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Vertex Pharmaceuticals Incorporated (VRTX) CEO Jeff Leiden on Q3 2019 Results - Earnings Call Transcript

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Q3: 10-30-19 Earnings Summary

Press Release SEC *10-Q* *Slides*

EPS of $1.23 beats by $0.07 | Revenue of $949.83M (21.07% Y/Y) beats by $1.45M

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Vertex Pharmaceuticals Incorporated (NASDAQ:VRTX) Q1 2020 Earnings Conference Call October 30, 2019 5:00 PM ET

Company Participants

Michael Partridge - SVP, IR

Jeff Leiden - Chairman, CEO & President

Stuart Arbuckle - EVP & CCO

Reshma Kewalramani - EVP, Global Medicines Development & Medical Affairs and CMO

Charles Wagner - EVP & CFO

Conference Call Participants

Salveen Richter - Goldman Sachs

Michael Yee - Jefferies

Alethia Young - Cantor Fitzgerald

Cory Kasimov - JPMorgan

Paul Matteis - Stifel

Phil Nadeau - Cowen & Company

Matthew Harrison - Morgan Stanley

Brian Abrahams - RBC Capital Markets

Liisa Bayko - JMP Securities

Geoff Porges - SVB Leerink

Whitney Ijem - Guggenheim

Michael Partridge

Good evening, this is Michael Partridge, Senior Vice President of Investor Relations. Tonight, we will review with you Vertex's business progress and provide our Third Quarter Financial Results. Making prepared remarks on the call tonight, we have Dr. Jeff Leiden, Chairman and CEO; Stuart Arbuckle, Chief Commercial Officer; Dr. Reshma Kewalramani, Chief Medical Officer; and Charlie Wagner, Chief Financial Officer. We recommend that you access the webcast slides on our website as you listen to this call. This conference call is being recorded and a replay will be available on our website.

We will make forward-looking statements on this call that are subject to the risks and uncertainties discussed in detail in today's press release and our filings with the Securities and Exchange Commission. These statements, including without limitation those regarding Vertex's marketed CF medicines, the continuing development and commercialization of our triple combination regimens for cystic fibrosis, Vertex's other programs, and Vertex's future financial performance are based on management's current assumptions, actual outcomes and events could differ materially.

I will now turn the call over to Dr. Jeff Leiden.

Jeff Leiden

Thanks, Michael. Good evening, everyone. 2019 has been a year of significant progress for Vertex across all parts of our business, as we continue to execute on our clear and differentiated strategy to create transformational medicines by investing in serial scientific innovation. Our significant growth in revenues from treating more people with CF globally has enabled continued investment in both internal and external innovation to create future medicines. And we are making rapid progress across our pipeline in our efforts to advance additional potentially transformative medicines both in CF and multiple other serious diseases.

Our strategy is working and has positioned the company for continued growth in 2020 and for years to come. I'm pleased to review with you some of our recent accomplishments.

First, to CF. I'm proud to say that last week's FDA approval for Trikafta, marks the most significant step to date in our more than 20-year journey toward our future goal of curing CF for every person with this disease. I joined Vertex as CEO, eight years ago, right before we received our first approval for KALYDECO to treat the cause of CF for a small group of patients in the US. Today, approximately 45,000 patients worldwide are eligible for one of our four CF medicines and we're treating thousands of patients in more than 30 countries around the world.

I would like to again thank the patients, families, caregivers, physicians and advocates as well as the CF Foundation who've been on this journey with us over the past two decades. The approval of Trikafta would not have been possible without the unwavering support of the entire CF community. I would also like to highlight the significant progress we've made throughout 2019 in securing reimbursement for our medicines outside the US. Most notably, we recently announced new reimbursement agreements were ORKAMBI and SYMKEVI in England, Spain, Australia, and Scotland. I'm pleased that eligible patients in these countries now have a medicine to treat the underlying cause of their CF for the first time and that we were able to work collaboratively with governments to reach agreements that will appropriately value the scientific innovation and clinical benefit of our medicines.

Now to our pipeline. Today, we have multiple different potentially transformative medicines in clinical development spanning five specialty diseases. And we're entering a period of significant clinical development progression and data generation for these programs. In fact, we expect multiple proof of concept data readouts and the initiation of key proof-of-concept studies, through 2020 that will represent important risk-lowering events for our pipeline. Our pipeline investments have for several years followed a disciplined strategy focused on causal biology, building highly predictive preclinical models, and developing biomarkers early in development to lower risk and increase our probability of success in the clinic.

And we only work on transformative medicines for serious diseases that create and sustain significant value for patients, society, and our shareholders. Our external investments are aligned with the strategy and encompass multiple therapeutic modalities. We have increased our external investment in line with our growing cash flow by acquiring new development programs and building a tool kit of new technologies that will enable us to develop breakthrough medicines in diseases such as Type 1 diabetes, Duchenne muscular dystrophy, hemoglobinopathies, and others.

Most recently we acquired Semma Therapeutics with a goal of developing a cellular therapy that both alone and in combination with an implantable device has the potential to cure Type 1 diabetes. This acquisition is a perfect example of our efforts to bring in promising development programs that complement our internal R&D efforts are aligned with our strategy and provide significant opportunities for further growth beyond CF.

The execution of our corporate and research strategies has produced a highly differentiated profile for both near-term and long-term growth, as we continue to expand access to our medicines worldwide and gain approvals for new medicines, we are well positioned for further revenue and earnings growth and for continued reinvestment in innovation to create future medicines. I look forward to updating you on our progress over the coming months and we'll now turn the call over to Stuart to talk in more detail about our commercial performance and the launch of Trikafta.

