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PRESENTATION

Cory William Kasimov *- JP Morgan Chase & Co, Research Division - Senior Biotechnology Analyst*

All right. Good afternoon, everyone. My name is Cory Kasimov. I'm the senior large-cap biotech analyst at JPMorgan, and it's my pleasure to introduce our next company, Moderna. Here to present for Moderna is the CEO, Stéphane Bancel, and please note that following Stéphane's presentation, there's a breakout just across the hall in the Georgian room. So with that, Stéphane?

Stéphane Bancel *- Moderna, Inc. - CEO & Director*

Thank you, Cory. Good afternoon, everybody. Thank you for joining us. Before starting, let me remind you, we'll be making forward-looking statements and there are risks associated with investing in Moderna, which you can find on the SEC website or on our website.

So let me start by capping a little bit 2019. The key highlights before looking at the future, what's coming. So today Moderna has 20 program in development. So of course, I'm not going to go through all of these. You can find the slides on our website. But I just want to note that we are preparing our first pivotal Phase III study, which is a big change from us being a discovery company to early development to late-stage development and there are other of things that have been moving in the right direction over the last 12 months. So let me just highlight a few products about 2019. The first one is CMV. So CMV, we believe, is a company builder for Moderna. So for those of you that are not familiar, cytomegalovirus is a virus that is a big issue for pregnancy in the developed world. You have massive neurological damage, 10% to 30% of children early to death in the first year of life. And there has been, despite a lot of efforts by a lot of great company, no vaccine launched in the last 20 years. So there's no vaccine on the market. If you think about this program, I think it really exemplifies the power of mRNA technology in each vial of our product, you can find 6 different molecules of mRNA. 1 coding for gB antigen and 5 coding for each component of pentamer, which is a very important antigen to provide protection through vaccination. So we shared several data in 2019. First, in September at our R&D Day, we shared the interim data after 2 dose of a vaccine. And last Friday, we shared data after the third dose. And we are very encouraged to see that for seronegative, healthy adults, meaning that they have never been exposed to a virus, we're able to see after 2 dose, 2 to 5x increase in antibody titers versus baseline of CMV positive. And after the third dose, we saw up to 10x. We were shooting for 1x to be able to move our program forward. We've also seen a good safety and tolerability profile, very similar to approved vaccines. And in CMV, a positive subject. We saw a very important boost. We have been able so far to see durability up to 12 months with very high titer, still at the 12-month point. So this data very encouraging, led us to start a Phase II study. The Phase II we announced on Friday has been started. We started dosing subjects. It's a study that's going to go pretty fast. It's U.S. focused. 12 sites, so it's going to enroll the 252 participants pretty quickly. We anticipate in the second half of the year to be able to share the interim data after the second vaccination. We are already preparing the Phase III, our first pivotal study in the company's history. The Phase III is going to be done in Europe and in the U.S., obviously, we anticipate to be able to get both efficacy and safety database with a study of less than 8,000 participants. And we are working really hard to get the study started in 2021. We have already started to make Phase III material in our factory in Norwood.

So let me share a few reasons why we are very excited about CMV. First, we believe that at peak sales, CMV should be a product of $2 billion to $5 billion of annual sales. It's interesting to see that Merck in their annual R&D day in June 2019, shared that they believe CMV is an opportunity larger than $3 billion of annual sales. If you assume a price like GARDASIL, we believe our gross margin is going to be around 90%, and that we should have an EBIT margin of around 50% for this product. One of the very important points is, we believe, that we will launch the CMV vaccine. And we believe that because there has been already studies done in the clinic using only gB antigen. And there was a very important paper done by Sanofi,

using a gB antigen showing that they were able to protect 50% in terms of efficacy in that Phase II study. And so because we're adding gB (inaudible) pentamer and because mRNA makes protein in human cells, we believe that the presentation to the immune system should lead to very good protection, and we're looking forward to be able to validate that in the clinic.

What is important to know is that Moderna owns the global commercial rights of this product. And so we really believe that this product because of its commercial potential, of its high probability of success of launch and the fact that we own it, could be a company builder. And really embodies and represents the mission of Moderna, which is to use mRNA technology to make innovative products.

The next product, I'm going to go very fast, is hMPV-PIV3. hMPV is the third respiratory virus, PIV3 is the fourth, we are designing a vaccine that combines antigen against those 2 viruses. We have a good Phase I data. We're now going to a Phase Ib of age de-escalation to go into children. We own the right of this product. Our personalized cancer vaccine that we are developing with Merck shown good data that we presented at ASCO, which have a good safety profile. We show T-cell response, and now we are doing the experiment, which is important to do, which is a head-to-head Phase II, KEYTRUDA monotherapy compared to KEYTRUDA plus PCV to see do we have in terms of response to the product or not.

