Vertex Pharmaceuticals Incorporated

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Reshma Kewalramani, Stuart Arbuckle, David Altshuler

Jessica Fye Analyst

Great. Good morning, everyone. Welcome. I'm Jess Fye, biotech analyst at JPMorgan. We're kicking off the 43rd Annual Healthcare Conference this morning.

And I couldn't be more delighted to introduce Vertex's CEO, Reshma Kewalramani. She's going to come on stage, give a presentation about the business. And then a number of other members of the senior management team are going to join us for some Q&A after the presentation. So silence your cell phones, send the questions on the iPads if you got them. And let's get into it.

Reshma?

Reshma Kewalramani Executive

Thank you. Thanks, Jess. Thank you to JPMorgan for hosting us. On behalf of the entire Vertex team, I'm delighted to be here with you today. Good morning to all of you.

And while I may not be the first, let me add my happy New Year greeting before we're officially not allowed to say that anymore. Before getting into the presentation, let me put up the slide here on the safe harbor statement. I'll give you a minute to review this. I will be making some forward-looking comments, and I encourage you to read our SEC disclosures that have more detail. I'd like to take this minute while you're reading to apologize in advance for my voice.

I'm getting over a cold and so I may not sound my best self this morning. But it is really a pleasure to be here. With that, let's get started. At Vertex, we have a unique business model. We have a unique corporate strategy, and that is depicted on the center of this slide.

We invest in scientific innovation to develop transformative medicines for serious diseases in specialty markets that require lower SG&A spend. This enables strong operating margins, profitability. It allows us to reinvest in R&D. And this is what perpetuates this virtuous cycle. The key pillars of our differentiated disease-first R&D strategy are detailed to the left of the slide.

We only pursue diseases where we understand causal human biology; diseases in which we have validated targets, usually genetic, but pharmacologic is just fine; diseases with biomarkers that translate from bench to bedside; and we only work on diseases with efficient development and regulatory pathways. This approach was designed to deliver disproportionate R&D success. And it has delivered. We now have 5 approved medicines in cystic fibrosis, an approved medicine in sickle cell disease, or SCD, and transfusion-dependent beta thalassemia, or TDT, and anticipated approval in acute pain. And our strategy enables us to unlock new disease areas, develop transformative medicines, create value for patients and shareholders, and do this time and again through serial innovation.

The power of this R&D strategy and our disease-focused approach is depicted on this next slide. Our cystic fibrosis leadership is an exemplar of this strategy. Since 2012, we've expanded our leadership position in CF by serially innovating, to deliver these transformative medicines to a growing number of patients. And with each medicine that we develop and get approved, we raise the bar. Today our CFTR modulators can treat up to 90% of CF patients.

In 2024, we delivered revenue outside of CF with the launch of CASGEVY in SCD and TDT. And we are positioned to accelerate revenue diversification through 2028 and beyond, as you see in the middle part of this slide, given pending regulatory approvals and multiple programs in late-stage clinical development. Two years ago at this conference, we talked about our 5 in 5 strategy, that is to say an ambition to have 5 launches in 5 years. We are well on our way to doing so. Beyond 2028, there are even more potentially transformative therapies in the pipeline, including for myotonic dystrophy type 1, autosomal dominant polycystic kidney disease, improved conditioning for CASGEVY, to highlight just a few.

Along with that diversifying R&D pipeline, which is broadening, clinical programs are now across 10 disease areas, we're also diversifying our revenue base and geographic presence. And let me use this slide to illustrate that. On the patient front, by bringing transformative, if not curative, medicines to more patients around the globe, we intend to serve more patients and grow and diversify our revenue base. We target expanding the current indications, which are in CF and in sickle cell disease, which, in aggregate, could be about 160,000 patients, we intend to go from 160,000 patients to over 5 million patients by expanding from cystic fibrosis, sickle cell disease, beta thalassemia, to type 1 diabetes, certain renal diseases, myotonic dystrophy type 1. And beyond that, we, of course, are so very excited about the opportunity to serve the 80 million patients with acute pain and the 10 million patients with peripheral neuropathic pain in the U.S.

alone. With regard to geography, in '24, we achieved our first product approvals in the Middle East. And we also established a clinical and commercial presence there to support the large patient populations with SCD and TDT. Indeed, the first patient treated with commercial CASGEVY was in the Kingdom of Saudi Arabia. We also now have clinical trials in numerous

regions, including in Asia for IgA nephropathy.

