Moderna Inc CMV Interim Data Conference Call

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PRESENTATION

Operator

Good morning, and welcome to the Moderna CMV 7-month Interim Data Conference Call. (Operator Instructions) Please be advised that the call is being recorded.

At this time, I'd like to turn the call over to Lavina Talukdar, Head of Investor Relations at Moderna. Please proceed.

Lavina Talukdar, Moderna, Inc. - Head of IR

Thank you, Shannon. Good morning and happy new year, everyone. At today's conference call, we will review 7-month interim data from the company's Phase I CMV vaccine program. You can access the press release issued yesterday as well as the slides that we'll be reviewing by going to the Investors section of our website.

Speaking on the call today will be Stéphane Bancel, Chief Executive Officer; and Tal Zaks, Chief Medical Officer. Also present in the room is Lorence Kim, Chief Financial Officer.

Before we begin, I would like to remind you that this conference call will include forward-looking statements. Please see Slide 2 of the accompanying presentation and our SEC filings for important factors that could cause our actual performance and results to differ materially from those expressed or implied in these forward-looking statements. We undertake no obligation to update or revise the information provided on this call as a result of new information or future results or developments.

I will now turn the call over to Stéphane.

Stéphane Bancel, Moderna, Inc. - CEO & Director

Thank you, Lavina. Good morning and happy new year, everyone. We're excited to be presenting new data from our 7-month interim analysis of our Phase I for CMV vaccine, mRNA-1647, and the announcement that we have begun our Phase II trial with the first participants dosed. This is the first-ever mRNA vaccine for infectious disease to move to a Phase II study.

I will start this call with a pipeline slide. As you see, we have evolved the slide to show now that CMV Phase III preparation has started, and we have moved down the slide the development programs that are still in preclinical. We'll be providing additional update on our pipeline at JPMorgan Healthcare Conference next week.

To help put today's data in context, Slide 4 summarizes the vaccination protocol: first vaccination or prime at month 0, second vaccination at month 2 and third vaccination at month 6. This is a common vaccination regimen, which happens to be identical to Gardasil's original dosing schedule at launch.

In September 2019, at our R&D Day, we shared the 3-month interim analysis after the second vaccination. As you recall, we were very happy with the high titers achieved in CMV seronegative study participants as well as CMV seropositives. Today, we share the 7-month interim analysis after the third vaccination. We are pleased to report neutralizing antibody titers in both seronegative and seropositive participants continued to increase from already

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unprecedented levels after the second vaccination. These results boost our confidence in the development plan for CMV vaccine. We are using the same dosing regimen, 3 vaccinations at months 0, 2 and 6 in the Phase II study, and we will use the same regimen in the Phase III.

With that, let me turn over to Tal to go over the clinical data.

Tal Zaks, Moderna, Inc. - Chief Medical Officer

Thank you, Stéphane. Let me just briefly remind everyone of the unmet need here. Cytomegalovirus or CMV is a common infection and the leading cause of birth defects in the U.S. to the point that approximately 25,000 newborns are affected annually. The burden of this disease is significant and causes a variety of neuro development disabilities, including vision and hearing loss. In fact, 10% to 30% of infants affected with severe CMV do not survive through the first year of life. Unfortunately, there are no approved vaccines against CMV.

We are energized by the data we have generated thus far with our CMV vaccine, mRNA-1647, and are eager to quickly develop it for the prevention of CMV infection. As a reminder, our CMV vaccine contains 6 mRNA sequences, 5 of which encode for the pentamer and one that encodes for gB. The pentamer is a complex antigen consisting of 5 distinct proteins that have to assemble inside the cell before they are transported to the membrane. Recall that we utilized 2 neutralization assays in our data, one assessing the ability of subject's serum to prevent CMV infection of epithelial cells and one that is using fibroblast. The pentameric complex is largely what the virus uses to enter the epithelial cells. gB, on the other hand, is a relatively simple single-protein receptor and is a port of entry for the virus into the fibroblast and, to a lesser extent, epithelial cells.