Another big milestone of 2019 is the delivery of our first IV product. So basically, this is an antibody encoded in mRNA so this is 2 mRNA in the same formulation to be able to deliver full IgG, heavy and light chain. So this was, as you can imagine, a pretty strong tour de force by our scientific and manufacturing teams. What you can see here is the interim clinical data. There were 3 dose. We tried the low dose, mid-dose and high dose. As you can see, we're able already at the mid dose, to exceed the target for the profile. You can see that the CV in between subjects is actually very tight, very similar to recombinant. And this product was given without steroids. The safety profile at the low dose and mid dose was pristine. The investigators or the subjects could not know if they were on active or on placebo. At the higher dose, we saw some injection-related reaction that went away without any medical intervention or medication. So we are doing more exploration in the clinic about this product.

Last but not least, is our rare disease program. We had both IND for MMA and PA opened by the FDA. Both programs have also got fast track designation by the agency. In MMA, we are actively recruiting patients. In PA, we are finalizing 2 set up sites to be able to recruit patients. One of the operational miss of last year was MMA. We were really trying to get MMA patient dose. We didn't succeed. Our team is working really hard to get MMA patient dose as soon as we can because we're extremely committed to those diseases and to rare disease in general.

So that's for 2019. And I would like to really recognize the Moderna team that has done a really terrific job over the year to be able to get us there. So let's talk about the future. And to be able to talk about the future, I need to go back into the early days of the company. Since we started Moderna, we have believed: the board, the management team, the early investors, the early employees, that if we could safely get an mRNA to approval, this will be a new class of medicine. It made no scientific sense that this would be a 1-drug company. It was going to be no drug or a lot of drug. And so we embarked on building this company as a platform and to think about how would you build such a platform? How would you de-risk it? Because it was very clear that if we were going to be successful, the product opportunity was going to be very large, secreted proteins, transmembrane protein, intracellular protein, combination of proteins, so very large product opportunity. Because mRNA is a platform, we believe that the probability of technical success of our drugs was going to be higher than traditional medicine, especially as you think about it, we are making human protein in human cells. I don't believe it could be worse than making them intracellular [electrolyte] cell. We believe that if we invested in technology, in IT, we should be able to go really fast because, again, of the power of our platform. We don't have to invent how to make drug every time all over again. We have a true platform. And then we believe that capital efficiency and cost of goods will be very interesting over the long run.

So if you believe that you have the potential to impact patients in such a profound way to build a new class of medicine, how will you build such a company? And what we decided to do with the team is to say, we have to obsess about managing risk, execution risk, obviously, financing risk but especially in our case, technology risk around mRNA technology and biology risk. And so what we decided to do, which was a pretty unusual experiment is not to pick 1 drug and go to the clinic as fast as we could and hope that we had picked the right technology. We decided to diversify what we're going to try in the clinic. And so we tried 6 different technology that you can see here on the x-axis, of different formulations, different route of administration, to diversify our risk because we didn't know where this technology was going to work best because no product has been approved for mRNA. And then in every 1 of those modalities, we try different drugs because we wanted to manage the biology risk. So that's how we build the company, which is why the pipeline today has 20 products, 20 programs in development. What we learned in 2019 -- and 2019 was a very important inflection point in the company's history, we believe -- we learned that our vaccines look really, really good. And we learned that we could inject safely, at a well-tolerated dose, the mRNA into an IV systemic delivery. And so the way we think about the company moving forward

is quite different now. We've always said we're going to try all those experiments in the clinic to learn in the clinic where the technology was going to work best. And once we have good positive signal in the clinic, we're going to do more because it becomes more of the same. This is where the power of platform is very interesting. So what we announced at JPMorgan, is that we're going to do more vaccines and with a more systemic therapeutic product.

We're, of course, continuing our commitment to exploration. That is very important to who we are. And if you think about it, today, we have 5 immuno-oncology drug in clinical trial combined with KEYTRUDA or with durva, where VEGF is dosing in people's hearts, AZ is running the study in Phase II as we speak. So we are very eager to see that clinical data. And as I said, we are working really hard to dose soon, MMA and PA, to try the systemic intracellular therapies of our company.

So we're going to do more of vaccines. We're going to do more of systemic secreted therapeutics. And the reason is very simple. It's a platform. We've invested so long. We have been very deliberate about how we build the portfolio. We have been very patient to not get ahead of ourselves. But today, we have a clinical data that are -- come in singles that what we should do for patients, that we should do for our shareholders is to do more of the same things that are working well. And for the obvious reason that I described before, once you get this derisked then you can go into leveraging the product opportunity. They're going to have probability of success. Think about CMV and the beautiful data we shared. We can do many more vaccines, where today, there is no vaccine on the market; like CMV, to go and help people to protect them so that they don't get infected.