Given time constraints, I'm going to focus the rest of my comments on just a few of the disease areas. I'll focus on CF, talk a little bit about the hemoglobinopathies and pain, and round out with the renal portfolio and type 1 diabetes. Let's start with cystic fibrosis. Overall, we see continued sustained growth in our CF franchise by reaching younger patients, patients living longer and expansion into additional geographies beyond our traditional countries of focus. Let me tell you a little more.

On the upper left, in those 2 wheels you see, we have increased the epidemiology in CF by 2,000 patients. We are revising upwards our estimates from 92,000 to 94,000 in our traditional areas of focus, that being North America, Europe and Australia where patients have -- this disease has the highest prevalence in patients. We estimate that about 75,000 of these patients in those, let's call them, traditional regions, are already on our modulator therapies. And so we have more patients we need to treat in these regions. Second, we continue to expand into additional geographies where there's health care infrastructure that supports high-value medicines and where there is pathways for formal reimbursement.

While these additional countries have lower prevalence of disease, in aggregate, there are another 15,000 patients who could benefit from our medicines. In these countries, we estimate that about 1/3 of the patients are already on our medicines. So there are more patients to treat in these regions as well. Lastly, this slide depicts our continued journey into serial innovation and bringing all of our CF patients to carrier levels of sweat chloride. That is a really important goal to us and it's a really important goal to the CF community, because at carrier levels of sweat chloride, our patients have no manifestations of disease and can live a long and healthy life.

Lastly, we had some big news towards the end of last year with the early approval of ALYFTREK, and let me go into that on the next slide. On December 20 of last year, ALYFTREK, our fifth medicine, gained U.S. FDA approval. And this medicine is quite remarkable in that it has met noninferiority on ppFEV1 to TRIKAFTA, which is no small feat given the profile of TRIKAFTA. It has bested TRIKAFTA in terms of sweat chloride reduction with even greater sweat chloride reduction, which many of you know, is a reflection of CFTR protein functioning.

This profile sets the stage for ALYFTREK to possibly set a new bar in CF treatment. For patients, let me outline what the advantages of ALYFTREK are. First, once-daily dosing. Second, higher CF protein function and lower sweat chlorides. Third, there are an additional 31 mutations beyond TRIKAFTA in the ALYFTREK.

And lastly, for the company, it carries a clinically meaningful, not a clinically meaningful, but a meaningfully reduced royalty burden, compared to TRIKAFTA and earlier medicines. As we launch ALYFTREK, we are equally focused on 2 patient populations. First, the about 6,000 or so patients who used to be on a CFTR modulator but are no longer on one. And second, patients who are on CFTR modulators but may wish to avail themselves of a lift truck either for once-daily dosing or because they want to have access to a medicine with greater sweat chloride improvements.

With that, let me move now to CASGEVY. In aggregate, in the countries that I described, in

North America, Europe and the Middle East, we have the opportunity for CASGEVY to serve 60,000 patients with the most severe forms of this disease. To reach these patients, we've been very pleased with the pace of regulatory approvals and we've also been very pleased with the pace of ATC, or authorized treatment center, initiations. These ATCs now number more than 50 across these 3 regions. In addition, we've already collected cells at more than 50 patients.

And we've infused multiple patients with their CASGEVY edited treatments. With regard to the payer landscape, in the U.S., we have not had significant obstacles for patient access to this life-changing therapy. Internationally, we're very pleased to have reached agreement with NHS England for the TDT indication last year, about 6 months after regulatory approval, which for many of you, know is quite fast. And we're also very pleased with the progress on the sickle cell disease negotiations.