Stuart Arbuckle

Thanks, Jeff. Tonight, I'll briefly review our commercial performance for the third quarter and discuss our expectations for the ongoing launch of Trikafta in the US. Our third quarter total product revenues were $950 million, a 21% increase compared to the third quarter of 2018. This increase is as a result of treating more patients globally with our medicines. Uptake across multiple products and in multiple populations drove revenue growth over the past year. Most notably from Symdeko and Symkevi in patients ages 12 and older. We also saw revenue growth as a result of expansion into younger patients including children in the US, ages 2 to 5 years for Orkambi and ages 6 to 11 years for Symdeko.

Outside the US, we continue to make progress in achieving reimbursement for our CF medicines Orkambi and Symkevi, as evidenced by our recent announcements regarding reimbursement in England, Spain, Scotland, and Australia. Together, our progress in these countries underscores the positive outcomes that can be achieved. When we and governments work collaboratively and flexibly toward providing access for patients.

Now to the approval and launch of Trikafta in the US. Trikafta is Vertex's fourth medicine to treat the underlying cause of CF and was approved by the FDA last week to treat people with CF ages 12 years and older with at least one F508del mutation. The speed of the FDA approval is a reflection of not only the strength of the Trikafta data, but also of the community's shared urgency to provide patients with a medicine that treats the underlying cause of their disease. And I am pleased to report that the first patients have already been prescribed Trikafta by their physicians, underscoring the strong interest in the medicine. The label for Trikafta is broad any patients in the US, age 12 years or older, with at least one F508del mutation is eligible. We estimate that there are approximately 18,000 patients in the US who fit this criteria. Representing by far the largest population of CF patients eligible for one of our CF medicines at the time of the launch. Of the 18,000 patients eligible for Trikafta, approximately 6000 are those with one F508del mutation and one minimal function mutation, who till now have not have treatment for the underlying cause of their CF. The remaining approximately 12,000 patients are those who were already eligible for one of our CF medicines and most of these patients are currently being treated with Kalydeco, Orkambi, or Symdeko.

Revenue growth in 2020 will be driven primarily by treatment of new minimal function patients and overtime we expect a vast majority of the 6,000 new minimal function patients will be treated with Trikafta. We also expect that a significant proportion of patients currently on Kalydeco, Orkambi, or Symdeko will switch to Trikafta over time. The large number of eligible patients coupled with the capacity constraints of CF centers to schedule and actually initiate such a large volume of patients are important factors in why it may take longer for the Trikafta launch to reach its peak level of uptake compared to prior launches.

Reimbursement is an additional factor in the launch of Trikafta. We expect to obtain broad reimbursement from both commercial and government payers in the US similar to our experience with prior CF medicines. We've already begun discussions with payers following the approval and the initial feedback has been positive. Based on the strength of the clinical data and payers understanding of the disease modifying benefits that our medicines provide. These dynamics are reflected in our updated total 2019 CF revenue guidance of $3.7 billion to $3.75 billion that we provided at the time of the Trikafta approval last week. We will also take these factors, as well as early uptake trends into account as we set guidance for 2020 early next year.

In summary, I'm pleased that we are bringing our medicines to many more patients around the globe and with the trajectory of our continued revenue growth. With that, I will now turn the call over to Reshma to review recent pipeline progress.

Reshma Kewalramani

Thanks, Stuart. I would first like to echo Jeff's comments about the significance of the Trikafta approval, both for Vertex and for the CF community, it's truly amazing to think that it was an early 2016 that our scientists first synthesized elexacaftor, the next generation corrector that became a key part of Trikafta. And in a little under four years, Vertex was able to bring that molecule from the lab through development and now to patients in the US. It's a remarkable story of drug development and I'd like to thank the entire CF community for their support in getting us to this milestone. As we celebrate this milestone,

we are also working diligently to bring Trikafta to more patients globally and to gain approvals for younger patients. We're on track to seek additional regulatory approvals for Trikafta outside the US. First in Europe, then in additional countries globally.

And we are also now enrolling a Phase 3 study of Trikafta in children ages 6 to 11 years. Outside of CF, we are entering a period of significant data generation and clinical development progress. We expect multiple important clinical data readouts from our pipeline beginning later this year and the progression of multiple molecules into Phase 1 and Phase 2 studies throughout 2020. In sickle cell disease and beta thalassemia, we expect to provide the first clinical data from the Phase 1-2 studies of the novel gene editing therapy CTX001 later this year with our partner Crispr Therapeutics. The data we expect to disclose will include measurements of safety and efficacy for patients with beta thalassemia and sickle cell disease treated with CTX001.

In our AAT program, we have now finalized the design of a Phase 2 proof-of-concept study for our first oral small molecule corrector VX-804 and expect to begin the study this quarter. The study is expected to enroll approximately 50 patients with AAT deficiency, who have two Z mutations and will evaluate multiple doses of VX-814 compared to placebo for 28 days. The primary endpoints will be the change in the level of functional AAT protein in the blood, as well as safety and tolerability. We expect to obtain data from the study in 2020.

In addition to VX-814, we're also developing a second AAT corrector VX-864, which is currently in Phase 1 development. In pain, we are advancing multiple selective NaV1.8 inhibitors through late stage research and early clinical development, including our ongoing Phase 1 study of VX-961. And in FSGS, we are on track to complete our Phase 1 study of VX-147 in healthy volunteers later this year. VX-147 is our first oral small molecule inhibitor of APOL1 function and if we are successful in Phase 1, our plan is to initiate a Phase 2 proof-of-concept study in 2020, where we would evaluate the ability of VX-147 to reduce protein levels in the urine. This would represent an important biological proof-of-concept for this program. And similar to other pipeline programs, we're advancing multiple additional molecule for APOL1 mediated kidney diseases in late stage research.

With the launch of Trikafta and the advancement of our pipeline of multiple other potentially transformative medicines across five serious diseases, 2020 is positioned to be a year of significant growth and pipeline progression for Vertex.

