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EDITED TRANSCRIPT

MRNA.OQ - Moderna Announces Publication in The New England Journal of Medicine of Non-Human Primate Preclinical Viral Challenge Study of its mRNA Vaccine Against COVID-19 (mRNA-1273)

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OVERVIEW:

Co. announced that a pre-clinical study evaluating mRNA-1273, its vaccine candidate against COVID-19, was published in The New England Journal of Medicine.

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PRESENTATION

Operator

Good morning, and welcome to Moderna's 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, Investor Relations at Moderna. Please proceed.

Lavina Talukdar - Moderna, Inc. - Head of IR

Thank you, Liz. Good morning, everyone, and welcome to the Moderna's conference call to discuss the publication of our nonhuman primate data for mRNA-1273, our vaccine against the novel coronavirus. You can access the press release issued this morning as well as the slides that we'll be reviewing by going to the Investors section of our website.

On today's call are Stéphane Bancel, our Chief Executive Officer; Stephen Hoge, our President; Tal Zaks, our Chief Medical Officer; and David Meline, our Chief Financial Officer.

Before we begin, please note that this conference call will include forward-looking statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Please see Slide 2 of the accompanying presentation and our SEC filings for important risk 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 revise the information provided on this call as a result of new information or future results or development.

With that, I will now turn the call over to Stéphane.

JULY 29, 2020 / 12:00PM, MRNA.OQ - Moderna Announces Publication in The New England Journal of Medicine of Non-Human Primate Preclinical Viral Challenge Study of its mRNA Vaccine Against COVID-19 (mRNA-1273)

Stéphane Bancel - Moderna, Inc. - CEO & Director

Thank you, Lavina. Good morning or good afternoon, everyone. Thank you for joining the call. I hope you and your loved ones are in good health.

Yesterday, we announced that the New England Journal of Medicine published the results of our COVID-19 vaccine, mRNA-1273, in a nonhuman primate challenge study. Challenge studies are often conducted during the development process of vaccines in order to understand if the vaccine candidates can provide protection against the virus. I am pleased to share that mRNA-1273 showed robust neutralizing antibodies and dose-dependent T cell increases in nonhuman primate, consistent with our Phase I study published also in the New England Journal of Medicine.

Vaccination of nonhuman primates with mRNA-1273 led to protection against SARS-CoV-2 in both the lungs and the nose of the nonhuman primates in the challenge study.

To our knowledge, mRNA-1273 is the first vaccine against SARS-CoV-2 to show protection in both the lungs and nose of nonhuman primates, which may prove to reduce transmission of the virus. Additionally, there was no evidence of vaccine-associated enhanced disease.

These results provide critical information on the potential profile of a candidate vaccine and complement the robust Phase I immunogenicity and safety data published in the New England on July 14.

With that overview, let me now turn to Stephen to go through the data. Stephen?

Stephen Hoge - Moderna, Inc. - President

Thank you, Stéphane, and good morning, everyone, or good afternoon if you're in Europe.

So as Stéphane mentioned earlier, our preclinical challenge models are often done during vaccine development. And the challenge studies have 2 parts to them, I just want to take a moment to describe them for context.

So first, animals are vaccinated, and we evaluate the type of immune response that's generated, in this case, both antibody and cell-mediated responses to that vaccination. The vaccination schedule in this study in a nonhuman primate with the same prime and boost schedule given 1 month apart that have been done in our clinical studies. We then wait a month, and 1 month after that boost vaccination, roughly week 8, the animals are then challenged with a high level of the virus, in this case, SARS-CoV-2. The dose of the virus that they're challenged with in the back of their throat and their nose was selected because it produces an infection that looks very similar to an infection in humans. They're then evaluated, the animals, for protection against the infection.

So on Slide 4, just briefly summarizing the results before we get into some of the data. We looked at immunogenicity and protection. First, in immunogenicity, after 2 vaccinations, the immune response that we saw in the nonhuman primate was very consistent with the profile seen in the Phase I human study previously published in the New England Journal of Medicine. At the 10 microgram dose, the geometric mean titer, this is the pseudovirus assay as measured by its pseudovirus neutralization assay, was 103, and that's comparable in magnitude to the geometric mean titer that have been seen in a panel of convalescent sera as reported previously in our Phase I study.

At the higher dose in the nonhuman primate, which, in this case, was 100 micrograms, binding and neutralizing antibody titers increased further, and the pseudovirus neutralization geometric mean titers reached 1,862.

Vaccination also led to a significant increase in T cell responses, and as I'll talk through in a minute, those were primarily Th1 CD4 T cells, which are desirable for helping establish long-term neutralizing antibody immunity.

So the second part of the study, looking at protection, both the 10 microgram and 100 microgram dose levels, both the low and the high dose level in the primate, provided protection in the lungs against inflammation following viral challenge. Inflammation is really the correlate of pneumonia that we'd be looking for to protect against with COVID-19.

Both dose levels, 10 and 100 microgram, also provided protection against viral replication in the lungs or the ability of the SARS-CoV-2 virus to make more copies of itself in the lung. And the 100 microgram dose level protected -- provided substantial protection against viral replication in the nose, which is also very exciting.

