our approach to serial innovation and focusing on transformative medicines for serious diseases is creating patients per incredible value for patients and for shareholders. So with that, let me open it up to questions.

Philip Nadeau Analyst

Sure. So I think investors are actually now focused outside of CF and probably most focused on pain. You referenced the positive data we saw from the pivotal trial for VX-548. For those less familiar, can you summarize the data briefly and talk about what Vertex is most enthusiastic about in the profile.

David Altshuler Executive

Sure. We're very excited about the data. We designed this Phase III program in consultation with the FDA with the goal of achieving a broad acute pain, moderate-severe acute pain label and the study met every expectation we had. There were 3 different studies. They all met their primary endpoint with very great statistical significance but also clinical significance.

So for example, the reduction in pain in both the abdominoplasty and the bunionectomy study was 3.4 points or about 48%, 52% reduction where actually 2 points and 30% is considered clinically meaningful. In addition, all the secondary end points that we studied, we did do the next study, which was it superior to the opioid comparator, which is actually a combination of opioid and Tylenol, but we used Norco because it's about 1/3 of all patients treated with acute pain -- treated with that. And the results were essentially very similar, and we can talk more about the bunionectomy, et cetera. Equally or perhaps important is the safety and tolerability.

So as people know, the problem with opioids is not that they don't have efficacy. The problem is they have significant safety and tolerability issues as well as addictive potential. I think the safety and tolerability is actually under recognized by some people in terms of how bad people feel many of them taking opioids. There's some people fairly good. They tend to be the ones who are more likely to get addicted, but a lot of people find the nausea sort of feeling spacey, the sleeping on the couch, not feeling like they can drive, et cetera, to be quite intolerable.

And the key thing about our studies was across the studies the number of -- there were no SAEs and number of adverse events is actually lower than placebo. When we saw those results, we all looked at each other because we couldn't think another with 3 studies, 2,300 people or 2,000 people in the placebo-controlled trials. The actual rate of AEs was lower. And

I think that, that -- a medicine that can provide that kind of pain relief and people actually feel good, they feel alert. They're able to go to their jobs.

They're able to like have energy and all that, I think, will be a transformative medicine.

One other point I want to make, and then I'll stop. Next question is we also did a study that was a broad -- those 2 states were a hard tissue model and a soft tissue model. bunionectomy and abdominoplaty. We also did a study 250 people with different kinds of pain conditions like broken bones or twisted ankles or other surgeries in a variety of settings, emergency rooms, hospitals, outpatient. And that study, 83% of people said they had a good, very good or excellent pain control.

So all the data is just that we thought we were looking for to get an approval for moderate-to-severe broad acute pain label, and we'll be filing midyear for that.

Philip Nadeau Analyst

We hosted a panel yesterday with pain experts and 1 point that they made is that they do want to see the full data. They want to see additional end points, in particular, one physician mentioned something called the double stopwatch tests with -- I admit I'm not all that familiar with. When will you announce the full data? What's other endpoints can we expect to see? And did you do that stopwatch test for [indiscernible] vanza.

David Altshuler Executive

So a couple of things. First, we will be presenting the data at a scientific meeting and publication. That's where we'll provide more information. I think we disclosed actually when we presented the data with some secondary end points are sort of usual things. With regard to rapidity of onset, there are 2 things.

But if you look, we saw rapid onset, much faster than placebo. And there's sort of 2 measures. One is like when actually the classical measures like when it drops 1 point, and then -- but we're more interested, frankly, in the clinically significant 2 point number. But those are all very rapid people we work on, very happy. And I think that something else that was said it's just not true is that any of that was important to approval.

We worked with the FDA. They worked with us. We designed the study. We know exactly what we need. We have what we need.

Philip Nadeau Analyst

And on the side effects, you did reference the AEs being less than placebo. Can you talk about that a little bit more that it not only were they less than the placebo, they're also obviously less than Vicodin. How important is that uptake to what do you attribute that?

David Altshuler Executive

Sure. Yes, they're better than placebo and obviously, they were better than the opioid. And the key thing to understand is that you cannot possibly separate the side effects of an opioid from the activity, the pain relief because they have the same thing, it's the same receptors. There's no way design in opioid that doesn't have all side effects. In fact, when I was a medical

school, I remember learning that the way opioids work, and it is true, they don't actually reduce pain.