Slide 7 shows the Phase I trial design and is helpful to orient us to the new data today. As Stéphane mentioned earlier, today's data are from the second interim analysis from this Phase I. We shared the first interim data analysis at the R&D Day in September of last year, and that data was at the 3-month mark. Today, we're reporting data after the third and final vaccination for 3-dose cohorts: the 30, 90 and 100 microgram doses from this Phase I trial. These data are at the 7-month mark. We're also sharing data from the 300 microgram dose cohort, and these are the post-second vaccination or at the 3-month mark.

Let's turn to the data, starting with the seronegative participants on Slide 8. On the top part of the table, you will see the neutralizing antibody titer levels against epithelial cell infection. Remember, this is the key assay that we focus on. The bolded rows in the table are the new data from the 7-month interim analysis. And I'll focus first on the GMT or geometric mean titers after the third vaccination.

What is remarkable here is the ongoing increase in neutralizing antibody titers against epithelial cell infection across all 3 doses to 16,000, almost 64,000 and 62,000. That is the level of dilution that one achieves neutralization titers with. Recall that to give us a sense of the magnitude of these titers, we compare against a benchmark calculated from the average titer of the seropositive individuals who entered our study. Some additional seropositive participants entered the study as part of Phase C and so our new average seropositive titer is 5,917 as you can see at the top of the table. And so the last 2 rows of this table, at 3 months, our GMT was 2.6 to 5.2x that benchmark at the 90 and 180 microgram doses.

At 7 months, those titers now exceeded tenfold the seropositive baseline at the 90 and 180 microgram dose levels. Even our 30 microgram dose exceeded the seropositive baseline. The ability to exceed seropositive levels has never before been seen with other vaccines to our knowledge. So obviously, we're very pleased with these results as they speak to the ability of a third dose of our vaccine to continue to boost the levels of neutralizing titers even beyond what we had seen following the second dose.

On the right, you can see our new data at the 300 microgram dose after the second vaccination. Comparing to titer of 43,000 to the lower doses, you can observe ongoing dose dependency here, which, of course, is helpful. And lastly, at the bottom, neutralizing antibody titers against fibroblast infection were also higher after the third vaccination. Here, we also compared against a seropositive benchmark. And on the last row, you can see that our titers were 1.3 to 1.4x higher than the CMV seropositive benchmark at the 90 and 100 microgram doses. This compares well against our 3-month data where we just approached seropositive levels. These data, again, confirm that our third vaccination is providing incremental immunogenicity.

Now the next slide shows the data for seropositive participants. In bold, again, are the new data from this 7-month analysis. Recall that boosting seropositive at all was an unexpected achievement with our 3-month results. Now here, if you look at the GMT or the geometric mean titer post third vaccination, we see a continued boosting of neutralizing antibody titers against epithelial cell infection at all doses to levels of 77,000 to over 200,000. To calibrate on these levels, we measure each participant's titer against their own baseline. Remember that they entered the trial with a preexisting exposure to CMV, and so they already have antibodies. This GMR or geometric mean ratio was already beyond our expectation post second vaccination with between 10- and 19-fold increases. By the third vaccination, the GMR was now 22-fold to 40-fold above baseline levels across all doses.

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On the right side of the table, you will see the titers from the 300 microgram dose level, which continue to show dose-dependent titers rising, in this case, to over 156,000 after the third -- the second vaccination. And lastly, at the bottom of the slide, neutralizing antibody titers against fibroblast infection were boosted fourfold to 6.5-fold over baseline after the third vaccination. This compares very well against the second vaccination where the boost was 2.5 to fourfold over baseline.

Now in terms of safety and tolerability, I'll show you 2 slides of data, one that compares the adverse reactions across doses after the third vaccination and another slide showing the data after the third vaccination. On Slide 10 are the second vaccination data. The new data shown in bold are from the 300 microgram dose cohort. These data show that safety and tolerability at the 300 microgram dose level was largely comparable to that observed at the 100 microgram dose level with some dose-dependent increases in rates in local and systemic adverse reactions.