Of note, none of the animals in the 100 microgram dose level had detectable viral replication in their nose compared to 6 out of 8 animals in the placebo group on day 2.

Moving to Slide 5 and some the data. If you look at the left-hand side of this chart, you'll see as a figure from the paper looking at neutralizing antibodies on a -- in a pseudovirus neutralization assay. This pseudovirus neutralization assay is the same that we've used to characterize our clinical data in the Phase I manuscript previously published in the New England Journal. What you're looking at the individual light-colored lines in blue and in red are individual animals following prime and boosting, and the solid lines in blue and red are the geometric mean. What you can appreciate is all animals developed some form of neutralizing titers. And if you look to the middle graph, comparing those on a more simple chart, you can see that the neutralizing titers that we achieved at the 10 microgram dose level were in line with the panel of convalescent sera that had previously been characterized in our Phase I cohort, roughly titers in the 100 range or a geometric mean log 10 of 2. The 100 microgram dose substantially exceeded that, reaching levels that were closer to a log 3 or above 1,000, as I said before.

We also characterize that immune response in a live virus neutralization assay. Now I'll caution you, this live virus neutralization assay, was different than the ones used in the Phase I study, which was a PRNT80 assay. In this case, this is a NanoLuc reporter assay, similar to the ones that others have reported. And as you can see there, we saw really strong neutralizing responses, both at the 10 and 100 microgram dose level in the nonhuman primate 4 weeks after boost, again approximately week 8.

Moving to Slide 6. mRNA-1273 also generated a robust immune response as measured by binding antibodies. And again, if you look on the left-hand side of the individual animals, you can appreciate the dose-dependent increases in priming and boosting of binding antibodies, and that, that benchmarks very comparably to that seen in convalescent sera in the chart in the middle. That panel of convalescent sera, again, includes most of the same human samples as in our Phase I study.

So how do we do the challenge? Moving to Slide 7, and this is the most exciting data we think from the manuscript. mRNA-1273 was protective in the lung and the nose in nonhuman primate, following challenge on week 8.

First, looking at the left-hand side of this chart, if you measure subgenomic RNA, and this is replicating virus, not the virus that you've installed in the back of the throat of the animal, but the virus actually replicating itself in the tissue, and that's measured by this thing called subgenomic RNA by PCR. If you measure that first in lung fluid, bronchoalveolar lavage, or BAL, fluid. What you can appreciate is that in the PBS control mock vaccinated animals, there's a very high level, 2 days after challenge of replicating virus in their lung fluid, and that does evidenced on day 2 in the gray squares. That falls a little bit, and by day 4 and by day 7 is mostly resolving, as you'd expect from the infection.

With 10 micrograms of mRNA-1273 in the blue, in the middle, we saw near complete protection in the lung. Only a single animal at day 2 had a very, very low level of detectable virus. That actually fell substantially by day 7. And at 100 micrograms, you also saw near complete protection, 7 out of 8 animals having no detectable virus, despite a very high dose challenge on day 2 and no detectable virus in any animal by day 4.

The most interesting finding perhaps was what we saw in the nose. If you look at the same measure of subgenomic RNA or replicating virus in the nose of animals, what you can see in a mock vaccinated animal or PBS is you usually see a substantial increase in the amount of virus and an increase from day 1 to day 2, as seen here, in the level of genome copies or a viral replication in the nose, and that's consistent with an establishing infection and shedding of the virus from the nose. That then resolves over to 16th week.

For mRNA-1273, at 10 micrograms, we saw a reduction, a substantial reduction in the viral load in the nose. By day 2, that was over a log reduction in terms of the number of genome copy. But importantly, at 100 micrograms, by day 2, there was complete suppression of viral replication. We believe this is the first report of a complete suppression of viral replication in the nose by day 2 in a nonhuman primate challenge model and provides great optimism to the potential for the vaccine to impact even the duration of transmission.

So we showed that there's a decrease in the viral replication, how do we do to the disease of inflammation. We move to Slide 8. mRNA-1273 did protect against inflammation in the lung of the nonhuman primate. SARS-CoV-2 infection in the control animals caused moderate-to-severe inflammation that often involved the small airways and alveolar interstitial and looked a lot like COVID-19 disease. Multiple lung cells, called pneumocytes, in the lung sections were positive for both the viral RNA, the virus that's replicating and the antigen itself for the proteins on the surface of the virus.

So how do we do compared to that benchmark of mock infected animals, the mock vaccinated animals that had moderate-to-severe inflammation? Well, animals that received the low dose, 10 micrograms, of mRNA-1273 had mild inflammation at best, and no viral RNA was detected on day 7. In fact, across 4 animals, only a single cell in a single animal was positive for viral antigen in day 8, providing direct immunohistologic evidence of decreased inflammation and control of the disease.

There was no substantial information at all observed in the lungs of nonhuman primates vaccinated with the 100 microgram dose, and neither viral antigens nor RNA were detectable at day 7 or 8 post challenge, providing complete viral control. By day 14 and 15, 2 weeks after infection, the vaccinated animal had no evidence of substantial inflammation, again, providing strong evidence of control of the disease.