I'll now turn the call over to Charlie.

Charles Wagner

Thanks, Reshma. In addition to Stuart's comments on the performance of our CF products tonight, I'll review our third quarter financial results, our 2019 financial guidance and make a few comments on our financial trajectory for 2020. All of the results and guidance I will discuss tonight are non-GAAP. As Stuart mentioned, we saw continued double-digit growth in total product revenues in the third quarter of 2019 compared to 2018 based largely on the uptake of Symdeko and Symkevi. Our third quarter 2019 combined R&D and SG&A expenses were $416 million compared to $379 million for the third quarter of 2018. A significant growth in revenues and disciplined spending in the third quarter resulted in operating income of $403 million, a 37% increase compared to the third quarter of 2018.

Net income for the third quarter of 2019 was $322 million compared to $282 million in the third quarter of 2018. Our year-to-date financial results show similar trends of strong revenue growth and disciplined spending, resulting in exceptional operating income growth. Our total CF revenues through the third quarter of 2019 were $2.75 billion, a 27% increase over the same period in 2018. Our year-to-date combined R&D and SG&A expenses were $1.2 billion compared to $1.3 billion for 2018 resulting in year-to-date operating income of $1.19 billion for 2019, compared to $763 million for 2018.

As our profitability and cash flow increase, as a result of treating more CF patients globally, we have a clear strategy and intention to reinvest in both internal and external innovation to create future medicines. To date in 2019, we have invested approximately $1.5 billion in cash in external innovation through new acquisitions and collaborations. We ended the quarter with approximately $4 billion in cash and marketable securities compared to $3.2 billion at the end of 2018. I would note, however, that we completed our $950 million acquisition of Semma Therapeutics early in the fourth quarter, so that outflow

was not yet reflected in our third quarter cash balance. As we look ahead to Q4 and 2020 and beyond, we expect continued increases in cash flow to provide more flexibility for additional deals to fuel our long-term growth.

Now to 2019 guidance and high-level thoughts on our financial trajectory for 2020. As you know, we revised upward our guidance of total CF revenues with the approval of Trikafta last week and we are tonight reiterating our 2019 guidance for total CF product revenues, combined R&D and SG&A expenses, and our anticipated effective tax rate. The midpoint of our 2019 revenue guidance reflects strong 23% growth over 2018 and we are well positioned to continue our trajectory of significant revenue growth in 2020, driven primarily by the launch of Trikafta in the US. The exact rate of revenue growth will depend in large part on the Trikafta launch dynamics that Stuart reviewed earlier, specifically the capacity of CF centers to schedule and initiate the large volume of new and existing patients likely to seek treatment with Trikafta.

With significant revenue growth expected in 2020, we will also increase our investments in innovation, particularly following our recent acquisitions of Exonics and Semma. While Vertex operating expenses have typically grown in the range of 10% to 14% per year over the last few years, our current expectation is that the rate of growth will be somewhat higher in 2020 as we invest in research and preclinical manufacturing for selling genetic therapies in support of our programs in type 1 diabetes, DMD, and other diseases.

Importantly, we expect our revenue growth to significantly outpace any increases in operating expenses, which will drive continued increases in operating income and expansion of operating margins. Currently, we plan to issue revenue and other financial guidance for 2020 at our Q4 earnings call, once we've seen a few months of the Trikafta launch.

I'm pleased with the continued performance of our business and look forward to updating you over coming months. With that, I will hand the call back to Jeff.

Jeff Leiden

Thanks, Charlie. As we near the end of 2019, Vertex is on track to meet or exceed each of the key goals we outlined for you at the start of the year. An important and often overlooked part of our success is the strength of the team we have in place to execute on our strategy and drive the success of the business. With the launch of Trikafta, increasing revenues from treating more people with CF globally, a pipeline that is expanding and progressing rapidly and a strong and diverse team committed to our strategy of serial innovation, we have never been in a stronger position than we are today.

With that, I will open the line to questions.

Question-and-Answer Session

Operator

[Operator Instructions] And our first question comes from Salveen Richter, Goldman Sachs. Your line is now open.

Salveen Richter

Thanks. Maybe just starting with a question on the reimbursement decisions that have played out recently in England and Spain and Australia and Scotland. How should we view the uptake trajectory in these regions and any implications for the fourth quarter?

Stuart Arbuckle

Yes. Salveen, thanks for the question. This is Stuart. So obviously we're thrilled. It's been a very productive quarter in terms of new reimbursement agreements, which is great, as we complete the journey from discovering these medicines to getting access for patients. In terms of the uptake, overall, I would say, really the consideration is up the same in each of the markets and the way I would think about it is, firstly, the various administrations have to put in place the process to allow physicians to prescribe these medicines. And as an example in England, they quoted that they were hoping to get that sold within 30 days. So obviously, there is a bit of a lag before we can even staff initiating patients.

And then after that, really, I would be thinking about the number of patients that we have there in each of those markets. We expect in those markets, much like the other markets around the world that we will over time initiate the vast majority of those patients on one of the CFTR modulators that's been reimbursed, across the world in general, across products, across geographies, we tend to see initiation rates in the 80% to 90% range. As you know, not everybody unfortunately can stay on the medicines, so we see persistence rates across products, across markets, somewhere in the 80% to 90% range and so when we do eventually reach steady state, it's a function of those two things then we need to factor in a compliance rate, the compliance rates are medicines are as good as I've ever seen in my time in the industry, they are across products tend to be in the 80% to 85% range.

So, those are the kinds of factors I would be taking into account. So that tells you a little bit about where we're likely to get to a steady state, really then question is how long is it going to take us to get to kind of peak levels of uptake and that really is given by kind of a couple of things, one is the size of the eligible patient population, if you take somewhere like England, it's 5,000 patients. That's a very large number. All of those patients are treated in the 40 CF centers in England. And so, just like here in the US, there is a capacity constraint that the centers have to actually being able to see all of those eligible patients and that's probably the biggest kind of rate limiter. So we certainly expect to get to the vast majority of those patients is just likely to ramp up over time.