And something on the systemic therapeutic.

And so we're going to do more infectious disease vaccine, and we're going to do more systemic therapeutics. In systemic therapeutics, what we're also announcing at JPMorgan is that Moderna is entering a new therapeutic area. After infectious disease, immuno-oncology, cardiology and rare genetic disease, we're entering autoimmune disease using the systemic therapeutic modality, meaning we're going to use exactly the same chemistry as we make our mRNAs, the same manufacturing processes. And we're also going to use the same formulation system, the same lipid, which are Moderna invented, and we own the IP on those lipids, to take those drugs into the clinic. So what does that look like? So we announced at JPMorgan, 2 new development candidates, mRNA-6231, which is an IL-2 long-acting mutine. We picked that 1 because as we go into new areas, we'll have to go after biology that is somewhat derisked. And as you know, there are several companies that are exploring in the clinic, IL-2 right now in autoimmune disease. The piece that's going to be new for Moderna is we want to keep exploring and learning about our technology. This is going to be our first product that's going to be subcu. The chikungunya data I shared with you was injected IV. So we're going to have an IL-2 injected subcu, where the mRNA is going to be taken to the cells, going to make an IL-2 long-acting mutine that's going to basically bind to the receptor to be able to expand Treg. So we have some very interesting preclinical data that we will present when we have a bit more time than today. And so the team is working to take this program into the clinic.

The other program that we're extremely excited about is the PD-L1 mRNA-6981. So again, let's be clear, this is not an antibody to PD-L1. There are a lot of those products on the market. This is a product that we believe is unique to mRNA technology, where here we inject IV, an mRNA coding for PD-L1 protein. The PD -- the mRNA gets uptake into the antigen-presenting cell, make the PD-L1 and it's designed as a membrane-bound protein which is, again, a unique feature of mRNA. We've done that before in our flu vaccine, in our CMV vaccines and many, many times again. And so the protein is designed to be made by the APCs and to be attached to a cell membrane to be able to do a handshake with a T-cell with a PD-1. So we believe this is going to increase the signal to basically being able to attenuate the immune response to be able to go after autoimmune diseases. So this is exactly in line with our strategy, use a technology that has been derisked in the clinic or formulation that has been used in the chikungunya antibody. And use biology that is somewhat validated. If you look at the label of an approved antibody to PD-L1, you will see a lot of autoimmune disease as side effects of a drug. So we think that there's a lot of rationale for this. And we are very excited to take this drug to the clinic. We own the commercial rights to both the IL-2 and the PD-L1 molecules.

So what does 2020 look like? So when you have 20 drugs in development, you can expect a lot of clinical data. Across all of our modalities, we expect very interesting data coming throughout the year. The other piece, too, is we expect new development candidates to be nominated as the year evolves.

So in terms of financials, if you look at it at the end of the year, the company at $1.26 billion of cash and cash equivalents on its balance sheet. Because we have quite a number of grant with BARDA for Zika program with the Gates Foundation, we have around $184 million of capital that we got funding for that is not on our balance sheet as we speak. But that on a quarterly basis, we basically get reimbursed for. So if you add those 2 numbers, that's how we get to the $1.45 billion of capital that we can invest into the company to create value. In 2020, we shared already at our November Q3 call that we intend to invest around $490 million and $510 million of capital in the company when you look at cash from operations as well as PPE or purchase of capital. So as you can see, we have a very strong balance sheet that we can use to invest, like when we saw in 2019, the good clinical data in vaccine and the fact we want to do more and something with systemic therapeutic. So if you look at the company at a 30,000 feet view now, we are preparing our first Phase III. We have 4 molecules that are either in Phase II or preparing for Phase II. We have 10 Phase I that are ongoing. And we have so far 10 clinical readouts, showing that we can, say, free inject mRNA into different applications, where we get the protein that we designed, produced in human and the protein being active.

If you look at the portfolio, it's a very [attacking] portfolio of products. We have 4 first-in-class vaccines. There is no CMV vaccine on the market. There is no RSV vaccine on the market. There is no hMPV or PIV vaccine on the market. There is no Zika vaccine on the market. That is how we want to deploy our capital and our technology to do products that are highly differentiated.

In immuno-oncology, we have 5 drugs in the clinic. We've always trying to answer the same question, can we improve the response of a checkpoint monotherapy? And we're trying this either by going intratumoral or we're trying this with our cancer vaccine application, both the personalized cancer vaccine, where every patient gets a different drug; or in our KRAS vaccine that has the 4 most prevalent mutation of KRAS that Merck is running the clinical study for us. Fibro disease program and with the JPMorgan announcement, 2 autoimmune disease program.