Slide 9 provides another correlate that -- providing demonstration of that same effect. So if you look at the lungs of the animals that were vaccinated or mock vaccinated and evaluate the amount of cytokine or inflammatory markers that are in the secretions in their lungs as measured by bronchoalveolar lavage, you can get a sense of whether the infection is producing any inflammatory segment. Sometimes, these markers can be extremely sensitive. And as you can appreciate in panel A in the upper left-hand corner, if you look at markers of inflammation, like interferon gamma, PBS or mock vaccinated animals, the control animals, had relatively elevated levels, whereas mRNA-1273, either the 10 or 100 microgram doses did not see elevations in their interferon gamma.

If you look at panel C in the bottom of that chart, you see 3 additional inflammatory cytokine: IL-1; IL-6; and MIP-1 beta. And just focusing on the IL-6 as an example, you can appreciate if there is evidence of inflammation in the secretion in the lung of the animals vaccinated with PBS, as evidenced by that elevated IL-6 signal, but it was largely controlled to background in the 10 microgram and 100 microgram vaccinated animal.

All of this provides orthogonal confirmation of the histologic finding and the viral replication control findings, as I said before. And all of it points to both the 10 microgram and 100 microgram dose of mRNA-1273 provided protection to infection and inflammation in the lungs of these animals.

Moving to Slide 10. We did take the opportunity to characterize more deeply the type of immune response we're seeing in the nonhuman primate, and we're able to see, in a way that was very consistent with our Phase I study, a Th1-biased CD4 T cell response to those animals. So first, looking at the upper left-hand corner, there were statistically significant increases in the memory CD4 T cells, the Th1-specific cytokine memory CD4 T cells, at 10 micrograms and 100 micrograms. And that's important because these cells are critical for locking in memory in the long-term immune compartment, particularly neutralizing antibodies. In fact, we went further and characterized whether those responses had any Th2 bias to them, and that has been described in the past in other viruses as possibly relevant for an enhanced disease. Unfortunately, we did not see any Th2-bias T cell response. This is entirely consistent with the response we saw in the Phase I human study.

Characterizing that a little bit more deeply, we look at 2 markers of activation in those CD4 T cells. First is CD40 ligand and the second is a T follicular helper cell marker, called interleukin-21. Both of those are complicated mouthful, but the bottom line is those are markers that demonstrate whether or not those CD4 cells we're generating are going to be effective in locking in its long-term T cell memory, neutralizing antibodies to help protect against the virus over the long term.

I'm pleased to report that, and as you can see in these charts here, both the 10 microgram and 100 microgram dose in the nonhuman primate led to increases in both of those markers, CD40 ligand and IL-21 in the T follicular helper cell compartment, providing strong evidence that we're generating the right kind of long-term memory response and T cell helps for locking in neutralizing (inaudible).

So moving to Slide 11. A quick recap of the data generated to date before we move into questions. So first, we've shown Phase I clinical data where we have neutralizing antibody titers that were observed in 100% of evaluated participants and the live SARS-CoV-2 neutralization assay in that

study, which is a PRNT80 assay. By day 43, the geometric mean titers at the dose level we're taking into Phase III were 4.1 fold above those used in the reference convalescent sera.

Now we've added to that a nonhuman primate data set, which shows 2-dose vaccination produces rapid protection against SARS-CoV-2. The magnitude of that protection and the nature of it looks very similar to what we saw in the Phase I. And when we take those animals 1 month after their prime and boost regimen, so 8 weeks after they start the study, and we challenge them with a high dose of SARS-CoV-2, what we find is protection in the lung and the nose, and particularly prevention of immune inflammation in the lung.

We also have mouse data pre-print, which is currently under peer review -- peer review, which provides additional confirmation of potent neutralizing antibody responses against SARS-CoV-2 infection.

And so the overall mosaic of data that's starting to emerge continues to give us a high degree of confidence in the potential for mRNA-1273 to work to prevent COVID-19 disease. It also gives us increasing hope that mRNA-1273 will be able to limit some degree of transmission or prevent some aspect of the infection by decreasing the duration of shedding, as evidenced by some of these preclinical data findings presented here.

We've moved very quickly through some of this data, and we continue to build more data as we move forward. But just to recap the time line of data over the last less than 2 months or 2 months now. The first interim analysis of our Phase I was announced on May 18. We've subsequently now, in just the last 6 weeks, have produced that preclinical mouse data, the Phase I data and now this nonhuman primate challenge data. And we do believe that overall mosaic starts to build a strong case for the potential for mRNA-1273.

Now let me hand it back to Stéphane to close.

Stéphane Bancel - Moderna, Inc. - CEO & Director

Thank you, Stephen. We're excited about these results and how they built upon the data we have generated to date for mRNA-1273. As Stephen said, the mosaic of data is getting stronger.