They change your perception of pain. So when my good friends broke his lower leg and we were at medical school and we went to the pre-emergency room, they put him on a morphine drip. When we went to saw him -- "how are you feeling" and he goes on the pain is unbelievably mild. I said, why are you smiling, because I don't care. That's true.

That's actually what opioids do to their CNS factor, but they also act on your gut to constipate you. They also suppress respiration. They make you dizzy, they make you sort of feel out of it and all that stuff. That's not separable.

Our medicine one is highly selective, 30,000-fold selective, for example, for other sodium channels, and the target, which is the only thing it hits, you also test it like hundreds of other receptors on that is only expressed in the pain-sensing peripheral neurons that's known from biology, that's known from human genetics, it's known from all this. So we are only acting in the peripheral nerve to block pain signaling, and that's why there's no CNS effect for diabetic peripheral neuropathy, we'll get to that later if you want. People used what's called Lyrica. I don't know if people know what Lyrica is. It's an anticonvulsant.

It's not a pain medicine. It's a CNS-acting medicine that suppresses brain function that was first developed as an anticonvulsant and then people tried for pain. And if you talk to anyone who's on it, when I was a diabetes doctor, at Mass General, the diabetes doctors who prescribe a lot of people for diabetic peripheral therapy, no one stayed on it because they come in and say, I don't feel good.

I'm saying so the point of pain medicine is not just to change in number on a scale, which it seems like sometimes when I listen to people is what they think, it is actually if the patients feel better. And part of the patient feeling better is how they feel on the medicine. So since our medicine is no CNS acting effects predicted and has none seen across 6 different clinical trials. I think the answer to the question is it has a totally different and unique mechanism of action never seen before. The last thing I'll say is there is a precedent for how much pain relief we ultimately should be able to get by blocking sodium channels.

I'm not saying [5, 4,] years there yet. Has anyone in the room ever had dental work and had Lidocaine or Novocaine. You know what that drug is, it's a sodium channel blocker. It blocks pain by blocking these sodium channels. That's the ceiling that you can go to.

Why don't we use Lidocaine and Novocaine like take pills or inject ourselves because there's also sodium channels in your brain and your heart, not safe. So what we did was make a medicine there's 30,000 fold selective that no one ever done before for the relevant pain channel, and so we can dose it up without any side effects. So that's why this is key. It's entirely new era of pain control. Nothing ever like that's ever been out there.

Philip Nadeau Analyst

I think one of the most controversial aspects of the data, both among investors and among the physicians is the lack of superiority against the opioid comparator. How does Vertex think about those data?

David Altshuler Executive

Yes. I mean we've said it all along. So this is not a change in story because of the data. The problem with opioids is not that they don't work for pain. The problem is safety, tolerability and addictive potential.

So somehow, people seem to believe, well, maybe they want to believe because they're prescribing it. Actually, you should talk to patients rather than doctors, to be honest to you as a doctor -- because like if you talk to doctors, they're happy writing the prescription, they said, oh, like my wife had her shoulder surgery last year at my hospital that I was at for 25 years. She had -- shoulder surgery is extremely painful, it lasts for like a year. She was sent home with 4 tablets from Mass General Hospital of opioids. She didn't take any of them, which most people don't because they don't want to expose themselves to opioids, and she was in pain for months.

That's reality.

Saying so, the reality is there's lots of undertreated pain. And even people who are given opioids they've given 48 hours, but their pain lasts for weeks. I'm saying. And so there's a great unmet need for a pain medicine that is safe and effective -- that is more effective. Obviously, people will take -- and should take Tylenol and ibuprofen first.

You can manage your pain with that, but then no one be given opioids of that work. So the question is for all of you and for the doctors and for the governments is do you want and force everyone to go through an opioid and only then try something else. Or do you want to try a non-opioid pain medicine and only using opioid if that doesn't work. That's the key question.

Philip Nadeau Analyst

And how do you convince the payers that they don't need to step through a generic opioid. Is there some way to convince them that that's the right strategy.

Charles Wagner Executive

Maybe you want to talk from just from a doctor's perspective, and then I'll cover the commercial...

David Altshuler Executive

So I would say this from a -- well, most important thing is a patient perspective. And I would say, pain is one of those things where I really would talk to patients, like go to someone who's postsurgical a week later, 2 weeks later and ask how happy they are, okay? Because that's reality. The doctor no offence -- write the prescription and send you home. They're not with you in your house.