If you think about the number of studies that we have done so far. We've started 16 clinical trials around the world. We have dosed more than 1,500 healthy subjects or patients. The team is strong of 820 employees between our Cambridge facility and our Norwood manufacturing sites, which is 200,000 square feet. I remind for those of you who are not familiar with the site, it's a fully integrated factories where we make our raw materials like plasmid, we make mRNA, we formulate mRNA. We fill the vials. We do all the quality control, both products and environment metering. So we're in charge of our destiny.

Our teams come from Big Pharma and big biotech. They have strong expertise in 21 CFR in GMPs because, again, we want to derisk the execution of our plans. We have a very strong partnership with Merck. We have done 4 partnerships over the years with Merck, we have done 3 partnership with AstraZeneca, and we're, of course, in an important partnership with Vertex, where we'll continue to explore where could we use mRNA for different applications. And this is exploring the use of mRNA into the lung. So it's still in the labs, which is why you don't see a CF program in the development pipeline. But it's very important to know that this is really who we are as a company. We believe mRNA can be a new class of medicine and want to keep exploring where we can keep expanding the possibility of using mRNA. And we talked about the balance sheet. So what are the priorities for 2020? The priority #1 is to, of course, execute on our development pipeline. We are very clear that getting the first product to approval, getting products moving forward from Phase I to Phase II, from Phase II to Phase III is very important. And amongst those, the most important priority is to complete the CMV Phase II, pick a dose for Phase III and start enrolling for Phase III of first pivotal study. As I shared before, we believe -- I believe that we will launch the CMV vaccine and we're getting the organization ready to launch the CMV vaccine. We have said before, we can launch our CMV vaccine from our current facility in Norwood. So again, we're in charge of our destiny. And of course, moving the other programs in the pipeline.

And as you can see, there's a lot to do. The team are very busy, but we're a very strong team so that makes it much easier. The second priority of the company is to keep creating value, keep derisking the company by nominating new development candidates that are important for patients. And we're going to do that in the 2 clinically derisked modalities that we spoke about today, the prophylactic vaccine and the systemic secreted and cell surface therapeutics using the chikungunya antibody technology. And as I said, we're going to keep exploring in new modalities because we are just getting started. So all in all, we are very proud of the progress we have made toward executing toward our mission. We believe that mRNA will be a very important new class of medicine for patients. And the entire team at Moderna is very committed to get our first drug to approval because, again, as I said, we know if we get 1 drug approved, we'll get many more drugs approved. With this, thank you very much for your attention.

QUESTIONS AND ANSWERS

Stéphane Bancel - *Moderna, Inc. - CEO & Director*

Okay. Well, good afternoon. Thank you so much for attending the session. Yes, so we'll be happy to take questions.

Matthew Thomas Holt - *JP Morgan Chase & Co, Research Division - Analyst*

Yes, sounds good. So I'll start off with the first question. And if anyone has any questions, just come up to the mic because we are being webcast. But let's start with the CMV data that you announced last week and discussed extensively in your talk. Can you expand a little bit on how you're thinking about the probability of success now that you have the 7-month data in hand?

Stéphane Bancel - *Moderna, Inc. - CEO & Director*

Yes. So I think it's a story in several pieces. First, there is what I discussed in the presentation, which is we know that gB is very important because of the Sanofi Phase II study that is in the New England Journal, where we showed 50% protection. So obviously, that's a very important starting point when you go after a virus for which there is no vaccine ever approved. That's number one.

Number two, if you ask infectious disease doctors that have worked across the world on this virus, some of them all their life, they will tell you, we knew 10 years ago, 15 years ago that the pentamer was critical. We just didn't know how to make the pentamer using the recombinant. So the pentamer component has always been important. And then there is, I think, first the realization that if you look at the industrial vaccines, there was a study published by MIT a couple of years ago, showing that the probability of success of a vaccine after a positive Phase I is north of 40%. And when you think about it, what is different in vaccine from therapeutics is that your Phase I population is healthy people, your Phase II is healthy people, your Phase III is healthy people and your commercial is healthy people. So what we saw in -- or signal in Phase I, which was not 5 subject, it was I think 150 or something like that subjects, is we start to get a good data set of what you could see into the commercial population of a product. And then I think it's the quality of the data we share. To give you a sense, before we saw our Phase I data, we were hoping to get 1x. Meaning, we're hoping to get the adults that were CMV negative, who had never seen the virus, to make as much antibody as adults that have been infected before, that are CMV positive. So that's what we were hoping for. There is a published study from Merck, which has been making vaccine for a long time, it's a great company in making vaccine. We have decided to take to a Phase II a CMV vaccine, where they demonstrated 0.9x of their seropositive with their assay. So if you look at the ratio because every company has a different assay. So looking at the absolute antibody titers actually means much scientifically. And so we were hoping for 1 because we saw a Merck data before, and we knew and it is believed in the field that if you can get the same antibody concentration as people who have seen the virus, it should be protective. So we are seeing our people get 1, maybe 1.1, that'll great.