As you know, we are pleased to have started on Monday our Phase III study. So what's ahead in terms of data? We look forward to be able to share the Phase I interim data for the 2 older age group, the age group 55 to 70 and the age group of 71 and above. We look forward to share with you the Phase II interim data and then the Phase III interim analysis. And as you know, our team is already working actively, both in regulatory clinical as well as in CMC for the BLA filing upon evidence of Phase III safety and efficacy data.

So with this, I just want to thank again our NIAID collaborators and scientists as well as our Moderna scientists for their hard work on this publication in the mRNA-1273 program.

With that, we'll be happy to take your questions now. Thank you. Operator?

QUESTIONS AND ANSWERS

Operator

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

Matthew Kelsey Harrison - Morgan Stanley, Research Division - Executive Director

I guess two for me. First, can you just talk a little bit about the subgenomic RNA and that data specifically related to the nose and your (inaudible) either your ability to protect asymptomatic individuals or stop transmission from asymptomatic individuals? And then I just have a follow-up after that.

Stephen Hoge - Moderna, Inc. - President

Thank you for the question, Matthew. You're breaking up a bit, so I'm going to restate it, make sure I understood it. It was a question about subgenomic RNA, in particular, our view on the ability to use this data to predict whether we would be able to prevent transmission in humans. Is that the question?

Matthew Kelsey Harrison - Morgan Stanley, Research Division - Executive Director

Yes. And specifically, I was wondering about the difference between asymptomatic and symptomatic individuals?

Stephen Hoge - Moderna, Inc. - President

Okay. So great questions. So first of all, I think we don't know how to correlate this to symptomatic or asymptomatic individuals. But presumably, if you're controlling viral replication, you're then controlling the potential for shedding of that virus, whether somebody is symptomatic or not. But obviously, I think we -- primates are more difficult to ask questions about symptoms than humans, and so I wouldn't try to draw too much connection there.

In terms of the ability to control shedding, I think we -- let me talk about the 100 microgram dose first. I think we are incredibly pleased by what we saw at day 2 there, which was essentially -- starts to look like sterilizing immunity in terms of the ability to prevent the virus from even getting a toehold. It's important to note that you're putting a very high dose of the virus into the nose of the animal and their throat. And so this speaks to you a really strong and robust local immune control. In fact, if you look in the supplemental figures of the paper, you'll see that there wasn't even boosting of the immune response, and this is described in the New England Journal paper. That's relevant because in order for there to be boosting, the virus has to escape and, for instance, get into other tissues. And the lack of boosting suggests that there was, in fact, very good local control of that virus. It never even got a toehold by which to establish replication and then shedding. I think that gives us reason for optimism.

Now this is a primate model, not a human model, but the fact that we were able to see -- establish that kind of biologic control locally at the 100 microgram dose, I think, provides additional hope. And as you know, in the Phase I -- Phase III study, we do have exploratory endpoints looking at the duration of PCR, in particular, which might -- or may or may not allow us to confirm that additional benefit.

Matthew Kelsey Harrison - Morgan Stanley, Research Division - Executive Director

Okay. And then just the follow-up is more of a technical question, but I just want to make sure I understand the robustness of this animal model versus what we're seeing in humans. It looks like control animals that you treated with PBS, after 7 days, their subgenomic RNA also came back to baseline. So could you just comment on robustness of the model?

Stephen Hoge - Moderna, Inc. - President

Yes. Well, so I think we feel pretty confident about this model. It's analogous to the model that everybody is using. At the end of the day, the dose that was selected of the virus was selected as described in the manuscript based on the fact that after a couple of days, the amount of viral replication you see is in line with what you see in human in terms of copies. And so we feel like that's representative in terms of replication.

Now it's true that the primates -- we're doing relatively low-end studies here. And so while there are 8 per group, and there's 24 animals overall in this study, you're probably not capturing the full spectrum of disease that you might see, both in the primate and in the human. But it is relatively reproducible from study to study.

And so I think we feel very confident about this model, as confident as you can about a preclinical model, that it is representative of the type of disease that we're going to see in humans. And therefore, it's probably the gold standard -- not exactly the gold standard, but one of the gold standard assay experiments that we would do to give us confidence preclinically that we're on the right track in terms of 1273.

There is a couple of other things that we will, of course, continue to look at and characterize, and we are also continuing to do additional work in this model to look at a range of other doses, and we'll share that data when we have it. But at this point, I think I'm as confident as I can get that we're on the right track.

Operator

Our next question comes from Salveen Richter with Goldman Sachs.

Salveen Jaswal Richter - Goldman Sachs Group, Inc., Research Division - VP

So I just wanted to get your comments as to what you're seeing now with regard to CD4 and CD8 and memory T cells with regard to establishing long-term immunity and how are you thinking about expansion versus just response? And what are you doing to measure this in the Phase II and Phase III?