They're not your spouse, [indiscernible] has been the spouse or the partner, the child of some who had surgery and asked how great is their pain control today. But as a doctor today, you're encouraged strongly not to write prescriptions for opioids. You're told to give as few medicines as you can.

In some states, you actually have to fill out multiple forms because they're tracking you because of the history of the use of opioids. And so I think that -- and then finally from a payer, and Charlie, can talk more about the government, there's a lot of interest at a high level in not having people take opioids, and that's because of the opioid crisis and all the debt. One thing that doctors -- again, I certainly don't mean sounding wrong. I mean I love being a doctor as professor at Harvard Medical School for 25 years teaching medical students. But let's say, the rate of opioid addiction is like 1%, which is people estimate to a doctor writing prescriptions, that may seem low.

How many people a year get those prescriptions for acute pain, $80 million. So even if it was 1 in 1,000, that would be 80,000. So I think people are just not thinking about this right.

For society, you don't want to put people on an opioid. And -- but on the other hand, an individual who's just looking right in front of their face might not see it, but I think payers do see it. I think hospitals see it, I think governments see it.

Charles Wagner Executive

Yes. And there are many hospital systems with the requirements to consider nonopioids ahead of opioids. The problem is there isn't anything effective. 18 states have legislation that require doctors to discuss non-opioid alternatives with patients before going to an opioid. 13 states have similar legislation in process.

At the federal level, just recently, bipartisan support for what's called the alternatives to Pain Act, which is aimed at the Medicare population with 3 primary objectives: one, to prevent the requirement of step through from an opioid to non-opioid. Two, to prevent the requirement for preauthorization for non-opioid and three, to equalize co-pays for opioids and nonopioids. So I don't think it's much of an argument at all. I think when you see that sort of response at the hospital system level, at the state level, at the federal level, I think people clearly understand the value of a non-opioid alternative.

Philip Nadeau Analyst

You referenced a midyear filing. Can you give us a status on that filing? And what has to be done before it's completed? And what label do you think you'll ultimately get?

David Altshuler Executive

As I said, our goal of has been a moderate to severe acute pain broad label. And that's in contrast to a lot of medicines they've gotten a label like for knee surgery or for shoulder surgery -- that's a much broader label. We worked with the FDA to design this trial. All the results are exactly what we saw. So we had to write the thing and send it in and answer any questions they have and do whatever they want to do, but I feel very confident based on the discussions with the FDA and the results we have.

Charles Wagner Executive

We expect to file the middle of this year is the timing...

Philip Nadeau Analyst

Yes, sorry. Coming back to where we were just before. So do you actually see the majority of payers allowing the use of your drug ahead of much cheaper generic opioids?

David Altshuler Executive

Well, I would say this. If you ask me where I think we're heading as a society, do I think the first-line therapy should be an opioid or a non-opioid, I can't tell you exactly who will do what at one pace. But if you ask me, there's a lot of discussion about having a non-opioid before an opioid.

Philip Nadeau Analyst

Is this within the patent life of your drug or...

David Altshuler Executive

A patent life is very long. But I don't mean in 20 years. I mean near term. So I think that here's the thing. I think there's lots of people who look at this and they're looking for a precedent, but there is no precedent for being in the middle of an opioid crisis.

It is a major societal issue with a new medication. I guess my question for you is, you're a doctor, would you prescribe an opioid to someone.

Philip Nadeau Analyst

No, I think I'm a doctor.

David Altshuler Executive

No, I think you were. Would you prescribe an opioid to someone who had a non-opioid alternative. If you think about the risk you take if you do that.

Philip Nadeau Analyst

Can you discuss the market size, both in terms of patient numbers and dollars? And I guess working into that conversation, what type of premium price do you think you could get to the generics for branded therapy.

Charles Wagner Executive

Yes. So maybe just start with acute and focus on the U.S. for the moment. We've talked about the fact that 80 million people receive prescription for moderate to severe acute pain over the course of the year. The average course of treatment is about 2 weeks.

That translates into 1.25 billion treatment days. 2/3 of those days are prescribed or influenced in an institutional setting, so either a hospital or a surgical center or at the time of discharge. We've done work on density and concentration around the U.S. 80% of that 2/3 is concentrated in 2,000 hospitals that roll up into 200 IDNs.

Long way of saying we've done our homework. We know what the coverage model looks like. We believe that we can serve this with a specialty sales force. We will augment our sales efforts with digital and other approaches. And then obviously, we're working to ensure that at

the state and federal level, there is a strong tailwind for non-opioid alternatives.