In the Middle East, we have secured a national reimbursement agreement with Bahrain. And in the Kingdom of Saudi Arabia, we have hospital-level agreements. Given the growing patient demand we are seeing for CASGEVY, we are investing to expand manufacturing and have just secured regulatory approval for an additional manufacturing site for CASGEVY with our partners at Lonza. As we look forward to '25 and beyond, we see the CASGEVY momentum built in 2024 continuing, and we are excited to treat more patients with this medicine. With that, let me now move to pain.

I'm going to start with acute pain, where we see enormous opportunity. Just like in CF, our commitment is to leadership and serial innovation. 80 million patients in the U.S. seek treatment for acute pain. This is prescription treatment for acute pain.

40 million of these patients get an opioid prescription, despite the high levels of concerns that physicians have about the consequences of opioid prescriptions. 10% of acute pain patients who received an opioid prescription go on to have prolonged opioid use. And 85,000 patients who are treated with an opioid go on to have opioid use disorder annually. The cost remains stubbornly high, including about $10 billion to $20 billion for health care costs alone, of opioid use disorder attributable to opioids initially prescribed for acute pain. Let me move to suzetrigine and tell you a little bit about how we see this fitting into the treatment paradigm in helping with the opioid crisis and how we see the launch of suzetrigine.

We believe our NaV1.8 inhibitor, suzetrigine, holds the promise to address this public health crisis, to address this high unmet need. And we believe we can build another multibillion-dollar franchise. The left-hand side of the slide demonstrates the unmet need. On the one hand, we have over-the-counter acetaminophen or NSAIDs. They don't have addictive potential, but they don't have the highest efficacy.

On the other hand, we have opioids. Opioids are effective medicines, but they have significant safety tolerability concerns. And of course, they have abuse and addictive potential. We see suzetrigine as being poised to fill this therapeutic gap. And as you can see on the data to the right, which is excerpted from the Phase III clinical trials, these Phase III clinical trials were the largest ever conducted in acute pain.

You can see the efficacy and the safety profile also look very good. It is a peripherally acting

medicine. Addiction and abuse potential are centrally-mediated phenomenon. So because of its peripherally acting mechanism, there isn't addictive potential. Combined with the strong policy tailwinds at both the state and federal levels, we are, therefore, working to establish the conditions for patient access and long-term commercial success for our pain franchise.

I'll share a couple of more details on this. With regard to the payers, we are making good progress with both commercial and government payers. And we're focused on accelerating formulary reviews, minimizing NDC blocks and limiting prior authorizations. In the institutional setting, we are engaged broadly with IDNs and with networks of integrated delivery, as well as with group purchasing organizations that serve these institutions. And what we are trying to do here is accelerate their P&T process, and we have line of sight to do so, so that suzetrigine can be supported for use in this setting.

And at the retail pharmacy, we are working to have broad stocking on approval. The feedback from the pharmacists suggest an eagerness for a non-opioid option for patients as well as interest and eagerness for this kind of medicine, which they tell us will simplify their dispensing work flows. Bottom line, we are launch-ready for suzetrigine in acute pain, which has a PDUFA action date of January 30 of this year. Let me continue beyond acute pain to neuropathic pain. PNP, or peripheral neuropathic pain, is another multibillion-dollar opportunity.

This significant opportunity is accentuated by the fact that the medicines that exist have high rates of discontinuation, polypharmacy and inconsistent use of medicines. Our development programs in PNP are well underway. The Phase III DPN study is enrolling and dosing. Following our Phase II study of suzetrigine in LSR, or lumbosacral radiculopathy, from last December, we continue our analyses. We continue working on optimizing clinical trial design, and planning forward for our end of Phase II meeting with the regulators to discuss the requirements to achieve a broad PNP label.