The next slide shows safety data post the third vaccination. These safety data were consistent with those reported at the 3-month interim analysis. There were no unexpected adverse events or any vaccine-related serious adverse events, and the most common local adverse reaction was injection site pain. The most common systemic adverse reactions reported were headache, fatigue, myalgia and chills.

Slide 12 is an update of a slide that we had previously shared, and it shows the new 7-month interim data against the preliminary 12-month data from a small cohort of patients that we had disclosed at R&D Day. While these are still small numbers, mRNA-1647 is clearly achieving and sustaining significant titers.

Slide 13 is a graphical representation of neutralizing antibody titers against epithelial cells for the seropositive subjects. While the data presented at R&D Day after the second vaccination, we were fairly surprised to see our vaccine boosting titers above natural infection in participants that began seropositive. This to our knowledge hasn't been seen before. And to see continued boosting after the third vaccination further validates the potency and safety profile of the vaccine, which ultimately bodes well for the seronegative population.

In summary, we're very pleased with mRNA-1647's emerging safety profile, its very strong immunogenicity at the 7-month time frame and the early evidence of neutralizing titers that remain above seropositive baseline levels out to 12 months. The ability of the third vaccination to induce ongoing increases in titers in both seronegative and seropositive participants is exciting with respect to the anticipated 3-dose regimen of the pivotal trial. And the totality of the data inclusive of the 300 microgram level supports our choice of dose levels of 50 or 100 and 150 micrograms in the Phase II.

We're eager to develop our CMV vaccine as quickly as possible given the unmet need and are happy to announce that the first participants in our Phase II dose confirmation trial have been dosed. We described this study in September, and the design remains unchanged with 3 dose levels being tested in 252 healthy adult volunteers, both seronegative and seropositive. The first interim analysis from the Phase II trial will occur 1 month after the second vaccination, which is at the 3-month timeframe. We expect data from this first interim analysis in the second half of this year, and we intend for these data to inform the Phase III dose selection. As a reminder, the Phase II trial is being conducted with the intended Phase III and commercial formulations.

Now we're actively preparing for the Phase III, which we expect will begin sometime in 2021. As you will recall, we received preliminary FDA feedback last year which pointed to a primary endpoint of prevention of CMV infection in a population that includes women of child-bearing age. We continue to believe that this endpoint can be achieved with a trial size of less than 8,000 participants. Manufacturing of Phase III materials and other preparations such as site selection across the U.S. and Europe are underway.

With that, let me turn the call back to Stéphane.

Stéphane Bancel, Moderna, Inc. - CEO & Director

Thank you, Tal. With this exciting clinical data, let me now talk to the commercial opportunity.

After thorough analysis, we estimate that mRNA-1647 annual peak sales could be in the range from $2 billion to $5 billion. This assumes a Gardasil-like average selling price, regulatory approval around the world and labels covering 3 indications that we intend to pursue over time: first, women of childbearing age; adolescents; and eventually, toddlers. There is an opportunity to eradicate CMV, like was accomplished for rubella, given humans are the only reservoir for CMV.

This commercial peak sales estimate was validated by Merck during their June 2019 R&D Day in New York City. This copy of the slide from that day shows their estimate that the global market opportunity for CMV vaccine is greater than $3 billion per year. Assuming pricing similar to Gardasil, at commercial scale, our CMV vaccine gross margins in the U.S. market are estimated to be higher than 90%. And consequently, EBIT margins are estimated to be around 50%.