In terms of '19, we haven't included any adjustment in our '19 guidance just because those reimbursement agreements have come so late in the year and obviously, we need to work our way through the administrative things I've just told you about before we can actually start initiating patients.

Salveen Richter

Great, thanks. And then just a second question about the AAT program, could you just comment on how many dose cohorts, you're looking at and what the doses are and could this transition into a registrational trial.

Reshma Kewalramani

Hi, Salveen, it's Reshma. So as I said in my prepared remarks, I think that you're going to see this Phase II dose-ranging study for VX-814 look and feel very much like our CF studies, it's going to be about 50 people or so, a few dose cohorts and a very reasonable timeframe. I'll stay away from the specifics around the doses and such. And I do think that this is going to be important in getting to our Phase 3 study because this is indeed in the study that's going to help us select the right dose. So in that respect, I think it's going to be very important.

Salveen Richter

Yes.

Operator

Thank you. And our next question comes from Michael Yee of Jefferies, your line is now open.

Michael Yee

Hi guys, thanks. Two questions. Congrats on all the progress and the Trikafta approval. Maybe you could just frame some of the expectations around the uptake of Trikafta early on and whether you would expect centers to prioritize all the het/min patients first, you would think that would be logical. So even though they're swapping from others. How much of a priority is that for the het/min's first? And then the other question relates to a follow-up on AAT maybe Reshma, I think we are less to the eight-hour workshop, but they seem to be quite interested also in functional data, so how confident are you that if we get positive data on AAT that a primary endpoint of just AAT would be sufficient for approval. Thanks so much.

Stuart Arbuckle

Hey, Mike, it's Stuart here. I'll take the Trikafta question and then Reshma will talk to AAT. So in terms of Trikafta, obviously we were thrilled to get the approval so quickly, as you know the label is broad anybody with one F508del mutation, that's approximately 18,000 patients here in the US. Of those 18,000, about 6,000 are patients, who have a minimal function mutation on the other allele and as you well know, those are the patients who

don't currently have a medicine to treat the underlying cause of their disease today. In terms of uptake, again, this is going to be governed by a couple of things, one is the absolute capacity at CF centers. This is by far and away the largest number of eligible patients we've ever had for any new product launch. For instance, more than twice as big as we had when we introduced Orkambi back in July 2015. So clearly, the capacity of centers is going to be a challenge. In terms of prioritizing patients, Mike, we've heard just about everything from every different center and I think if you talk to one center, you'll get response. If you talk to another, you'll get another, some have said that they will prioritize het/min's, some have said that they will treat the most severely impacted patients irrespective of what their mutation is, others have said they were going to treat patients as they are coming in.

So I'd love to tell you there's one answer to how patients are going to be treated, but I think it's as individual as individual centers. What I can tell you though is to a center; they will tell you that they expect to treat the vast majority of those minimal function patients over time and indeed expect the vast majority of those who are currently being treated with Symdeko and Orkambi also to transition over time. But the real rate limited to that's going to be just their ability to process all of those patients through the limited number of centers that there are. Reshma AAT.

Reshma Kewalramani

Right. With regard to the AAT workshop that took place, just a couple of months ago, we were really pleased to be there. It was nice to be invited to be with the community and with the agency. I thought that there was real recognition of the disease, the gravity of the disease and the high unmet need. It was also interesting to see that our approach a small molecule corrector remains the only one that holds the potential to treat both the liver and the lung disease. With regard to where the agency is, I found them to be very open-minded and acknowledged that the -- the augmentation companies to date have gotten their approvals based on AAT levels and that's the data point that's there. And I was also encouraged by their comments that they are going to work with each individual sponsor, based on their approach to determine exactly what the Phase 3 trials could look like.

Michael Yee

Okay. Thank you.

Operator

Thank you. And our next question comes from Phil Nadeau of Cowen & Company. Your line is now open.

Stuart Arbuckle

Phil, you're there.

Operator

And Phil, if your phone is on mute please unmute. And our next question comes from Alethia Young of Cantor Fitzgerald. Your line is now open.

Alethia Young

Hey guys, thanks for taking my question and congrats on all the progress you've made. I guess kind of two, I wanted you to talk a little bit about the Semma deal and how it fits in your world of innovate medicines, but still it's a kind of a much bigger addressable market and different angle from where you guys are going. And separately, like in the United Kingdom, I know that there, you said 5,000, do you think there is like a scenario where people, there will be some sorts of controls as far as kind of, I would assume all the patients are warehouse to some degree. So is there any kind to management that might happen there that we should think about in our models, things.

Jeff Leiden

Yes. Thanks, Alethia. This is Jeff. I'll take the Semma question and then Stuart, will take the England question. With regard to Semma, I'd just start off reminding you that type 1 diabetes is a disease that fits our strategy perfectly right, it's a serious disease, about 1.25 million patients in the US that are treated in a relatively small number of centers by endocrinologists, so you can certainly reach them with a specialty sales force and interestingly, despite the fact that insulin has been around and has saved their lives for almost 100 years now, it turns out that insulin therapy for these Type 1 patients is not

really a very good long-term way of returning them to normal glycemia or normal hemoglobin A1c levels and so they, as you know suffer from very high rates of cardiovascular disease as well as from multiple hypoglycemic episodes.

So there is a large unmet need, obviously with this patient subset and it fits our strategy. We also knew for more than 15 years that if you can successfully transplant islet into these patients, you can essentially cure the disease. There were a number of studies of small numbers of patients, who were transplanted with cadaveric islets under immunosuppression and maybe those patients were not only cures, they were long-term cures, some of those patients were up more than a decade. So there were really two issues with Type 1 diabetes, and we've been watching it as one of our diseases of interest for some time. I'd say obviously David Altshuler, is a diabetologist as well as the geneticists, so he has been keenly interested in this disease.