Following these discussions with the regulators, we intend to advance to Phase III development. We expect that this body of work will complete by about the summer of this year, and I look forward to updating you on where we are at that time. Let me move from pain now to our growing renal franchise. Two quick highlights on this slide, and then I'll dive into povetacicept in a little bit more detail on the following slide. In primary APOL1-mediated kidney disease, or AMKD, we continue to enroll and dose patients in the Phase III portion of what is called the AMPLITUDE trial.

I am pleased to share that we expect to complete enrollment in the interim analysis cohort of this study this year, which positions us to file for potential accelerated approval in the U.S. once this cohort completes 48 weeks of treatment. We also expect to initiate another trial, this one called AMPLIFIED, in patients with 2 APOL1 alleles but with additional comorbidities, such as diabetes. What this does is it brings the population that could be treated with inaxaplin from 150,000 with primary AMKD to about 250,000 patients. And in ADPKD, this is autosomal dominant polycystic kidney disease, we expect to complete the healthy volunteer study and start the Phase II proof-of-concept study also this year.

Let me turn my attention now to povetacicept and give you a little bit of a map as to where we are and where we're going. Povetacicept is our pipeline and a product that we added to our

portfolio with the Alpine acquisition. And I'll focus on 3 points here with the lead indication in IgA nephropathy. First, we believe pove has best-in-class potential given its mechanism of action, the preclinical data, and the clinical data, which at the last showing at ASN last year had a 66% reduction in proteinuria at 48 weeks, as well as convenient, once-monthly, small volume, subcutaneous administration. Second, the global Phase III RAINIER study is well underway.

RAINIER is a placebo-controlled, on top of standard of care, randomized, double-blind, 80 milligrams of povetacicept versus placebo on top of standard of care. It's designed with the preplanned interim analysis to support potential accelerated approval in the U.S. I'm pleased to share, we also expect this study to complete enrollment in the interim analysis cohort this year. This positions us to file for potential accelerated approval in the U.S. once the cohort completes 36 weeks of treatment.

And lastly, I'm really excited to announce and share the partnership with Zai Lab that you heard about late last week. Zai Lab is a leading biopharmaceutical company in China and the broader region. And together, we think that we can bring this medicine to that population where the prevalence of disease is high. In China alone, there are an estimated 750,000 patients diagnosed with IgAN. Let me move on now to the last spotlighted program for this morning: type 1 diabetes.

We are so excited to be in pivotal development with this program, previously known as VX-880, now known as zimislecel. This is a medicine that has the potential to be a functional cure for the about 125,000 patients with type 1 diabetes who have the most severe form of the condition. To be clear, to bring forward a transformative, onetime, potentially functional cure for type 1 diabetes, the required element, the required element, is fully differentiated, stem cell-derived, glucose responsive islets that can be manufactured at scale. And let me also be clear that that is exactly and uniquely what we at Vertex have. These cells are the foundation for all of these programs.

The cells have already demonstrated proof of concept, and I'll talk more about VX-880 on the next slide. But in keeping with our serial innovation approach, we also have approaches using these cells with something called VX-264. These are the cells encapsulated in a device so as to avoid the need for immunosuppression. We have research-stage programs with alternative immunosuppression, as well as in trying to edit these cells to create hypoimmune cells. On the next slide, let me focus on the lead program, previously known as VX-880, now known as zimislecel.

We are so very pleased to be in Phase III development. We converted the Phase I/II/III study into a Phase III study after global regulatory discussions, including with the FDA. The Phase III pivotal program is a total of N equals 50 patients. And the primary endpoint is the proportion of patients achieving insulin independence without symptomatic hypoglycemic episodes. The current zimislecel program will seek approval for about 60,000 of the 125,000 patients with the most severe form of the disease.

And we're going to get to the full 125,000 patient population after that. The zimislecel program is moving quickly. This is another program where I'm pleased to share that we will complete not only enrollment but enrollment and dosing this year. That sets us up for filing

for a potential approval when that cohort has 1 year of follow-up after treatment of insulin independence. On the right side, I included the data once again from the recent EASD data set.