We believe our CMV vaccine now has a very high probability of success to launch for the following reasons. Prior CMV vaccine candidates, like Sanofi's vaccine, showed 50% vaccine efficacy in a Phase II study back in 2009. Their

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vaccine targeted only the gB antigen. This study was published in the New England Journal of Medicine. The scientific infectious disease community believes that targeting the pentamer in addition to gB is critical. We showed you in September the unexpected immunogenicity of our CMV vaccine after 2 vaccinations, which gives us confidence to moving ahead to a Phase II. Today, with this data post third vaccinations with even further increases in titer and therefore validation of the potential of vaccine, we believe even more in our chance for success. So we believe that we will launch our CMV vaccine.

We are already starting to prepare the Phase III, but we're also starting to recruit marketing and commercial talent to prepare prelaunch commercial activities during the Phase III. Commercial ramp in the first quarter and year after launch and peak sales are highly dependent on the quality of prelaunch activities, and we want to maximize the commercial uptake in the launch years as well as ensuring we will maximize our peak sales.

And as you know, Moderna owns the commercial rights for mRNA-1647 around the globe. We are passionate about bringing this vaccine to market in order to prevent this debilitating infection for thousands of newborns each year, and the whole team at Moderna is committed and focused on launching this vaccine. Our goal is to eradicate CMV so no more families suffer from the consequence of a CMV infection, an objective which embodies our mission.

As we shared in our shareholder letter last Monday, we believe that infectious disease vaccines will be an important backbone for growth and cash flow generation for Moderna and that our CMV vaccine would be a franchise builder. With that, I would like to thank all the study participants who helped us in this Phase I and those that are enrolling in our Phase II and all our investigators. I would like also to thank our Moderna colleagues, the quality of the science, the quality of the process development, manufacturing and quality teams, the quality of execution of the clinical teams and of course, all the colleagues that are supporting this effort. It takes a village to develop this medicine.

With that, we're happy to take your questions.

QUESTIONS AND ANSWERS

Answer – Operator: (Operator Instructions) Our first question comes from Matthew Harrison with Morgan Stanley.

Answer – Matthew Kelsey Harrison: I guess 2 for me. One, could you just comment on updated thoughts on dose now that you have some of the preliminary 300 microgram data? And then second, one of the questions I get a lot is we can see that you can raise titer levels significantly. Internally, what's your view on threshold? And I know you talked about this at the R&D Day, but any updated thoughts on what's the most important threshold, what's the most important marker from the various assays, whether it's epithelial or not, in terms of the full changes you've been able to achieve in titer levels?

Answer – Tal Zaks: Thanks, Matthew. This is Tal. Let me take those. I think the dose-selection question is a really good one and obviously one that we are continuing to look at the totality of the data. What's important here is how we end up threading the needle between showing the benefit for seronegatives and making sure that it is as safe and tolerable for the entire population. The -- I think if you look at the -- while the 300 microgram continues to boost the titers, if we use the baseline of achieving seropositives or above, then clearly the sense that somewhere between 90 and 180 is likely going to be sufficient for what we're trying to achieve here.

And so I think we're well positioned for the doses in the Phase II, and we're going to have to look at the data at the Phase II, which is why we're doing the larger Phase II dose confirmation here, not just to reaffirm the titers but to gain more confidence as to the adverse event and safety profile here before we go into a very large Phase III. So that's sort of where our thinking is on the dose. We didn't see anything at the 300 microgram that would make us want to change our mind in terms of the Phase II design.

Now in terms of what's the right threshold, I think it's a combination of 2 things. As Stéphane said, we're starting -- or in our mind, we're starting from a 50% efficacy threshold that the gB is giving us. And if you look at our titers versus historically how that gB vaccine performed, we're probably there even higher, and that was only on the fibroblast front. Now the pentameric complex is largely measured by the epithelial cell, and there, again, I think the fact that we're seeing above the baseline is very positive for us in terms of what we expect ultimately efficacy to translate to.

So I'd say it's a combination of these 2 assays. The floor, if you will, is set by getting to seropositive levels or slightly above with the fibroblast, and that's precedented on Sanofi's vaccine, and then the upside is having a pentameric complex that gives you such significant immunogenicity here in our vaccine. And these are the 2 parameters that we'll continue to monitor versus the tolerability profile as we look at the Phase II data.