And the two problems were there weren't enough cadaveric islets and so you need a different way to naked islets and the other problem was the need for immunosuppression was potentially limiting to the number of patients that you can reach. So we were watching companies who are addressing those two problems for the last two, three years. And over the last six to eight months, we were convinced that Semma has actually solved both of those problems. So on the first front, they have figured out how to take ES cells or even iPSC cells and successfully differentiate them into human -- into human cells in an industrial fashion, so they can make industrial levels of a human islets and they've shown that those islets and animal models actually are able to cure diabetes when they're transplanted. So that was the solution of the islet number problem and then they've also invented a device that is able, in which you can put the that's able to protect them from the immune response.

And so, Semma really has two products, they have what we call naked islets that they can transplant into the liver just like cadaveric islets are transplanted into the liver that does require immunosuppression. And they have a second product, which is the islets in the device, which we believe can be transplanted ultimately without immunosuppression and that obviously opens up the number of patients, that could be treated substantially.

So in summary, it's a disease that fits our strategy perfectly, it's a specialty disease, it's a disease of high unmet need, and it's a disease in which these recent scientific breakthroughs have given a new approach towards the transformative therapy, so it's a perfect fit and when we saw that we were able to move pretty quickly.

Stuart Arbuckle

And Alethia, on expectations for England, I really go back to kind of what I said earlier about uptake in all markets. As you said, there's about 5,000 eligible patients in England for the various medicines and across the various age ranges and genotypes that are included in the agreement we struck with the NHS. If you look at the uptake rates around the world for those products across patients and genotypes and age ranges, it's as I said in the 80% to 90% range in terms of how many of those patients have been initiated in similar markets around the world. Again, not every patient can stay on the medicine, the persistence rates again are somewhere in the 80% to 90% range. So if you factor those two things and I think about where might we be when we get to kind of steady state, then that could be somewhere around 3,500 patients could be persistent on a CFTR modulator, if you just take those assumptions and kind of pick the mid-range of all of those other markets around the world.

In terms of warehousing that in something that we've heard discussed in the UK. Obviously there has been a lot of pent-up demand for these products. And so we've heard about people wanting to be initiated. I have not heard of people saying that they're likely to warehouse their patients in anticipation of the triple, clearly that's something that could happen. As I say, it's not something that I've heard talked about in the UK.

Operator

Thank you. And our next question is from Cory Kasimov with JPMorgan. Your line is now open.

Cory Kasimov

Hey, good afternoon guys. Thanks for taking my questions. I'll ask one -- about one of the few countries, you don't have a formal agreement in yet with France. So, can you remind us how many patients are already on one of your approved CF drugs over there and how we should think about revenue recognition once a deal ultimately comes through in that country. And then on the pipeline side, regarding CTX001 for beta thal and sickle cell. Are you able to elaborate at all on the type of data, we could expect to see later this year in terms of patient numbers or duration of follow-up, you would have at that point? Thanks.

Stuart Arbuckle

Cory, it's Stuart. I'll start on France. You're right. France is one of the few markets now, where we don't have a reimbursement agreement in place. We are in very active discussions with the French authorities and I'm certainly hopeful that we'll be able to bring those discussions to a successful conclusion, as we have recently in Spain and Scotland and England and Australia. You're correct, there are a number of patients who are taking Orkambi in France. Orkambi was available through an early access program for patients 12 plus and within the French system, there's approximately 1100 or so patients who are currently receiving Orkambi. In terms of revenue recognition and how that might change, I'll turn that over to Charlie.

Charles Wagner

Yes. Cory, this is Charlie. For revenue recognition, we have been recording revenue at a relatively low value for sales into France currently, when we land on an agreed-upon price, we will book a catch-up of prior period revenue, which will equal the difference between the negotiated price and the price at which we've been booking revenue that revenue as it comes through the prior period revenue, our intention would be to non-GAAP that out, as obviously it won't repeat. And then going forward, we'll book revenue at the contracted price.

Reshma Kewalramani

Cory, with regard to CTX001 and beta thalassemia and sickle cell programs, here's kind of where we are. We have about half a dozen sites open for beta thal, about a dozen sites open for sickle cell, the studies are enrolling. I think you must have heard our partners at

Crispr comment on the fact that we will be in a position to share data this quarter. I think what you should expect to see is safety and tolerability first and foremost unsurprisingly in this Phase 1-2 study. And on the efficacy side, certainly hemoglobin levels, hemoglobin F levels will be very interesting amongst other things.

Cory Kasimov

Okay. Great. Thank you very much.

Operator

Thank you. And our next question comes from Paul Matteis of Stifel. Your line is now open.

Paul Matteis

Great. Thanks so much and congrats on the progress. I have a couple of questions with one on AAT and one on the triple in the UK. On AAT, I was wondering if you could talk a little bit about the mechanics of the assay, you're using to corroborate the functionality of the AAT levels produced by VX-814 or I guess secreted, how important is that assay and the output from it to the top line readout and validating the efficacy of the drug. And then as far as discussions with any, Jeff or Stuart, I was wondering if you could just give us the latest on where your conversations are regarding reimbursement for the triple and whether or not an agreement there is gated by EMA approval. Thanks so much.

Reshma Kewalramani

Sure, sure. This is Reshma. Let me tackle be AAT assay question. So as you've seen, our data in the animal models, you'll remember the Slide to the left panel shows you what happens with a VX-814 and with VX-864 treatment and the Y-axis there is actually functional AAT levels. So what we've been measuring in the animal studies is what we will be measuring in the human studies and it's a reasonably easy, I never like to say easy in terms of a clinical trial, but it's a reasonably simple assay and it's the same a functional assay that you've seen us do in the animal studies.