Stephen Hoge - Moderna, Inc. - President

Thank you, Salveen. Thanks for the question. Good to speak to you. The T cell responses, so I think we're -- well, first of all, we're focused on -- I think when we describe T cells or when we describe neutralizing antibodies, we are describing correlates of protection. We're describing things that we think will predict protection in humans, and we're trying to describe them in preclinical model and in human. But the most important thing is that they have to correlate with protection. And so what we're doing here in models like this and like in the mouse model that was the -- in the preprint is, we are putting forward the challenge as the gold standard for what you want to measure against, what you want to benchmark against. And in this case, the things that correlated with protection were both the neutralizing antibody titers as well as the CD4 T cell responses. And that makes sense for a lot of respiratory viruses, particularly for coronaviruses. It does appear that antibody responses are important in terms of protection. In fact, most of the therapeutic interventions that people are pursuing right now are monoclonal antibodies or are hyperimmune passive transfer of antibodies essentially from people who've recovered from the virus. And so we do think those are the -- among the most powerful correlates, if you will, of protection because of that correlated mechanism of action.

Now in terms of this study, what we saw here was strong CD4 responses of the Th1 bias, as I said, which looks nearly identical in magnitude and character, at least wherever we characterize it, to what we saw in the Phase I. So I think it provides confidence that this correlate of CD4 responses that we're seeing looks a lot like what we saw in Phase I. And therefore, the probability is that this protection that we're seeing in the primate is likely also going to be essentially there in the human study.

The nature of the CD4 response, as I said, was -- looked like one that would lock in a long-term memory, in particular, the T cells with their helper cell component, which is a kind of characterization you can do in a preclinical study, but you can't quite take that much blood always in a human study, provides us a really clear evidence that we think we're getting the right kind of CD4 response that will generate that long-term memory. And obviously, there's the good news of continuing to see no evidence of Th2 or a vaccine-enhanced disease.

It is interesting that we didn't see any CD8 response here at week 8, but I would comment a couple of things about that because in relation to your question was CD8. The first is there's a lot of talk about CD8 right now, as you all know, but perhaps not enough focus on when you measure it. And I think it's implied by your question, Salveen, about expansion versus contraction. It's important, we think, when you look at the CD8 response,

which no doubt is there and generated by our platform, I would point you to our work in cancer vaccines or our prior publications in that regard. But it's important to characterize the CD8 response or any of these responses more in that long-term convalescent phase and not acutely right after vaccination. And so in this case, we're characterizing and measuring the amount of CD8 response 28 days after the boost. This is 8 weeks after they started the study, but a full month after the boost. And that matters because what you will see immediately following a boost in immunology is an expansion of that CD8 compartment for about a week and then a contraction relatively quickly, and it will return to some form of steady state. We think it's most relevant not to be measuring that expansion phase, let's say, 7 days after a boost, but really that convalescent phase out of 28 days, which is really your long-term circulating memory compartment.

And in this case, we did not detect a meaningful amount. It is low to no as described in the manuscript, but it didn't appear to have any impact on the ability of those animals to fight off that infection. In fact, in the 100 microgram dose level and the 10 microgram dose level, there was no clear impact at all. There was good virologic control locally in tissues and no pathology in the lung.

So I think the question of whether or not we had enough CD8 or the balance of CD4 to CD8 is -- I would actually sort of flip it on its head and say, this was the level of convalescent protection -- or sorry, correlates that were needed and correlated with protection. We saw protection in the animals. We saw good Th1 responses in their peripheral blood still at 8 weeks. We didn't measure detectable amount of CD8, and we saw good neutralizing antibodies. And those features now figure to us to be the correlates of protection that's most important.

Operator

Our next question comes from Michael Yee with Jefferies.

Michael Jonathan Yee - Jefferies LLC, Research Division - Equity Analyst

Two, if I may. One is maybe just make a comment on your 100 microgram dose in the human Phase III study and trying to correlate that, of course, to what was a bit different in neutralizing antibody levels at 10 and 100 here in the nonhuman primate study and trying to predict both disease symptomology, but actually preventing infection, which I think you've made a lot of comments about here. So your thoughts on trying to read toward 100 micrograms in the key secondary endpoint of preventing infection.

And then my other question is, if you just take a step back, maybe we could take a step back and think about the Phase III. Could you just maybe make a comment on, obviously, the start of enrollment recently, but visibility on how that's proceeding in terms of patient interest? And also whether there will be any OUS sites, and whether there's any implications to needing any OUS sites in the study?

Stephen Hoge - Moderna, Inc. - President

Of course. So I'll let Tal handle the second part -- the second question on Phase III in just a minute. But first, on the 100 microgram dose and how we think about that relative to human. So it's always a tricky thing to move between species, even primate species of humans to nonhumans. The reason we provide all of these measures of the immune response, characterization of immune response prior to challenge in the primate is because they allow us to triangulate around what we think that relative performance is. I think the place where you can most probably directly compare is the pseudovirus neutralization assay, where it is technically the same assay, and we're running the same convalescent sera benchmarks through that assay. And in that case, what I think you can infer is that the 100 microgram dose in humans, so our -- the Phase III dose that we carried forward, is somewhere between the 10 and 100 micrograms in terms of the type of immune response it's generating. If you look at the GMTs at, say, day 57, it's maybe 2.5x or 2.3x above where we are at the 10 microgram in the primate. Not at the same level as the 100 microgram in primate, but somewhere in the middle, maybe a half log step in between. And so I think the way I would -- and if you look at all the other correlates, they sort of directionally point in that way.