Answer – Operator: Our next question comes from Ted Tenthoff with Piper Sandler.

Analyst: Edward Andrew Tenthoff, Piper Sandler & Co., Research Division - MD & Senior Research Analyst

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Question – Edward Andrew Tenthoff: Looking at the Phase III trial design, I'm impressed by the activity and want to just go back to your thinking about the size and duration of that potential Phase III, understanding that there's still more to learn this year from the Phase II study. But when could that start? And what are your current thinking on the Phase III design?

Answer – Tal Zaks: Ted, this is Tal. I'll take that. The -- I think the size, as we've discussed, is really going to be driven by our assumptions for efficacy and the incidence rate in the population that we treat. And so if one assumes an incident rate of 1.5% infection per year and one would want to see durability beyond 1 year, so let's say 2 years for the sake of discussion, then we're looking at a 3% event rate over 2 years in the population that we will monitor. And then the size of the trial is going to be a function of what you estimate the point efficacy of that trial to be and getting agreement with regulators obviously. So that kind of, if you will, gives you the bounding factors of how we think about this. My inherent assumption is that this vaccine will be somewhere between 70% and 95% effective. And so somewhere within that range, we will use to power the study and inform that size and duration question that you asked.

In terms of study start, our goal is to start it next year. Obviously, a trial of this magnitude going after healthy participants with the goal of registration would need some further regulatory discussion along the way to ensure we're aligned there.

Answer – Operator: Our next question comes from Salveen Richter with Goldman Sachs.

Answer – Salveen Jaswal Richter: So 3 for me. One is, when we think about the CMV study, how long would it take to enroll a 8,000-patient trial? Secondly, strategically, just given the success you've seen with the prophylactic vaccine platform, does it make sense to accelerate some of the other programs in that modality versus other modalities as you look to kind of allocate your resources? And then lastly, on the MMA program, I'm going to use this as an opportunity to ask about that. But could -- do you think you'd have to lower the threshold age of enrollment there just to kind of accelerate the program?

Answer – Tal Zaks: Thank you for those questions. On how long to enroll, I think our estimate is somewhere in the 18 months' timeframe. We hope to exceed it. That's what typically it takes for large Phase III trials, just as a general statement, and we'll be looking at that.

The question on accelerating other programs, I'm actually going to let Stéphane take that. I can tell you, from my perspective as a clinical developer, I'm really super excited about the fact that both the vaccine modality seems to hit home run time after time as we look at immunogenicity and the overall safety profile. And with these data, certainly excited to think of what else could we do. But I'm also really buoyed by the data we had shown for the monoclonal antibody program and our ability to translate protein at therapeutic levels for a systemically secreted protein. And I think we're looking at those 2 areas carefully.

And finally, on the age at MMA, that -- I will say that, that is a point of continuing discussion with the agency. Obviously, the lower the age, the higher unmet need there. And I think if we were able to go to a lower age group, we should be able to recruit better. We remain committed to that program. And I hope to be able to advance that as soon as possible to address the unmet need in that population.

Answer – Stéphane Bancel: Yes. Thanks, Tal. I think your question is spot on. I mean, if you step back and you think about at the company's strategy, which we've communicated years ago, is -- given the unknown, unknown on the technology, we said we're going to try this technology across many different applications. And to derisk the biology, we're going to try several vaccines. And so it kind of makes sense once we get type -- this type of clinical data to kind of harvest the platform. That's why we build the platform that we build now. So I think your question is very relevant, and I will confirm future discussions.

Answer – Operator: Our next question comes from Cory Kasimov with JPMorgan.

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

Question – Matthew Thomas Holt: This is Matthew on for Cory. I wanted to ask on the T-cell reactivity assays. Can you talk about whether you saw dose response for the gB antigen in your assay? And what needs to be done to complete development for the pentamer-based one?