That dataset had 12 patients who received single infusion of a full dose of the drug. And in that data set, all 12 patients who received the drug achieved hemoglobin A1c levels less than 7, which is the ADA recommended threshold. The 11 of our patients either had elimination or reduction of exogenous insulin, and 9 patients were no longer taking any exogenous insulin. Clearly, the dataset is impressive and continues to fuel our enthusiasm for bringing this to patients as a potential onetime curative therapy. The safety continues to look very consistent with the transplant procedure as well as with immunosuppression itself.

Let me wrap up quickly now with 4 slides, and I'll start with this slide on the pipeline. We are committed at Vertex to our patients as well as to our shareholders. And therefore, I'm very pleased to say that we're well on track with our 5 launches in 5 years goal that we set in 2023. Second, I'm really very pleased with the progress of the late-stage pipeline. And last year, we had this important milestone in Q3 with 3 programs moving into Phase III development.

And lastly, equally pleased with the earlier-stage programs with things like VX-407 in ADPKD and VX-607 in myotonic dystrophy type 1. Next, let me show you a slide that you can keep as a reference for milestones that we expect to achieve in 2025. I'm going to bucket this into 4 categories. First, we have 3 products that have either recent or anticipated approvals. The continued launch of CASGEVY in SCD and TDT globally.

The early launch of ALYFTREK in the U.S. And we are launch-ready for suzetrigine in acute pain. Next, there are 3 programs where we are either going to complete enrollment or complete enrollment and dosing in the cohort for either accelerated or full approval. The first is inaxaplin in AMKD, the second is povetacicept in IgAN, and the third is VX-880 in type 1 diabetes. Next, in the mid-stage, we are looking to advance VX-407 to Phase II proof-of-concept in autosomal polycystic kidney disease.

And lastly, in the last bucket, we have 2 data releases that we expect to share this year. The first is VX-522, our mRNA program in partnership with Moderna, for the last 10%, the last 5,000, 7,000 patients with CF. And another data release with Phase I/II data from our VX-264 program in type 1 diabetes. I'll finish off here with some highlights of our financial profile. Our attractive financial profile is created by our differentiated business model.

Revenue guidance on our November call was $10.8 billion to $10.9 billion for full year '24. That represents the potential for the tenth year of double-digit revenue growth. This profitable revenue growth, and our specialty business model, allows us to deliver high operating margins while also continuing to invest internally and externally in innovation. As a result, our balance sheet is strong even after funding nearly $5 billion for the Alpine acquisition, and provides significant flexibility for us to continue to invest in innovation, driving that virtuous cycle I mentioned at the top of the hour. To conclude, here's a slide that we show every year and that you can follow, to follow along on our priorities and our progress.

In CF, we aim to continue our leadership. We also aim to diversify across our revenue base, geography as well as disease areas. Next, we are looking to rapidly advance the pipeline,

which I've highlighted a few programs for you today. And lastly, we look to deliver industry-leading financial performance.

We are well positioned for '25 and for many years to come, and we look forward to continuing to serve patients and shareholders. With that, I'm going to turn it back to Jess, and I'm going to invite the management team up to the stage. Jess, over to you.

Jessica Fye Analyst

Great. Thank you for the presentation. So we're joined on stage by CFO, Charlie Wagner; Chief Operating Officer, Stuart Arbuckle; Chief Scientific Officer, David Altshuler; and obviously, Reshma, who just presented. I guess I wanted to start out, you guys have 2 significant launches this year: in CF and in pain. And I feel like this is a good venue for you guys to kind of set expectations for those launches.

I know you've talked about the process to get reimbursement for pain, maybe like you expand a little bit there. And on CF, you talked about kind of these 250,000 patients who weren't eligible for CFTRs before, the 6,000 patients who had discontinued CFTR and then transitioned from TRIKAFTA. And how should we think about that kind of playing out this year?

Reshma Kewalramani Executive

Stuart, do you want to cover CF first and then go on to pain?