We did select these doses, the 10 and 100 microgram doses, to book end, if you will, that performance because you wanted to get a sense of what a lower immune response would do and what a higher immune response would do. And so I think we have good reason for optimism that we are at least as good as that 10 microgram and probably somewhere closer -- somewhere in between there in the 100 microgram. But beyond that,

very much directional sense. I think it's quite hard to draw conclusive evidence. And I think that's why we need to run the Phase III study and hopefully develop evidence of that protection directly in humans.

Tal, do you want to take the Phase III question?

Tal Zaks - Moderna, Inc. - Chief Medical Officer

Yes, sure. Happy to. Michael, thanks for the question. So look, the enrollment is going well, and we're day 3 into it. So obviously, too soon to provide any meaningful color. But we're on track, and there's tremendous interest out there. And our investigators are busy at the sites enrolling.

At this point, I don't expect us to have any sites outside the U.S. Unfortunately, the pandemic situation in the U.S. will likely translate into a significant number of cases. And so with that and given the time line here, I think it's very unlikely that we would end up opening sites outside of the U.S.

Operator

Our next question comes from Gena Wang with Barclays.

Huidong Wang - Barclays Bank PLC, Research Division - Research Analyst

I have two sets of questions. First is regarding the CD8. I think that's very helpful. Just wondering, BioNTech Pfizer has almost identical drug candidate now with your candidate. Firstly, do they infringe your IP regarding lung measure superiority? And second, I understand they test CD8 T cell earlier, 1 week after boost, and yours a little bit later. Other than the timing, what will be the reason that they have CD8 T cell response in that lipid nanoparticle play? How important lipid nanoparticle play a role there?

And the second question is regarding the timing for Phase III data readout. Pfizer basically said they're hoping to have a drug approval maybe by October or late September, October time frame. Since they have almost identical trial design and the same starting date versus your Phase III, will you also have the data around the same time? Or what could lead to the earlier data reports?

Stephen Hoge - Moderna, Inc. - President

Gena, thank you for the question. I'm going to take the first couple, and then I'll hand it to Tal to talk maybe about the development portion of it.

So first, on sort of the specifics of the comparison of the assay. Again, I think it's always -- you want to be careful about directly comparing between assays. But I would highlight a couple of things that are different. The first you've already hit on, which is measuring T cells 7 days after a boost, we all know, is going to have a higher level of T cells than 14 days after, which is what we've reported in our Phase I, and it's then 28 days after here. It's really not the convalescent phase. It's an expansion phase. And that matters because you're getting -- not every CD8 cell is the same. There are different compartments in an infection and in the resolution and in memory. And so you're seeing an expansion of effector cells. You may not be seeing an expansion of memory cells. It can be highly dynamic in your early stages. And so I wouldn't want to compare absolutely between the day 7 and, let's say, day 28 or even day 14.

I would also ask -- I would also caution about comparing between assays because the amount of stimulation you do actually determines to, some degree, how strong a response you see. And in some assays, folks will do a lot more stimulations so that you will increase the volume of the response we're seeing.

Generally, though, we feel like the CD8 responses that we're seeing in the Phase I study, as well as here in our preclinical work, are in line with those that we've seen before. There's clearly a CD8 component. When you measure it, it is there. And we think measuring the convalescent phase of that is probably the best way to get a sense of what the long-term memory compartment will look like, as opposed to the acute phase of that.

JULY 29, 2020 / 12:00PM, MRNA.OQ - Moderna Announces Publication in The New England Journal of Medicine of Non-Human Primate Preclinical Viral Challenge Study of its mRNA Vaccine Against COVID-19 (mRNA-1273)

I won't specifically comment on IP or infringement or anything like that. I will note that they have recently ended up with their vaccine that looks a lot like ours, and we take great confidence from that. I think it points to all of the work we did over the last 5, 10 years to build a platform and select the vaccine. And many of the choices that we made in January for mRNA-1273, we hope are now being validated.

Tal, do you want to take the Phase II decision -- or sorry, the Phase III clinical result, excuse me.

Tal Zaks - Moderna, Inc. - Chief Medical Officer

Yes. Happy to. Yes. So Gena, I think you asked a question around the time line. And my answer would be, look, I think we've been very transparent about the underlying assumptions, the statistical design of our trial and what is going to drive our ability to see data. I think, beyond that, it is likely -- it is a function of rates of infection in the vaccinated population and compared to placebo, and this is per FDA guidance. I'm aware that Pfizer has given more concrete time lines. However, you're going to have to ask them what are their design elements that would lead them to expect that.

Operator

Our next question comes from Cory Kasimov with JPMorgan.

Cory William Kasimov - JPMorgan Chase & Co, Research Division - Senior Biotechnology Analyst

I have two for you as well. First, just regarding the T cells, do you have plans to test for T cells at earlier time points, acknowledging that you think the later time points are more relevant?