And after the second dose, we saw 2 to 5x, which was extremely surprising. We're, of course, extremely pleased. And as we shared last Friday, after the third dose, we're now at 10x at the 90-microgram or 180-microgram per human. So it's a very, very tiny dose, which has very interesting manufacturing benefits, of course. And so that's why we are -- with a stronger belief that we will launch CMV. I don't know yet the protective -- protection we're going to get from CMV, but given the medical need that is just very important. And the fact that gB is already doing 50%, we think that we are now ready to launch this product.

Matthew Thomas Holt - *JP Morgan Chase & Co, Research Division - Analyst*

Okay. So we'll get into the Phase II study and the Phase III studies in a little bit. But before that, you've guided to having another interim update for the Phase I at some point. What are you hoping to see in that or learn in that, relative to what we we've already seen?

Lorence H. Kim - *Moderna, Inc. - CFO & Treasurer*

Sure. So we -- as you might recall, back in September at our R&D Day, together with our 3-month data, we showed an early cohort of subjects that had been followed out to 12 months. And we saw very nice durability of neutralizing antibody titers out to that 12-month time frame. We'll continue to follow our participants in our study here from this 7-month time point out to 12 months. And really, this goes to the durability of that immune response. And so far, we've seen quite compelling durability where these seronegative subjects that we've vaccinated maintain a level that's multiple folds higher than seropositive levels for that time frame.

Matthew Thomas Holt - *JP Morgan Chase & Co, Research Division - Analyst*

Okay. Great. And then also, in your 7-month update, you presented new data for your higher-dose cohort, the 300-micrograms. Just curious to get your thoughts on that and your confidence that, at least with all we know right now, that doesn't need to be explored in a Phase II study?

Stéphane Bancel - *Moderna, Inc. - CEO & Director*

Yes. So I think there are a few thoughts there. I mean the first one, you need to know, we decided to go for the 300-microgram just to understand the dose response and to not miss the dose. Again, we have never done a vaccine in the clinic with 6 mRNA in each virus. So when you think about it from a mass standpoint, that is actually much less per component. Our flu vaccine saw great titers at 25-microgram in our hMPV+ PIV at 100 and above. So it just gives you a sense -- and so as we're doing the study, we just say let's just push with those so we understand the dynamic range of the dose response. And if you look at the data we shared at the 7 months, I mean, at 90-microgram, like at 180-microgram, with 10x about what we're hoping to achieve. So we think that dose-wise we are wrong and which is why if you look at the dose, we are dosing, as we speak, in the Phase II, 50-, 100-, 150-micrograms. So we tightened a little bit the dose range to try to really land the right dose. It's, of course, critical to get the right dose. And as we said, the Phase III, to get approval between safety database and efficacy database, we think we should get that with around a little bit less than 8,000 participants.

And so you want to get the dose right before you're going to go vaccinate 8,000 people. And so we just want to make sure in the formulation we're going to be using with a commercial product, which is a lyophil as we've communicated. The Phase I was done with a liquid product. And so we want to make absolutely sure, again, with the same mindset to derisk this program to try the product that we're going to be using in the Phase III. So there's not a manufacturing surprise in the Phase III. This is going to be exactly the same product form.

Matthew Thomas Holt - *JP Morgan Chase & Co, Research Division - Analyst*

Got it. And then, I guess, for the Phase II, and you somewhat answered this. But you're trying to find a dose or select the correct dose. And so when you update us in the second half of 2020. What are the key parameters or the order of importance that you're going to look for in those doses.

Stéphane Bancel - *Moderna, Inc. - CEO & Director*

So if you ask people that have successfully launched vaccines, then we are lucky, we are surrounded by them, both as consultants or on our Board of Directors. It's always a trade-up between efficacy and tolerability. Because if you have great tolerability, but the vaccine doesn't work, it's not going to be selling very much. And it's not going to be helping people very much. And so what you want to really find the right balance, where you have very strong anticipation of efficacy and the tolerability profile that makes -- people will get vaccinated or come back for their boost because if we only get the prime, they might not be really protected or fully protected. And so that's the trend.