Stuart Arbuckle Executive

Sure. Yes. So we're certainly very excited about the approval of ALYFTREK, which came through a little bit earlier than our PDUFA date. Fortunately, the teams were launched ready and we're already executing on that launch. And whilst it's very, very early, the reaction from customers has been exactly as we expected.

They're very excited about the clinical profile and the fact that it's once-daily dosing. We've already had patients enrolled on ALYFTREK into our patient services program, which means they're on their way to getting a prescription, which is fantastic. So the launch is underway. As you said, there's really sort of 3 populations that I think ALYFTREK is going to be particularly interesting for. The first one is patients who are currently on a CFTR modulator like TRIKAFTA but would like the benefits of greater CFTR function and also the convenience of once-daily dosing.

Then there's about 6,000 patients globally who have discontinued one of our previous CFTR modulators. And we know they're going to be potentially interested in a new CFTR modulator that has the kind of benefit-risk profile ALYFTREK has because they know that they would be better controlled if they could be on something that addresses the underlying cause of their disease. And then the last group, as you mentioned, there are 31 additional mutations, which are on the ALYFTREK label, which aren't on the TRIKAFTA label even after the expansion of the TRIKAFTA label which came on the same day as the ALYFTREK approval, talking to the increased potency that you get with the vanzacaftor triple combination. So incredibly excited. In terms of actual rate, we haven't talked about the rate of switching or the rate that we are

going to get, patients who are currently discontinued, onto a CFTR modulator.

But we do expect the majority of patients who are on one of our CFTR modulators who are discontinued to transfer onto ALYFTREK over time. And then in the pain launch, again, we're launch-ready, as Reshma said. We are doing all the things you would expect us to do in terms of prior to approval, all the things that we can do compliantly, as Reshma mentioned, with payers on the government and commercial side, working with institutions on the formulary side. And also, as Reshma said, very importantly, working with the retail pharmacy chain so that we can have broad national distribution of suzetrigine at approval. Because once a patient gets a prescription for it and they turn up at their retail pharmacy, we certainly want to make sure the product is there.

These patients are in acute pain; if the product isn't on the shelves, they're going to abandon that prescription and get a prescription for something else. So retail distribution is also very important. So we are eagerly awaiting the PDUFA date on January 30. And as Reshma said, we're launch-ready and we can't wait to take suzetrigine to the market.

Jessica Fye Analyst

Maybe sticking with suzetrigine and this acute pain opportunity, one of the questions I get a lot from investors is, what's the right way to think about price? I get the sense the Street is kind of all over the place on this. I don't know if you're going to do a big unveil right now. But maybe talk about the framework. Kind of how are you thinking about it?

Reshma Kewalramani Executive

Maybe spoiler alert, Jess, I don't think Stuart's going to be unveiling the price, but I'm sure he's going to be able to talk through the context and frame it up for you.

Stuart Arbuckle Executive

Yes. It's obviously a very, very important question. And the price that we are going to select is really looking to balance a couple of things. The first one is to ensure that we can get broad and equitable access to suzetrigine for the 80 million patients in the U.S. who suffer from moderate to severe acute pain every year.

The second thing is that we want to make sure that we're establishing the right value for this medicine. We've been working on this target for well over 20 years. And we imagine that this is going to be the first of what will be a portfolio of medicines for acute and, indeed, neuropathic pain as well. We imagine we are going to be transforming the treatment of pain exactly in the same way that we've transformed the treatment of cystic fibrosis. So suzetrigine is a great medicine.

We're really looking forward to bringing it to the market for acute pain. We're developing it for neuropathic pain. We also have follow-on molecules, which we believe could have even better properties than suzetrigine, even higher levels of efficacy in terms of new NaV1.8s. We're also working on NaV1.7 inhibitors, which could be used either as monotherapy or in combination with something like suzetrigine to create even greater levels of pain control. So we are going to be in this market for decades to come.

So the price that we established for suzetrigine really is going to be the foundation that's going to set the value for this franchise for many, many years to come. So we want to make sure that we are pricing it in that sweet spot that allows us to get access for patients whilst at the same time reflects the clinical value of suzetrigine, the cost offsets that it will have in terms of reducing the opioid epidemic here in America, but also reflects the significant investment we've made over literally decades to get to this point.