Stuart Arbuckle

Yes. Paul, just on the UK, just to be crystal clear, the current agreement, the one that we announced last week, the current commercial agreement does not include the triple combination, it includes Kalydeco and its approved indications Orkambi and Symkevi. So triple is not included. Obviously, there is a very high level of awareness of the triple combination, both in the CF community and at NHSE, but access to the medicine in the UK is going to be governed by our ability to get EMA approval in the first instance.

Operator

Thank you. And our next question comes from Phil Nadeau of Cowen and Company. Your line is now open.

Phil Nadeau

Good afternoon. Thanks for taking my question. Sorry about before, I think it was on mute. First on the Trikafta launch in the US, I think you've mentioned a couple of times that capacity will be limiting to getting new patients on therapy. Do you have a sense of exactly what the capacity is at CF centers, how many patients could see their physician every month, every quarter, every year during 2020?

Stuart Arbuckle

Yes. Phil, it's Stuart. Yes, capacity of CF centers is we hear from the CF centers, all the time, we heard it in the run-up to the launches of Orkambi and Symkevi and we've heard it when talking to them about how they planning to approach the launch of Trikafta. Essentially the rate limiting step there, just to be clear, is it's the same 275 centers were seeing, all of their CF patients and whilst there is a huge amount of enthusiasm about Trikafta, they've got other patients who are coming in for their regular visits, they've got patients who are not yet eligible for Trikafta, obviously they've also got people sadly who are being admitted with exacerbations and things like that. So while Trikafta is very, very important to them, they have a lot of other things that are going on as well.

As I said, in total, there is 18,000 patients who are eligible for Trikafta in the United States, who will be treated at the 275 or so CF centers. As I said, it was about 8,5000 patients who were eligible for Orkambi, about 12,000 for Symkevi. And so that's why we think,

whilst we think we're going to get to a very high levels of uptake overall over time, it may be that it takes us a little bit longer to get to those kind of peak levels of uptake than it did with Orkambi and Symkevi.

Phil Nadeau

Got it. Okay, thank you. And then second question, just a follow-up to Paul's prior question on the UK. The press reports about the current agreement that you have mentioned that in order for the triple to be reimbursed in the UK, it'll be subject to a NICE -- an evaluation by NICE, can you talk a little bit more about that process, is that a different process than what you've had before to secure reimbursement or is the triple kind of starting from the ground floor and need to go through the whole process that you're medicines have had to go through in the past.

Stuart Arbuckle

Yes, great question, Phil. So yes, we will be submitting the triple combination to NICE pending EMA and CHMP positive recommendation. We've said that we will submit that and discuss the timing of when we will submit that with the NHS and NICE and we've agreed and we made public that we are planning to do that in around January 2021. The reason for that is a couple fold, one that it will allow us to collect additional long-term data, as we are currently in the US through our open-label extension studies and we know how important that long-term data is in terms of demonstrating the benefit of CFTR modulators, we've seen that with Kalydeco, we've seen that with Orkambi, and now Symkevi. The more data we get, the more you get to see the long-term benefits that these types of agents have.

The second reason why that timing, we think is an appropriate time to be submitting is the NICE is currently undergoing a review of its methodology. As you may know, and as we've made quite public, we have some concerns about the approach that NICE takes to evaluating medicines in terms of their ability to truly value, appropriately medicines like ours that have the kinds of long-term benefits that ours have and we're hopeful that through that methods review that there may be some changes to the evaluation methodology, which allow them to better value. The types of benefits that our medicines

bring. So we're committed to submitting the triple January 2021 is when we've said that we will do that and hopefully that's explained the reasons why we've agreed on that timeline.

Phil Nadeau

Perfect. That's very helpful. Thanks for taking my questions.

Operator

Thank you. And our next question comes from Matthew Harrison of Morgan Stanley. Your line is now open.

Matthew Harrison

Great. Good evening, thanks for taking my question. I was hoping maybe we could spend a minute on 147. Can you just talk about exactly what data you expect to have available next year and given that data, I assume on some renal parameters, what you would expect to look at in terms of the next study?

Reshma Kewalramani

Sure. So just to catch everybody else up to speed on VX-147. This is the molecule that's targeted at the APOL1 axis and there is -- there is a known disease called FSGS, focal and segmental glomerulosclerosis, a type of kidney disease that unfortunately is relentless and really has only one outcome and that is progression to either end stage renal disease transplant or death, it's really a very significant renal disease. The way it manifests itself is proteinuria, that is to say protein in the urine. So where we are right now with the VX-147 program is we are in Phase 1 during the SAD/MAD. We anticipate that we're going to be ready to go to Phase 2, the dose-ranging study next year 2020.

And while it's too early to call exactly when we're going to have results, I expect it to be a very modest size study given the small patient population that has this disease and the very grievous nature of the disease. So in that dose-ranging study that will get off and

running in 2020, I anticipate the endpoint there is going to be proteinuria, which is very convenient because that is the endpoint of significance and it is the proof of biological activity.

Matthew Harrison

Reshma, you want to talk about the other molecule into the --

Reshma Kewalramani

Yes. Sure, sure. You know, just like in cystic fibrosis and what you've seen us do there, we have a portfolio of molecules for this as well for the APOL1 mediated kidney diseases, so while VX-147 is the one that's in the lead and going through its SAD/MAD, there is a whole portfolio of molecules, behind that in late preclinical and those will also be making their way through the clinic.

Operator

Thank you. And our next question comes from Brian Abrahams of RBC Capital Markets. Your line is now open.