Answer – Tal Zaks: Yes, this is Tal. Let me take that. The data are too preliminary for me to give you more granularity, if you will. I think the salient point for me is that we did see T-cell responses, and frankly, that wasn't really a surprise. I mean we see T-cell responses from this platform across the board, and I think the most informative program is the personalized cancer vaccine, which uses the same formulation ultimately and where the goal is solely T-cell epitopes, right? It's well known, I think, in the field that gB is likely more T-cell immunogenic than the pentamer in terms of our ability to measure it in assays. But look, I'll point you back to the fundamentals here, which is the antibody response, right, this level of increasing titers. And not only that, but over time, the sense of the decreasing

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slope and improvement in the quality of the antibodies that we think we're getting is evidence of T-cell health at the end of the day. That's how you get to boosting of antibody titers.

And so I wouldn't -- I'm -- even though I'm a cancer immunologist and spend my entire life looking at T-cells, frankly, in this one application, I'm far less interested in the T-cells than what the antibodies tell us. Because, remember, at the end of the day, we believe that conferring protection against infection here, especially in the context of an in-utero baby, is really dependent on the antibodies. And so we'll continue to look at that data. We'll get it to the best of our ability. But looking forward in Phase II and Phase III, our focus is really going to be on the antibody titers. It's a much clearer assay and one that we believe is much more relevant.

Answer – Operator: Our next question comes from Geoff Meacham with Bank of America.

Answer – Alec Warren Stranahan: This is Alec on for Geoff. Just a couple on safety. Are the AEs, particularly the grade 3 AEs, well-managed? And are they dose dependent in your view? What kind of safety profile would sort of make you satisfied and confident of the ultimate market adoption? And lastly, has anything been modified with the Phase II formulation to improve tolerability? Or are you mostly trying to attain this through dose modification?

Answer – Tal Zaks: Thank you for that question. Let me go through them. I'm just jotting it to myself so I don't forget any of them. In terms of dose dependency, I do think that we see, overall -- again, it's a very small study, but you do get a sense that as you go up on the dose, you see more adverse reactions and perhaps a little bit more severe. These are very small numbers. It's a Phase I dose, and it's why we're actually doing the larger Phase II dose confirmation. The grade 3s are, by and large, well managed. They happen a day or 2 after the vaccination. They go away. These are all solicited as per usual FDA CBER guidances. And so we collect diaries, and this is what you typically see in vaccines. So the type of adverse events we see are typical.

Your point about threading the needle and making sure that what we -- the dose we pick ultimately straddles both a good tolerability profile while maintaining a very strong immunogenicity is going to be a critical one ultimately, both for Phase III and for acceptability in the market, as you point out.

I will say, at the end of the day though, that for vaccines, just like for medicines, it's a question of benefit versus risk. And I think in this really high unmet need, if you think about the chance of a woman in the U.S. to give birth to an infected baby is between 1 in 50 and 1 in 150 or so, if you think of those numbers and what we're trying to prevent here and you weigh that against the tolerability profile, I think that's the choice ultimately that both the regulators and individual people will have to make, and I just hope to be able to enable that choice with a vaccine that works.

The formulation question, I think it's been optimized. It's going to be a lyophilized formulation. It's the formulation we believe is going to be the one that we can bring into the commercial space already. That really is what it's been optimized for. I don't think there's any -- I don't expect changes in the safety profile at all with that formulation. I expect us to replicate pretty much what we've seen today.

Answer – Operator: Our next question comes from Yasmeen Rahimi with Roth Capital Partners.