In terms of the market today, it's a -- for acute pain, it's a $4 billion market at entirely generic pricing. Given the numbers that I quoted around the number of treatment days, you really don't have to imagine much of a market share at branded pricing for this to be a multibillion dollar opportunity for us.

And that's just an acute pain alone. We haven't commented on pricing yet. So as we get closer to launch, that's something we can discuss. Similarly, on the neuropathic side, 10 million people a year received prescriptions. That is -- translates into about 2.3 billion treatment days, so twice as many treatment days as the acute pain market.

Again, you don't have to use much imagination to think about a multibillion dollar opportunity. So we're -- we do get a lot of questions around how big could it be, how small could it be, et cetera. Our view is that it's a multibillion opportunity well within reach and something we can serve with our specialty sales model.

Philip Nadeau Analyst

Turning to the diabetic neuropathic pain data that you released last year. I think one of the more controversial comments on the panel yesterday was how they frame the data versus how investors saw it. So investors looked at the data said that you numerically beat Lyrica, that's impressive. It's also impressive that all 3 doses had approximately efficacy [indiscernible] yesterday said you guys are looking at that all wrong. Sometimes they are okay...

Charles Wagner Executive

Actually fit this panel.

Philip Nadeau Analyst

I would throw open the phone book for you guys -- and this was unexpected. You guys are looking at it all wrong. Sometimes Lyrica fails. So how do you know that this isn't just all placebo in this trial. So could you...

David Altshuler Executive

Multiple ways to look at that. So the first is that you have to say -- I don't know who these people are, but you have to say that all 4 that you had for such things because Lyrica looked exactly like Lyrica looks you have to say that was a false positive somehow, in all 3 of our arms, which unfortunately, the PK was such that they were overlapping and high all had false positives. And then while it's true that there have been in the hundreds of studies with Lyrica, some failures, if you look across at the results of Lyrica exactly what we saw.

So I don't know what they're talking about. I'm curious. I don't understand it. Like I mean, I guess if you notice sometimes people look at one piece of data, they don't look at the context of the world. But you'd say then that Lyrica is a placebo for the last 20 years because the Lyrica results were exactly what it's seen with Lyrica before including the side effects.

Unknown Analyst Analyst

I just wanted to follow up on the earlier question. I think that convincing the docs based on the legislation for the government as well as just the opioid crisis to write this your drug is easier, but it's to be more of a cost issue for the insurance. I'm not saying that's right, but it's comes down to [indiscernible] drug. So I'm wondering, as you engage that will you be engaging the insurers about where the pricing is you can't tell us. And what's been their response or them to make you right tier, and we not giving them like a 90% due date to...

Philip Nadeau Analyst

Question is Vertex going to work with the payers about the pricing?

Charles Wagner Executive

Yes. And the answer to that is, of course, we're -- we haven't even filed yet. So there are limits on the conversations we can have regarding the profile of the medicine and pricing, et cetera. So yes. But we -- the conversations that we can have at this point, we feel, are very positive and constructive.

Philip Nadeau Analyst

In terms of the safety profile that you showed in the Phase II, can you discuss in a bit more detail how it compared to Lyrica and how important is safety and long-term chronic therapy like this?

David Altshuler Executive

Yes. I think it's important to talk about safety and tolerability because it's not that we're saying that like Lyrica is a medicine that's going to kill you, it's not. I'm saying I probably shouldn't say that. We're not saying anything about Lyrica. What we're saying is it has known side effects if you look at its label and you see them in our study, right?

So you see the weight gain, you see the different side effects that are in there. We don't see any of them.

So in terms of the safety and tolerability, like there's a positive control, if you want, in the study, which as you see the side effects that are on the label of Lyrica and we don't see them. Now again, as a physician, here's a bit of data for you for my opinion. If you look at people with diabetic peripheral neuropathy, I think by the numbers right, like 70% of them take 2 medicines. High fraction will take 3 medicines. There's constant turnover in the medicines.

People were so happy with the medicine. Why do they keep changing it? I'm saying. And so I think the reason is not so much the efficacy. Again, the key thing is you have to actually talk to the patients.

People don't feel good on those medicines, generally because of the CNS side effects. And it's not surprising because they're CNS depressants like that's how they work. It's not like you're saying, well, that's really weird. Why would something like I wrap your ankle, why would you feel dizzy. It's because the medicines were used because they're CNS depressants.