Brian Abrahams

Hi, thanks so much for taking my questions and congratulations on all the progress. Two questions from me on Trikafta. I guess, first off, just given how early this was approved, anything that you guys need to do in parallel more than typical post marketing clinical work preclinical tox to maintain it on the market and then any educational awareness that you plan to do around some of the side effect nuances versus Orkambi or Symdeko, I'm sort of curious how we should think about compliance and persistence ending up, given the cocktails overall benefit risk, maybe relative to say Symdeko. Thanks.

Reshma Kewalramani

Sure. Let me start this off and then I'll ask Stuart to comment on education then on compliance persistence. So obviously, we were thrilled with the quick approval of Trikafta and I do think it reflects the benefit and the very nice tolerability of this medicines. With

regard to what to expect in the post-marketing setting, nothing really unusual or different. You know that we have a study in F gating an FRF patients that we had already initiated. So those are continuing, but no, nothing else that's different or unusual. Stuart?

Stuart Arbuckle

Yes, Brian, in terms of Trikafta and its benefit-risk profile, as you would expect we will be being as fulsome as we can in our discussions with physicians on both the benefits of the molecules and the adverse events that we've seen from the studies, as you know, the benefit-risk profile is very positive, as a result of that in terms of what we expect, in terms of compliance rates, I would expect them to be very high, just as they have been with our other CFTR modulators, as I mentioned earlier, we see them in a very tight range across Orkambi, Symdeko, and Kalydeco, they're in that sort of 80% to 85% range in terms of compliance with the medicine, given the benefit-risk profile that we've seen with Trikafta, I would expect it to be right in that range if not towards the top end of that range. Obviously, we'll see how it plays out in the real world, but that would be my expectation.

Brian Abrahams

Thanks so much.

Operator

Thank you. And our next question comes from Geoff [ph] of Bank of America. Your line is now open.

Unidentified Analyst

Hey guys, thanks for the question and big congrats on the fast approval of Trikafta. So a question for Stuart for the roll out, I guess what are the lessons that you guys have learned with getting reimbursement secured with Kalydeco, say going back years ago or Symdeko more recently, it's really focus on how you can reduce see insurance access barrier? So that's question one. And the second is what percent roughly would you assume need some sort of co-pay assistance and what are you guys doing for that? And I have a follow-up.

Stuart Arbuckle

Yes. So Geoff, in terms of what have we learned in terms of getting access here in the US, I would say going back all the way to Kalydeco through Orkambi and Symdeko, we've seen very broad reimbursement and actually that reimbursement has been put in place pretty quickly. Now, obviously it's a range across all of the government and commercial payers and so some move faster than others, some move slower than others, but in general, we've seen them move pretty quickly and we've ended up with kind of rapid and broad reimbursement. I think the thing that gives me hope that that will happen is obviously we've been out there with these payers now for seven years in the US, they have a very, very good sense of how severe this disease is, the benefits that our medicines have and the team is out there now talking with payers. And today, as I say, in terms of the reaction we've had, the reaction to date has been very positive. So I feel very good that our team is very well prepared to secure broad access.

In terms of insurance barriers, yes, there will always be some, we have a great team here which is trained to do justice to help patients out and provide support to them as they navigate the insurance barriers. In terms of what are we going to do in supporting those patients who may have financial needs, we have the standard suite of offerings that you would expect and certainly our commitment is that we are going to do everything we can to make sure that no patient is left behind because of their ability to pay.

Unidentified Analyst

Okay. And then, and then just a follow-up for Reshma or maybe even, Jeff. When you think about opportunities to diversify outside of CF, you guys have a lot and it seems like everyone's been working pretty hard, but on the pain program, most of them are early though, so I want to ask you, what is the capacity or even how much of a priority is bringing on later stage assets. As you begin to see the leverage in the P&L from the Trikafta launch. Thank you.

Jeff Leiden

It's a great question Geoff, maybe I'll take that one. We have been working hard, the entire team on getting these deals. I was showing our Board today that I think we've done more deals in 2019 than we've done -- than we did in 2016, 2017 and 2018 combined and that's a good thing. Obviously, we have both diversified our pipeline and we've also considerably built our toolbox and you should expect to see us continue to do that. I think we've been pretty consistent all along in saying what you probably shouldn't expect to see us do is to buy on-market assets or very late stage assets to essentially buy revenue growth. We don't really need revenue growth; our CF franchise will provide that well into the 2020s. And so, we're in a very nice position of being able to invest in earlier stage assets, where by the way, we think we can get much better value and also add much more value from our own internal development and regulatory group, so that we can build much, much better value both for patients and for shareholders.

So you should expect to see us to continue to do deals early stage assets, where we can add value, technology is particularly that bolt on to our gene editing strategy, which as you know we have broadened considerably over the last year and more of those deals, but I don't think you'll see us do the very late stage, certainly not on market products or very late-stage products.

Reshma Kewalramani

I just wanted to add to that. You mentioned the pipeline and where we are, you already talked about pain. It's actually interesting to know how many molecules we have already into mid-stage development. So CTX001 is already in Phase 1, 2, AAT we expect to be in Phase 2, it'll start this quarter 2019 and FSGS, I expect to be in Phase 2 next year.

Unidentified Analyst

Great. Okay, thank you.

Operator

Thank you. And our next question comes from Liisa Bayko of JMP Securities. Your line is now open.

Liisa Bayko

Hi, thanks for taking my question. I just wanted to ask you to help with questions about the pipeline. The first is for the AAT program, I noticed you're focusing on patients with two Z mutations. Can you maybe just break down the AAT population into its kind of mutation types to better understand what kind of group you're addressing with that small molecule corrector, the first one.

Reshma Kewalramani

So you are right that there are different subgroups of patients who have alpha 1-antitrypsin deficiency, but the majority of patients have the Z mutations. The majority of patients who are ill have the Z mutation. So 90% plus have the Z mutation, so no surprise that that's the group that we're focused on.