Analyst: Yasmeen Rahimi, Roth Capital Partners, LLC, Research Division - MD, Senior Research Analyst & Co-Head of Biotechnology Research

Question – Yasmeen Rahimi: Congratulations on the continued great work and timeliness of this data ahead of JPMorgan. We have 2 questions for you. So the first question is can you enlighten us what this grading rate is of seropositive versus seronegative? What did you observe in your Phase I study just to kind of help us guide for Phase II? And then maybe an update in terms of manufacturing. How much supply do you currently have? When would you be ready to go? I mean as you're starting Phase III in 2021, would you be ready for commercialization as well? And then I apologize, maybe one more question. How do we think about infection rates as you're enrolling in Phase III in the U.S. versus ex U.S. as you're thinking in the 285 sites?

Answer – Tal Zaks: Thank you, Yasmeen. So this is Tal. I'll take questions 1 and 3, and then I'll let Stéphane answer the question around supply. The grading system is the typical CBER grading system. Happy to share it. It's available publicly. It is what you look at. It is mostly a combination of looking for the solicited local adverse events as well as the systemic ones. There is no difference between looking at seropositives or looking at seronegatives in the sense that we are using the same grading system and it's the same scoring system overall.

What you do see in the data is that there is a somewhat higher incidence of the adverse events in seropositives, and that is even more pronounced after just the first dose. And after the second and third dose, you still get a sense of that, but it appears somewhat less so. These are very small numbers. So I think it's hard for me to comment conclusively on any of that. I look forward to having the Phase II data with larger numbers per group, where we hope to be able to characterize those trends much, much more stronger.

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In terms of infection rates against -- across the different sites, there's a difference. I don't think the difference is going to be so big between U.S. and Europe per se as a geography. The differences tend to be sort of in the micro level depending on the sites, the actual participants we get, socioeconomic status, number of previous kids in the household, et cetera, et cetera. These I'll correlate with both the screening rates of how -- what percent of the population is seronegative to begin with as well as then their risk of infection during the trial. Both of these are obviously parameters we'll be looking at. We'll have some assumptions before we start the Phase III. But as that Phase III enrolls, remember, you can monitor in a blinded fashion the ongoing rates of infection and make sure that, if you're undershooting or overshooting, you can course correct in terms of the operational complexities of the trial. So we'll be looking at all of that to inform making sure that we run the most efficient trial that we can.

And let me give it over to Stéphane for the question on supplies.

Answer – Stéphane Bancel: Yasmeen, so on manufacturing, I think this is where having a platform like we have and having invested in Norwood is really where it's going to be a big differentiator. The way to think about it is we look first at the mRNA and the formulation and then at the vial filling. So if you think about the dose, just speak to the midpoint dose of a Phase II at 100 microgram, it is 100 microgram per human. So if you looking 1 gram, you're going to make product for a couple of thousand people, just to give you a sense of how the math works on the mRNA front and formulation.

Then of course, you have to fill the vials.

And so if you look at then the Phase III and then launch with this kind of framework, given the size of our Phase III, we're talking a few grams to make the material for the entire study when you put in stability material and everything else you need to do -- as you manufacture your products. And filling these type of volume of vials, we can do it now. Obviously not a problem. We have a filling line capacity and so on. So I think the [question] in terms of capacity is an easy answer.

In terms of readiness, that's where the platform beauty comes in place and the fact that we have been investing in technical development for a long time and that, for us, investing at risk to do scale-up work is a very smart use of our capital. Why? Because the team doesn't really care if it's for Zika or CMV or MMA or -- it's the same process. And so what we have done now for several years is really invest ahead of the curve so that CMC is not on a critical path to studies or to commercial launches. So the team has already started making material for the Phase III, having the right discussions to figure out all the crossing of the Ts, dotting of the Is here so that we do not slow down the enrollment start date or the ramp of Phase III recruitment because of CMC issues. So we feel very good about the Phase III.

So now let me talk about the launch. As we've shared in the past, Norwood has been designed to be able to launch commercial products. It is not ready today because we have to do more work in terms of validation, but this is work that is very well understood by the team. The team comes from large pharmaceutical companies, having dealt with commercial products for a long time. And so that is work that is to happen between now and launch to get ready for launch, but we feel really comfortable that we can launch out of Norwood. The plant has been designed from a utility standpoint and from a process standpoint to be able to accommodate commercial launch under 21 CFR.