And then my second question is off topic, so I apologize for that, but I was just wondering if you could comment at all, maybe Stéphane, on the media reports that started coming out last night about Moderna trying to charge \$50 to \$60 for 1273. And we've seen some companies apparently charging as little as low single digits and others around \$20 per dose. So can you just kind of talk about your strategy on this front and what you maybe believe is most appropriate?

Stephen Hoge - Moderna, Inc. - President

Cory, thank you for the question. So let me first take the T cell portion, and then I'll hand it over to Stéphane.

So first of all, we're -- we have not found evidence here in the preclinical literature that says that CD8 responses correlate with protection. In fact, we're finding evidence that, at least to the extent that you measure it in the convalescent phase, it's not correlating with protection, and that's, I think, what this New England Journal publication in the primate model shows. So I think the question maybe goes on to the other side of that, why would you start tracking that in humans? It is an operational lift to take the blood to go measure those sorts of early T cell responses early in Phase III. And again, in the absence of any preclinical evidence that it's relevant for protecting, let's say, primates in a challenge model, we don't think it's an appropriate burden to put on participants in the study. And so we aren't characterizing it further at this time. Obviously, if we'd seen a strong evidence that it was going to be necessary, we might take a different approach. But I don't see evidence right now that suggests that's worthy of the investment or the burden on people in the study.

Cory William Kasimov - JPMorgan Chase & Co, Research Division - Senior Biotechnology Analyst

Okay. Understood.

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Stephen Hoge - Moderna, Inc. - President

Stéphane, do you want to take the question on pricing?

Stéphane Bancel - Moderna, Inc. - CEO & Director

Sure. Thanks, Stephen. So we will not provide comments on price at this time because, as we've said before, we are highly aware of our obligation during the pandemic phase to be responsible in how we price mRNA-1273, so that we ensure broad access of our vaccine.

Operator

Our next question comes from Geoff Meacham with Bank of America.

Alec Warren Stranahan - BofA Merrill Lynch, Research Division - Associate

This is Alec on for Geoff. So two for me. In the Phase I study, you saw a similar Th1-biased CD4 response, which is encouraging on the safety side. But could you speak to any observation of vaccine-associated enhanced respiratory disease in any of your preclinical models or in the literature with the COVID-19 vaccine? I know this has been seen in other respiratory infections. How real of an issue do you think this could be as multiple COVID-19 vaccines advanced into late-stage study? And then I've got a follow-up.

Stephen Hoge - Moderna, Inc. - President

Yes. Well, thank you for the question. So at this point, we've -- I think we could say, in our 1273 program, we've never seen that evidence to date, certainly not in the preclinical species where you would investigate it most aggressively. I would point to multiple lines there. But essentially, as we look, even at subtherapeutic doses in some of these preclinical species, as was put out in the preprint, we do not see an expansion of immune pathology in the lung. In fact, even the low doses are providing -- and extremely low doses and subtherapeutic doses are providing protection, and that bears out here in the primate. The 10 microgram dose level decreases the disease. It doesn't provide any evidence of enhancement of disease. So I think we're, again, very -- as confident as you can be scientifically that there's not evidence of that. We will carefully monitor for it, obviously, in the Phase III and continue to monitor for it across all of our clinical development programs because we have an obligation to demonstrate that there is no harm done by the vaccine. But I think the body of evidence that's emerged over the last, let's say, 3 months, and not just ours, but I would point to the publications of others, suggests that this really isn't a specific concern in SARS-CoV-2, even if there may have been in other respiratory viruses that evidence.

Now to be fair, 6 months ago, when we started this journey together, nobody had that data. And so it was reasonable to be asking these questions, and we asked them ourselves. But I think the data that we now have in hand says it's reasonable to assume that there's not going to be a vaccine-enhanced disease.

Alec Warren Stranahan - BofA Merrill Lynch, Research Division - Associate

Great. And looking at the methods of the preclinical study, it looks like the monkeys were followed for about 5 weeks after prime boost, which is in the ballpark of the follow-up presented in the Phase I. But were any of the monkeys in the study followed past 7 days after COVID exposure or rechallenged to COVID? Just trying to get a sense of the durability of protection that you're seeing?

Stephen Hoge - Moderna, Inc. - President

So durability of protection, so we -- all animals were challenged 4 weeks after boost, and so all of the characterization of the immune response is day 57 and then they are challenged the next day. And again, we were looking to get into that convalescent phase, so get out of the week after

boost, get out of this week 2 after boost, go get down into the sort of steady state week, 4 weeks later, and then challenge the animals. We can and will evaluate longer-time horizons over time, but to be fair, I think our Phase III data may even catch that preclinical work at this point.

The animals are then challenged and then we want to do histopathology. And so some animals are taken down on day 7 and 8, a week later, and some animals are taken down on day 14, 15. And so all animals were -- exited the study by 2 weeks after challenge. And so -- and if you look at the 2 weeks post challenge, which I think is maybe the core of that question, you see the same story that you saw 1 week post challenge, which is that, essentially, the animals that have been vaccinated had more rapid resolution of their -- of inflammation or no inflammation at all.

Operator

Our next question comes from Hartaj Singh with Oppenheimer.