They too press action potential broadly in the brain in the case of that and in the case of opioids, they continue to have these effects throughout the body. So that's -- to me, what's really striking is we've done 6 studies with VX-548. We also did 3 with VX-150. The results of our studies are remarkably consistent. I remember people asking us a year ago or 6 months ago, everyone knows the psychiatric studies and pain studies, you often get like 2 out of 3.

Would that be good for you? If you saw 2 out of 3, would you be happy. We're 9 out of 9 at this point. The results are extreme also highly to 9, including 3 for VX-150.

Multiple different pain types always anticipate significant, always similar size of effect, always clean safety and tolerability profile. That gives us great confidence. And I guess the question will be, does society want such a medicine. And I guess, I believe they will. And I think the other thing when people think about payers and all that.

Just one thing you also -- we don't date on this, so I'm not suggesting we have data. But one of the things that does take time and money is people coming back because they're like not doing well. So you have to also factor in how many patients come back to see the doctor again because they're in pain or go to the emergency room because they're in pain because if you're able to -- concerned about those things. You have to think more than just like the -- there's a total cost of the procedure, there's how much of branded pain medicine would be and there's both how well you do in terms of all the other issues we were talking about and patient satisfaction, but also what -- do they just go home and do well? Or do they come back?

Philip Nadeau Analyst

Maybe just 1 or 2 more questions on pain before moving to your base business. In terms of the path forward in neuropathic pain, you're talking about meeting with the FDA to design a pivotal trial this year, also starting Phase II in LSR. So I guess, first, what does the pivotal likely look like? And second, we've heard LSR is a tougher indication because it's part osteoarthritis or can be a part of peripheral neuropathic pain. Does that have to succeed?

Is that on the critical path? Or can you just get a label on DPA?

David Altshuler Executive

A few different questions there. So the first I go, what's our goal? And then I'll talk about LSR and then I'll talk about -- With regard to our goal, our goal is a broad PMP label, a broad peripheral neuropathic pain label. And we have not yet had that discussion with the FDA. That's the discussion we're going to have.

Philip Nadeau Analyst

Does anyone have that label, Lyrica is just DPN.

David Altshuler Executive

Not in America -- not in America. There's also no approved medicine for LSR, okay? So the goal is that. And when we met with them about acute pain, we came up with the study design with them, which was 1 study in bunionectomy, 1 study in abdominoplasty in this 250-person

study. That's the discussion we want to have with them.

This jump or saying, what if LSR doesn't work? What if we can't do that? Yes, we could, of course, just do a pivotal trial and just trying to get a label in DPN. But our goal is to get the broad label. This is like 20% of people are DPN with PMP, 40% are LSR and other 40% are a wide variety of things.

So we get all of them in one label. That's our goal.

Now with regard to LSR, LSR is not osteoarthritis, but if you start with back pain, you're going to have both. So this is the mistake. If you say back pain, I have lower back pain. That could be everything from a strained muscle or tendon to some sort of osteoarthritis to LSR, which is if you hold back off -- you have a hole in your spine. The nerve goes through it, okay?

It gets pinched somehow. That's LSR, okay? And it's a pure neuropathic disease because the nerve is firing. It doesn't hurt the person. That's not osteoarthritis.

Now if you just take someone that you who has lower back pain, you're going to have a mess. And if you look at other studies people have done, they tried to treat lower back pain.

Philip Nadeau Analyst

So that's been the confusion.

David Altshuler Executive

That's not what we're doing. In order to get into our trial, you have to have a clinically clear LSR. What does that look like? The distribution of pain when you have one of these pinch nerves is wherever that nerve goes. And for example, sciatica, which is the most common form, which soon you made had or known about, is a very funny distribution.

So if someone walks into your office, as a doctor and they say, "I had this weird pain, I got acutely, it is on one side of my body, it's sort of my butt -- back on my leg, it goes to the side of my calf and into my toes. That's sciatica. There's nothing else that does that because that's the travel of the nerve. That's sciatica. So we -- that's the only way you get into our trial.

That's not osteoarthritis.

The osteoarthritis might have been involved in why the nerve is pinched, but that's not the pain because the pain, if you have like spinal or tendon or muscles back here. So it's actually very easy if you design the study for LSR, it's hard if you try and interpret LSR from lower back pain.

Philip Nadeau Analyst

Got it. Okay. I do want to touch on a few other aspects of the business.