Liisa Bayko

All right, that makes sense. And then sort of similar question. I know a little bit about FSGS, you kind of qualifying these as mediated by APOL1 is that -- is that again the majority of FSGS cases, just curious about that one.

Reshma Kewalramani

Sure, sure. So that one is a little bit different. So FSGS is a heterogeneous group of etiologies that results in that, FSGS is actually named after it's finding on pathology. But there is a right homogeneous group within that that is mediated by APOL1. So we are not pursuing all FSGS, we are pursuing APOL1 mediated FSGS, it's a group, it's a homogeneous subgroup of all of FSGS and it turns out that there is actually other groups renal disease that are also mediated by APOL1, but the one we're focused on is APOL1 mediated FSGS.

Jeff Leiden

And the reason Liisa is because there is very strong human genetics evidence that APOL1 is the cause of that disease.

Liisa Bayko

Okay, great. And then how -- I guess how do you know that the FSGS is related to that and I guess of FSGS patients, what -- how prevalent is this particular group?

Reshma Kewalramani

So you know I happen to be a nephrologist, so I really like this topic, but I'll keep it short and here's what I'll say maybe there's two, three important points to mentioned are amongst African-American patients, who have FSGS, 70 plus percent have FSGS that's related to APOL1, so the vast, vast majority, and the only other important point I'll make for today's call is that there are studies, really nicely done studies that looked at patients who have APOL1 mediated FSGS versus not, those patients have more serious disease that is more progressive. As Jeff said, it is the causal factor here and that's why we are so interested in this disease and in this pathway.

Jeff Leiden

And the way you know is just by sequencing. This is [indiscernible] that's been described in literature.

Liisa Bayko

Okay, great. Thank you.

Operator

Thank you. And our next question comes from Geoff Porges of SVB Leerink. Your line is now open.

Geoff Porges

Thank you. Thank you very much. And just to change the direction a little bit. Charlie, could you tell us what the free cash flow was in the quarter and then give a little bit more clarification on operating margins. And then, Stuart, could you tell us the total number of patients on one of your CF medicines and the breakdown of Kalydeco US to the Kalydeco, Orkambi, and Symdeko, just so we kind of level set our models. Thanks.

Charles Wagner

Sure, Geoff. On the free cash flow in the quarter, we can follow up with you afterwards on that. As I highlighted, we ended the quarter with about $4 billion in cash that did not include the Semma -- the disbursement for Semma, which happened shortly after, what you can see though with our performance this year is that we are on track to end the year with more cash than we started the year. And that's even after spending nearly $1.5 billion on business development during the year, so the operating leverage and the cash flow generation continues to be very strong.

Second part of your question was around operating margin, we've run in the kind of low to mid-40s in the first half of the year. We do expect, you've seen -- you saw a little bit of a ramp up in expenses in the third quarter, an additional ramp up in the fourth quarter. So we should end the year in that low to mid-40s range. Again, a significant increase over last year, which was around 39% and so with the continued growth of the business on the top line and disciplined spending, we continue to drive operating margins up and you could expect that into 2020 as well.

Stuart Arbuckle

And Geoff, in terms of the breakdown of I think it was just Kalydeco you wanted US, ex-US.

Geoff Porges

Well, the three markets.

Stuart Arbuckle

Okay. All right. I got all three. So Kalydeco US was $163 million in the quarter, ex-US was $87 million, Orkambi was $199 million in the quarter in the US, $98 million ex-US and Symdeko Symkevi the US was $349 million and ex-US was $55 million in the quarter.

Charles Wagner

Geoff, this is Charlie. I would add, you've been pretty consistent in looking for the details on this. Going forward, we're going to move away from some of this detail. Obviously, now with the triple approval, we've got a portfolio of medicines that are going to allow us to

treat the vast majority of patients within the medicines, there is a significant level of label overlap and we see a significant level of switching and we would expect even more switching with the triple. As a result, the very, very detailed breakdown by product becomes less meaningful over time. So moving forward, our intention would be to report total CF revenues and break that out by product. We will also break out our US and ex-US revenues, but we will move away from providing very detail product by geography.

Geoff Porges

Perfect. I will know what to expect. Thank you.

Michael Partridge

Operator, we have time for one more question.

Operator

Thank you. And our last question comes from Whitney Ijem of Guggenheim. Your line is now open.

Whitney Ijem

Hey, guys thanks for taking the questions. A couple of quick follow-ups. First on Semma. They had previously guided to a first half 20 start for the naked cell program, I believe, is that still on track? And then for FSGS, just curious, are there any plans to do sort of a basket study of renal diseases driven by APOL1 or as you mentioned, are you kind of specifically focusing on FSGS for the near term?

Jeff Leiden

Yes, Whitney, this is Jeff. I'll take the Semma question and Reshma will take the FSGS question. In terms of Semma, we are very pleased actually with the progress in both programs, the naked cells and the device plus cells, I think it's a little early -- as they're in discussions with regulators to sign a precise date to when they will start clinical trials. But I do anticipate it to be in the near future, meaning this isn't a program, it's three to five years out or anything like that, but stay tuned as they and we finish our discussions with regulators, we can give you a little more certainty.

Reshma Kewalramani

With regard to the FSGS question, it's a good question about basket trials. But, no, that's not our approach. The FSGS component compared to for example non-diabetic kidney disease that also has an APOL1 mediated component. They're actually different enough that the FSGS patients are much more sick, the progression is faster and the levels of protein are very high, so we think that there is a real high unmet need there that we have to go at it first and get there and then we'll get to the other. So our focus here is FSGS, APOL1 mediated and we're going to do that as a standalone trial.

Michael Partridge

Thank you, everyone, for tuning in and analysts for their questions. If you have additional questions, the Investor Relations team will be available in the office tonight. Have a good evening.

Operator

Ladies and gentlemen, this does conclude our conference call. You may now disconnect.