The piece about launch and, of course, volume, so I go back to speaking on mRNA formulation on the one hand and the vial filing on the other hand. Again, because of a very low dose of a product, given the potency of our vaccine, you could make a lot of vials, I mean -- or material in Norwood for filling initially millions of vials. We do not have capabilities to fill millions of vials in Norwood. And so the plan that the team has and they're already working on is with contract manufacturers because vial filling is capabilities that is available readily, that is very well understood because of literally [must be billions] of vials that are filled every year around the world. And so we believe that Norwood is able to handle very, very large volume of manufacturing of mRNA and formulating that mRNA for initially millions of -- dozens of millions of vials and then we'll work with contract manufacturers for vial filling. So all in all, to answer your question, that's a bit of a long [answer], but for both Phase III and for launch, we feel confident that we're in a great place to be able to support the product.

Answer – Operator: (Operator Instructions) Our next question comes from Alan Carr with Needham & Company.

Analyst: Alan Carr, Needham & Company, LLC, Research Division - Senior Analyst

Question – Alan Carr: How far out are you going to follow these patients in the -- or volunteers in the Phase I trial? And what's your -- based on the data that you've seen so far, what's your expectation on how long these patients are going to be protected by the vaccine?

Answer – Tal Zaks: Yes. Two great questions. I think I don't want to commit on the Phase I right now because we're having active discussions on getting a subset there to look for longer duration so that we can have those data. In terms of how long do we expect the protection to last, I think it's hard today to say -- clearly beyond a year. I'm hoping for 3 years personally at a minimum to maintain those levels above baseline. But we're going to have to follow that data. And I think the more relevant piece is likely going to come only from the Phase III because, remember, we don't

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actually know what the threshold required is for protection, right? So I think the Phase III is the first place where we're going to be able to start to understand any relationship between how high an antibody titer one needs and how much are showing that you have protection against infection.

If you look -- as a way to explain that maybe one level more in depth, if you look at the graph of where the seropositives live, you'll notice that actually in the population, at least in the log scale graph, there's not that much variability in terms of antibody titers, right? It's a chronic latent infection. And so the question of how much would somebody be protected if their titers are halfway there has never been answered by nature. So we don't really know. But it's entirely conceivable that for a woman to not transmit this to a baby, you don't need that high of a titer. That's just an unknown. So we're using this as a benchmark to gain confidence that, indeed, we will prevent infection based on all the corollaries I described. But then to ask what is the level of antibodies required to maintain -- in order to maintain a continued protection, I think that becomes a very different question and one that ultimately only years down the road, as we look at the follow-up for the Phase III, we'll be able to answer.

Question – Alan Carr: I have a follow-up on the Phase III. Is it your assumption for powering that, that it's 0.65 -- based on your Slide 5 there, 0.65% of newborns infected annually. Is that your -- is that the figure you're using for powering?

Answer – Tal Zaks: No. That is a good question. That would be the figure I would have had to use had I been powering the study to look at infections in newborns. But this study is actually powered to look at infection in women of childbearing age. And so any pregnancy that we happen to catch, we'll catch and we'll obviously follow them, but the primary endpoint here will be prevention of infection of the woman of childbearing age. And then only later in the post-marketing phase do we expect to demonstrate that, that indeed translates into prevention of infection of the newborn. That's why I cited incidence of 1.5% a year or so of infection rates in these women.

Answer – Operator: And I'm currently showing no further questions at this time. I'd like to turn the call back over to Stéphane Bancel for closing remarks.

Answer – Stéphane Bancel: Thank you for joining the call and for your questions. We look forward to seeing many of you next week in San Francisco. So safe travels, everybody, and have a great day.

Answer – Operator: Ladies and gentlemen, this concludes today's conference call. Thank you for participating. You may now disconnect.

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