If you look at Shingrix, which I think is the most recent example of a very innovative vaccine that was launched by GSK. Everybody that has got Shingrix, I'm sure people in the room have been vaccinated with Shingrix, all my friends who have got Shingrix told me this was the most painful vaccine they ever got. But if you look at the label, it's at 98% efficacy. And so I think for an important pathogen like CMV, for women in the age of bearing a child who want to protect their baby from getting neurological damage or from dying, I think we're going to tend to err on the side of

efficacy even if they're a bit more painful or they are sore or redness or a tiny bit of fever that goes away after a good night of sleep, to make sure that we have a very, very strong efficacy.

Matthew Thomas Holt - *JP Morgan Chase & Co, Research Division - Analyst*

Okay. So next, I want to discuss the Phase III design or preliminary thoughts on the Phase III design, which you did provide some detail on your conference call. But you've said that you can treat -- you think you only need to enroll 8,000 patients or less. Can you help us understand how you're thinking about, assuming that sample size, enrollment time lines? And then also through your discussions, either with FDA or looking at the prior literature, how long would you need to follow these patients? Or how are you thinking about this when designing a trial in order to see a benefit?

Lorence H. Kim - *Moderna, Inc. - CFO & Treasurer*

So clearly we need to land on the final trial design and communicate that transparently to the world, and we'll be doing that after we select a dose in the Phase II and after we talk to regulators and health authorities. That said, the numbers that you're referencing, Matt, refer to some early assumptions that we're making about how the trial will be sized and powered.

So you're right, we think that the Phase III pivotal trial can be run in under 8,000 subjects. If you look at various benchmarks for how quickly that number of healthy adults can get enrolled, that feels like about 18 months. And again, we'll come back with further granularity. I'm thinking about why that -- that can be done in that time frame. And then really, follow-up is determined by event rate. And as we go to the literature and look at the percentage of subjects that we'll seroconvert in any given year, that number varies from about 1% per year to 3% per year. And so in order to get an adequate number of events in our study in both arms, we think that, that follow-up looks like about 2 years at this point. And again, we'll be further testing those assumptions as we get closer and closer to finalizing that Phase III design.

Matthew Thomas Holt - *JP Morgan Chase & Co, Research Division - Analyst*

Great.

Stéphane Bancel - *Moderna, Inc. - CEO & Director*

Allow me to add a couple of things to what Lorence shared. I think know it's important to know that we already had the Type C meeting with the FDA where we wanted to discuss the approvable endpoint, which, of course, is very important. And what we discussed was to you as an approvable endpoint, protection against primary infection of women in childbearing age. So we are not going to try to track -- to vaccinate women, track when they become pregnant and their 9-month pregnancy and is the baby infected or not. FDA agreed with us because there's such a strong database of women who are CMV positive and the incidence rate of transmission to the baby, that being able to show prevention of primary infection was the right endpoint for this study. So this is behind us. We talked about it with the agency, and we will continue to refine discussion with the agency on CMC and other things, again, to make sure that we really have a good dialogue with the agency to be able to cross all our Ts and dot all our Is just to make sure the Phase III, when it's started, we have a very clear line of sight on how we're going to take this to be refined.

Matthew Thomas Holt - *JP Morgan Chase & Co, Research Division - Analyst*

Okay. Got it. And then, I guess, just the other part of the Phase III, how are you thinking about the cost and logistics of running such a large Phase III trial? And how heavy of a lift is -- is something like this for a company of Moderna's size?

Stéphane Bancel - *Moderna, Inc. - CEO & Director*

Yes. So let me start there and Lorence can add what I'm going to miss. So first, we said this is going to be U.S. and some European country studies. And it will not be a global study at this stage. As we said publicly before, the likelihood, we launch this product in 140 countries by ourselves is low. And so we think finding a partner or several partners in different geographies to help us is going to help there. So let's focus on U.S. and Europe.

This has been done before, actually much, much bigger studies have been done before. And so what we've done, like we've done in the past to reduce execution risk is our infectious disease team has done that before. Of course, not in Moderna, in bigger companies, the team that's running (inaudible) operation has done pivotal Phase III of even bigger size, the team leading the project has also done that in other companies. And so if you think about the number of sites that you need to get to get to this point, it is actually something that's really doable for a company our size.

Matthew Thomas Holt - *JP Morgan Chase & Co, Research Division - Analyst*

And then on the cost side, any preliminary thoughts?

Lorence H. Kim - *Moderna, Inc. - CFO & Treasurer*

We haven't, of course, guided since we haven't finished the trial design at this point. What I can reference perhaps is benchmarks that you can get from the industry for vaccine studies. So just as when you look at oncology studies, you'll often see cited costs that look like $150,000 to $200,000 per patient in a cancer study. What you'll often see in vaccine studies are benchmarks that look more like $20,000 to $40,000 per subject. Again, that's only a very preliminary benchmark assumption. And again, we will be coming back as we design our study with more granular assumptions for how we think about our costs.