Unknown Analyst Analyst

[indiscernible] the strategy as it relates to commercial, global commercialization of the opportunity. So is this something that you're in to obviously just Europe or reducing or developing regions of the world, low middle income countries and so...

Philip Nadeau Analyst

Questions about global commercialization of the pain front.

David Altshuler Executive

Yes. And the short answer is we're focused on the U.S. right now for acute pain. We think that there is a huge opportunity there. We would like to demonstrate the value in the U.S.

And then we'll talk about the rest of the world at some other time.

Philip Nadeau Analyst

Maybe a few questions on the base business. Your guidance this year seems 8% growth at the midpoint. What are the pushes and pulls in guidance? Could there be upside? Are there risks to hitting that?

Charles Wagner Executive

Yes. So the guidance for total product revenue, which includes both the CF portfolio and CASGEVY is $10.55 billion to $10.75 billion, 8% at the midpoint, you're right. Another really strong year. Importantly, that's roughly $800 million of incremental revenue over last year. So very significant at this scale.

We feel confident about it within -- in the CF, we're going to be treating more patients. The growth drivers in CF are patients who initiated medicine last year annualizing. We're continuing the rollout in the younger age group in 2 to 5.

We are working on reimbursements. There are a handful of smaller countries where we don't have reimbursements. And of course, we're preparing for future growth by continuing to pursue an mRNA therapy for those 5,000 patients who don't benefit from CFTR modulators today. And then, of course, we've got vanza, which could help us address the roughly 6,000 odd patients or so who've discontinued one of our medicines for one reason or another. So a strong growth year for CF, strong growth into the future.

And I guess, importantly, we did recently raise our estimate of the number of patients with CF in North America, Europe and Australia, to 92,000, roughly 20,000 of those weren't on our medicine -- one of our medicines as of the beginning of the year.

So significant opportunity for growth in CF in 2024 and beyond. And then, of course, CASGEVY, as I mentioned, will contribute to revenue this year and kick off that area of diversification for us there. We've commented that we are incredibly excited about the opportunity. We see CASGEVY as a multibillion-dollar product over time. This first year, we're working on getting the launch right, patient journey is long.

There are multiple stages and multiple months in the patient journey. So it will be a gradual build over the course of the year and we look forward to updating people with a few metrics.

Notably, our progress on authorized treatment centers. We don't see that as a rate limiter. We're targeting 50 treatment centers in the U.S., 25% in Europe. We have, to date, activated 12 in the U.S., 3 in Europe and 1 in the Middle East, and that's going very quickly now. So we

don't see that as a rate limiter.

And overall, we feel very confident about the year, and we'll update in future quarters as we go.

Philip Nadeau Analyst

Maybe one last question. We're just about out of time. In terms of cystic fibrosis, I think the #1 question we get from investors is how quickly will the transition to the vanza triple go. What are Vertex's thoughts on the rate that you'll switch people, specifically the switches from TRIKAFTA then?

Charles Wagner Executive

Yes. And the answer is to be determined. TRIKAFTA is a fantastic medicine. We saw with the launch of TRIKAFTA that the switching from previous generations of medicines, ORKAMBI SYM was instantaneous and complete pretty much but TRIKAFTA is a fantastic medicine and a lot of people are driving significant benefit from it.

That said, we think vanza is a better medicine, and we look forward to educating patients and doctors around the benefits and we know that we can get more patients to carrier levels. And we think that, that is a really exciting opportunity that's going to be compelling, especially for younger patients. So we've not commented on the rate of switching at this point. I guess, importantly, we're not going to look to drive it per se. All of the switching that's happened with our previous medicines, and we would expect the case of vanza is really patient and physician driven, and we're here to support that.

David Altshuler Executive

So one quick statistic is 95% of the people on vanza in this trial, had a sweat chloride below the diagnostic threshold. So the way you get diagnosed with this disease is you show up with symptoms, you have your sweat chloride measure, 95%. That's in the 6 to 11 group. If you're a parent and you're making this decision, why would you put yourself your kid on a medicine that has you like with a level that's above that as opposed to below that. That's just an example.

Other people were happy and comfortable we'll have to decide some people have stopped or whatever. But I think that's an important statistic in terms of what would you do as a parent.

Philip Nadeau Analyst

Makes sense. With that, I think we're out of time. Thanks for interesting discussion.

David Altshuler Executive

Thank you.

Charles Wagner Executive

Thanks, Phil.