Jessica Fye Analyst

Maybe turning to neuropathic pain. You guys gave us the LSR Phase II results, I guess it was December, along with the announcement that you intend to move to Phase III. I think that was met with some surprise on the part of investors. So walk through your confidence. Why should investors think that this makes sense to advance?

Reshma Kewalramani Executive

David, do you want to make some comments there?

David Altshuler Executive

Absolutely. We remain committed to bringing medicines to patients with PNP, and our goal is a broad PNP label. And when we look at the results of the study, clearly, the efficacy of the results was as expected. The safety was as expected. And the surprising result was the placebo effect was larger than we expected.

And there wasn't a lot of data in the past. There were only 2 studies actually that were 12 weeks. There were no Phase III studies, there were no approved medicines. And so looking at that, we believe that we can learn from that data. We can work on the design of the study and then with regulators to bring forward this medicine, with the potential not only with our Phase III study -- studies in DPN -- study in DPN, to bring it for patients with DPN but have a real shot to bring it with all patients with PNP.

And that is such a significant unmet need, such a large opportunity. And the medicine is effective, it's got a great safety profile, the MOA. We feel confident that bringing it forward is the best opportunity for patients and also for Vertex.

Reshma Kewalramani Executive

Jess, the only thing I'll add is, I agree with everything that David has so nicely outlined, if you're going to work in the pain space, you have to learn to deal with the placebo effect. It's just part and parcel of what you have to do. Part of that is coming up with better and better medicines and learning how to work with the biology and chemistry, and we're well on our way to do that. You heard Stuart talk about the NaV1.7s, 1.8s alone or in combination. And the second half, and it's an and, the second half is learning how to do clinical trials where you can manage the placebo effect.

If anyone can do it, I would bet my money on team Vertex.

Jessica Fye Analyst

Maybe switching to povetacicept. You've got compelling data so far, we're going to see how

that matures, and have kicked off the pivotal trial. There are multiple players pursuing this IgAN space, right? How do you think about the TAM in IgAN? And what's going to drive kind of the market share split among these multiple assets?

Reshma Kewalramani Executive

Yes. Great question. I'm going to ask Stuart to comment. But I'll start by letting you know that: 3 or 4 things in the clinical realm. One, we had a chance to very carefully look across all therapies being developed, because while IgAN was in what we call our sandbox, we did not have an asset internally.

So we had the chance to look very broadly and very carefully. And we chose Alpine and we chose povetacicept because of the dual BAFF/APRIL inhibition, because of the AFFINITY and potency data preclinically, because at that time we had already seen some amount of the clinical data, which has now come to light at the International Society of Nephrology Meeting and at ASN with 66% proteinuria reduction. And also because in biologics, the way in which the drug is administered is really, really important. This idea of once-a-month, subcu, at-home, small volume administration, that's critically important. And if you look at the history of biologics, it's not always the case that drugs that didn't have that were able to be very successful.

It's often the case that it's the drugs who had that that were able to be successful. Stuart, do you want to talk a little bit about how you see the market?

Stuart Arbuckle Executive

Yes. It's really going to be, as it always is, it's going to be about the efficacy profile, it's going to be about the adverse event profile. And as Reshma said, we anticipate that povetacicept is going to have a best-in-class clinical profile. And then very, very importantly, in these chronic indications, just as Reshma said, the route of administration, dosing frequency, volume are incredibly important differentiators. And we see that in many of the biologics market.

RA is a great example where the best product with the best route of administration, the best dosing frequency often wins. And I very much expect that's how it's going to play out with povetacicept if it delivers the kind of profile that we think it's going to deliver.

Jessica Fye Analyst

Great. I think we are just about out of time. So we should stop there, so we don't get cut off anyway. Thank you.

Reshma Kewalramani Executive

Jess, thank you so much.

Stuart Arbuckle Executive

Thank you.