Matthew Thomas Holt - *JP Morgan Chase & Co, Research Division - Analyst*

Great. And then, I guess, so going back to the CMV data, how do you think about the state of translating to the other programs you have within prophylactic vaccines and then also to the rest of the pipeline?

Stéphane Bancel - *Moderna, Inc. - CEO & Director*

Yes. So if you look at CMV first, this is not our first vaccine. This is our sixth vaccine that we have in the clinic. And so what we show consistently is that we can make transmembrane antigen, we [treated] the Flu, with RSV, with hMPV, with PIV, with gB and with pentamer. And if you look at the response we have, it's very actually consistent. What I think that I think is the most interesting about the platform that we have for vaccine is the consistency of titers. If you look not at the average, but if you look at the titers of every subject and you follow them, it's not like you have 50% of people at high titers and then the rest are very low titer and we'll just show you the average and it's kind of okay. The vast majority, if not all, the subjects -- go back to -- this we shared publicly. In the H10 study, we show that 96% of the subject got titers above the 40:1 ratio, which is the FDA approvable endpoint. In the H10 study in Germany, we showed 100% of the subjects got their titers above the target we were setting. And so it's pretty remarkable to see how broad the response is of our antibodies induced by the antigen made by BMI. And so we feel pretty good about where we are now, which is why we've announced at JPMorgan this year that we really want to double down on vaccines.

There are still quite a large number of pathogens that do not have vaccines on the market. They are literally thousands, if not millions, for some of those viruses that are heard every year. And so we want to keep focusing on what we have done before, like CMV, hMPV, PIV, RSV, Zika. There's still a lot of viruses that do not have a vaccine on the market. And we think this is where we can really apply the technology in a beautiful way. And this is where I think the platform is going to really show its power. For years, we've invested in science. We have invested hundreds of millions of dollars, which is a scale that is really hard to match in this business for new technologies in science, in manufacturing. So think about the next vaccine we're going to move to development. It's going to be made with the same chemistry to make the mRNA, with the same manufacturing process in Norwood. The lipid we're going to use to make the formulation is going to be exactly the same chemical composition with the same manufacturing process as our produced products. And so the efficiency of this platform is quite remarkable. I used to work in Big Pharma and every drug, you have

to reinvent everything. Here, the ability to move extremely fast. And the other piece, I think, that's quite remarkable about mRNA for vaccines is we mimic biology. Think about what Big Pharma does, they make a recombinant, they inject you with product which just go into circulation in your blood. And you are hoping that the B-cell recognize the right configuration of a protein to make the right antibody. Think about how it works with mRNA. You inject mRNA, it gets into a cell, it gets presented as a transmembrane with exactly the same configuration as if you had a natural infection in a human cell. I don't think it can be worse than when you're getting a protein in intracellular [electrolyte] that you inject and it just goes systemic. Even the 3D configuration of a protein is not the same. So the antibody is not as strong, as potent than what we have seen using mRNA. So which is why now is the time to double down and to really use vaccine as a very strong backbone to build the company so that we can keep exploring other opportunities, and we get to market with a vaccine that we can generate cash flow and profitability so that we can be a sustainable company. That's all about it.

Matthew Thomas Holt - *JP Morgan Chase & Co, Research Division - Analyst*

Got it. Makes sense. So I guess we have a question from the audience.

Unidentified Analyst

Once the CMV vaccine comes to market, are you considering the indications both for prophylaxis as well as for prevention of reactivation?

Stéphane Bancel - *Moderna, Inc. - CEO & Director*

Sure.

Lorence H. Kim - *Moderna, Inc. - CFO & Treasurer*

So I think we haven't settled on development for further indications. Our focus for execution and for development at this point is prophylaxis for congenital CMV infection. I think we'll be examining all future paths as we progress and settle on this path to approval first.

Unidentified Analyst

So in your recruitment of women in the Phase III, they would all be seronegative?

Lorence H. Kim - *Moderna, Inc. - CFO & Treasurer*

So we will be -- for the vaccine efficacy Phase III, those will be seronegative individuals. We will be recruiting seropositive individuals because we need to establish a safety database for that package for the BLA.

Stéphane Bancel - *Moderna, Inc. - CEO & Director*

Thank you.

Matthew Thomas Holt - *JP Morgan Chase & Co, Research Division - Analyst*

So in the last 5 minutes or so, I want to just quickly talk about the rest of the pipeline. And let's start with MMA and PA. And just help us understand how you're thinking about enrollment over this year and potential time lines to data?