Hartaj Singh - *Oppenheimer & Co. Inc., Research Division - Research Analyst*

I just have a quick question on the potential for the BLA filing going forward. It seems like this is preclinical data with the nonhuman primates that could actually be part of the BLA filing. And you've also got a CMC section that I'm sure you're working on. Could you just give us a quick update as to where you are with those 3 sections, the preclinical, clinical and CMC section? How you're tracking? And then how that will correlate with assuming you hit one of the interims or the final readout in the Phase III when you can turn around and go ahead and file the BLA?

Tal Zaks - *Moderna, Inc. - Chief Medical Officer*

So Hartaj, this is Tal. I think we've been working really in close collaboration with the agency on exactly this topic. I anticipate that as the various modules come together, we would be able to file it in a rolling BLA manner. We've got Fast Track Designation. And I think even beyond this -- the agency has a very immediate and direct line of sight into everything we're doing. So I can't give you more specifics, but absolutely, we're setting it up such that there is minimal, if any, delay between our ability to unveil the efficacy at the first possible instance that we will know that it is efficacious and then completing a filing.

Operator

Our next question comes from Mani Foroohar with SVB Leerink.

Mani Foroohar - *SVB Leerink LLC, Research Division - MD of Genetic Medicines & Senior Research Analyst*

I have a quick question on the Phase III and some of the practicalities of clinical trial execution. So first of all, how do you -- what should we expect you to disclose about recruitment, interim analysis, timing along the way? Sort of what's your communication plan with us and investors?

And then secondarily, as you accrue the relevant number of events, as you discussed before, should you achieve a significant results on of those primary endpoints, would you then unblind the study? With the follow-up question of, if you do unblind, how will you kind of accumulate enough safety data to meet the FDA's guidance around what would be appropriate for a broad label, what would be expected for recommendations into guidelines globally? And conversely, if you keep the study blinded, how do you even do that ethically given the risk of patients on placebo getting infected with and potentially passing away from COVID? And I'll stop there, and I have a quick follow-up question.

Tal Zaks - *Moderna, Inc. - Chief Medical Officer*

Mani, this is Tal. Let me take those. Look, I think on recruitment, I would expect us to communicate when we've completed enrollment. That's typically what we've done in the past, and I think that would be appropriate.

In terms of the interim analysis, I think when one triggers to the point that we have a material understanding of our safety and efficacy, then we would communicate that appropriately. Obviously, this would be determined, first and foremost, by the independent NIH-appointed data safety monitoring board. And then we'd have the appropriate conversations with both our partners at NIH and, ultimately, FDA to guide the communication plan here.

You asked a very good question on blinding, and the truth is, at this point, I don't know. I think that is going to be up for a discussion and debate based on the data, how much data we have, how much safety data has accumulated, whether there are subpopulations within that body of data that should or should not continue to be unblinded or what is the relevance to the trial in its totality. I -- there are going to be the obvious competing considerations here of ensuring the trial integrity and our ability to monitor safety for the longer run, as you rightly point out, versus a sense of obligation to participants on placebo in case of early overwhelming efficacy. So that is going to, I think, require dialogue based on the actual data when we have it at hand, again, between us, our partners at the NIH and, importantly, the FDA.

Mani Foroohar - SVB Leerink LLC, Research Division - MD of Genetic Medicines & Senior Research Analyst

Great. That's really helpful. And on a follow-up, looking forward, presuming that we see attractive -- very attractive benefit on the early interim, presuming an Emergency Use Authorization or similar and on the path to full approval, we've seen a number of supply agreements with companies producing your mRNA competing vaccines, other approaches with the U.S., U.K., et cetera. How would you plan to, on accounting basis, recognize revenue from supply agreements? Is your general practice when manufactured, when delivered? And how do you plan to think about that?

And secondarily, one of the comments that was made by -- on Pfizer's call is that, like many other indications, although at the other end of the spectrum than say, rare disease, you'd expect pricing for a SARS-CoV-2 vaccine candidate, once approved, to be inversely related to volume. In other words, could we see a broad band of global pricing with government contracts for smaller volumes priced higher than government contracts for very large volumes?

David W. Meline - Moderna, Inc. - CFO & Principal Accounting Officer

Yes. This is David Meline. Maybe I can take the first one on the accounting. So we'll give an update on August 5 at our quarterly call on some of the key elements as we start to anticipate moving from a clinical phase of the business into one where we're generating revenue and having normal production. And what we'll do is, of course, the accounting for those elements will be following GAAP accounting rules, so we'll give you an update at that time.

Stéphane Bancel - Moderna, Inc. - CEO & Director

Yes. And it's Stéphane. As I've mentioned to Cory earlier this morning, we will not provide comments on price at this time, but to be assured we will do it at the right time. Thank you.

Operator

I'm showing no further questions in queue at this time. I'd like to turn the call back to Stéphane for closing remarks.

Stéphane Bancel - Moderna, Inc. - CEO & Director

Well, thank you, operator. Well, thank you, everybody, for joining the call. We look forward to having you next week on August 5 for our Q2 business update. Stay safe, and have a great day. Bye-bye.

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Operator

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

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