Stéphane Bancel - *Moderna, Inc. - CEO & Director*

Yes. So if you think about rare disease, those are always more complicated to recruit than vaccines of -- in oncology. If you think about it, in vaccines, you recruit healthy subjects. So you have clinical trial sites around the country and people do a lot of studies. We have PIs do a lot of studies, we have teams do a lot of studies. I used to it. In oncology, it's the same thing. You go to those big teaching hospitals where we do clinical trial for a living. Think about this, there's never been an MMA clinical trial run before. So we really have to do a big heavy lifting to help to understand the community, to help to -- the PIs to understand our technology. And so it's just much more like a process that is much more complicated because it's the first time for everybody involved. You cannot go hire somebody who has run an MMA clinical trial. There's never been an MMA clinical trial run. So whoever you put on the team doesn't know the disease by design. And so you have all those constituents that have to learn everything and they learn about each other build trust also. So it's just slowlier (sic) [slower] and we've learned a lot on the way. So I think there's a lot of lesson we can use for the other programs. But that's a bit where we are today. So -- but the teams are working really hard to get the first MMA patients. We're finishing activating the PA sites. And so hopefully soon, we can share some new news that we will be enrolling in -- soon after dosing around first Q.

Matthew Thomas Holt - *JP Morgan Chase & Co, Research Division - Analyst*

Okay.

Unidentified Analyst

So for the CMV vaccine, it's a multiple dose, right?

Stéphane Bancel - *Moderna, Inc. - CEO & Director*

Yes. It's -- currently, the data we shared was 2 dose of 3 dose, very similar to a vaccine -- that GARDASIL, the Merck vaccine for HPV. It was launched with 3 doses and then it evolved to a 2-dose vaccine later on after long.

Unidentified Analyst

So have you optimized the interval between doses? Would it be required for the approval?

Stéphane Bancel - *Moderna, Inc. - CEO & Director*

So what we've used is a pretty typical schedule that as you look at previous vaccine and you look at the immunoresponse that we're trying to activate is a prime. You go back to boost 2 months after and then you let the memory build the antibody with maturation and then you hit the immune system again at 6 months, kind of giving it a last boost to get the optimal profile.

Unidentified Analyst

So you haven't actually tested? But it was with -- benchmark the other vaccine product?

Stéphane Bancel - *Moderna, Inc. - CEO & Director*

So we tried the -- in preclinical models, we did a lot of testing in preclinical model. In the clinic, the only protocol we have tried is the 0, 2 months and 6 months.

Matthew Thomas Holt - *JP Morgan Chase & Co, Research Division - Analyst*

Great. And then, I guess, since you announced your IL-2 and PD-L 1 assets or developmental candidates. I'm curious if you can expand on why you think mRNA is particularly suited for the autoimmune space and what advantages you might get compared with other modalities?

Lorence H. Kim - *Moderna, Inc. - CFO & Treasurer*

So I think PD-L1 is a really ideal place to start on that topic. And so recall that we're using the same LNP delivery system for these autoimmune indications as we are for our chikungunya antibody program and our other system therapeutic programs. As a consequence, what we've learned is that we can drive expression of both secreted proteins as well as cell surface proteins as well as intracellular proteins in a variety of ways. And so with PD-L1, what we're doing is we're driving transmembrane expression of a native PD-L1. And we're going to anticipate doing that on the surface of antigen-presenting cells. And that is a unique characteristic of mRNA in order to be able to drive that cell surface expression. As a result, you'll get -- in that immunological synapse with a T-cell, you'll get this co-inhibitory signal being delivered to those T-cells, which in autoimmune disease, of course, are hyperactive. And the intent is to use that PD-L1 signal to tamp down an immune response and ideally to induce some form of remission. It's a unique set of attributes so that when an mRNA confers against this particular protein that we're expressing.

Now on the IL-2 side of the equation, what we're trying to do is we're creating a secreted protein. And here, we have seen some validated target biology with recombinant forms. We think that we are going to advance the ball here though, primarily by taking mRNA for the first time into a subcutaneous administration, right? We've previously done IV administration and here, we're going to see for the first time, not just protein expression, but also potentially pharmacology in the form of inducing Treg cells in a potent way and we'll be able to benchmark importantly against recombinant forms of these IL-2s. And for us, that'll be a source of a lot of really important information.

Matthew Thomas Holt - *JP Morgan Chase & Co, Research Division - Analyst*

Great. Thanks. I think we'll stop it there since we're out of time.

Stéphane Bancel - *Moderna, Inc. - CEO & Director*

Thank you very much.

Lorence H. Kim - *Moderna, Inc. - CFO & Treasurer*

Thanks.

Stéphane Bancel - *Moderna, Inc. - CEO & Director*

Good night.