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EDITED TRANSCRIPT

MRNA.OQ - Moderna Inc COVID-19 Variants Announcement

EVENT DATE/TIME: JANUARY 25, 2021 / 9:30PM GMT

OVERVIEW:

Co. announced results from in vitro neutralization studies of sera from individuals vaccinated with Moderna COVID-19 Vaccine showing activity against emerging strains of SARS-CoV-2.

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PRESENTATION

Operator

Good afternoon, 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. - Senior VP & Head of IR

Thank you, operator. Hello, everyone, and welcome to Moderna's conference call to discuss results from in vitro studies against variants of the SARS-CoV-2 virus. You can access the press release issued today 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; Tal Zaks, our Chief Medical Officer; Stephen Hoge, our President; 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 update or revise the information provided on this call as a result of new information or future results or developments.

On Slide 3, please see the important indication and safety information for our COVID-19 vaccine, which has been authorized for emergency use in the United States and in many other countries around the world. Please review it at your own leisure.

I will now turn the call over to Stéphane.

Stéphane Bancel - Moderna, Inc. - CEO & Director

Thank you, Lavina. Good afternoon or good evening, everyone. Thank you for joining us.

There has been a lot of questions recently about the new SARS-CoV-2 strains and vaccine efficacy. For context, we have followed SARS-CoV-2 mutations since January 2020. The virus has mutated many times. It is an mRNA virus, and it will continue to mutate. And we will, obviously, continue to monitor closely mutations.

We were pleased to announce this morning and post online a blueprint of data generated by our teams in collaboration with Dr. Fauci at the NIH. The vaccination with Moderna COVID-19 vaccine produces neutralizing titers against all key emerging strength tested, including B.1.1.7, first identified in the U.K., and B.1.351, first identified in the Republic of South Africa.

No significant impact on neutralizing titers against B.1.1.7 parent relative to prior variants. A sixfold reduction in neutralizing titers was observed with the B.1.351 variants relative to prior variants. Despite this reduction, neutralizing titer levels with B.1.351 remain above levels that are expected to be protective.

Out of an abundance of caution, we also announced our clinical strategy to proactively address the pandemic as the virus continues to evolve with a new candidate, mRNA-1273.351 that Stephen will describe in a minute.

With this introduction, let me now turn to Stephen.

Stephen Hoge - Moderna, Inc. - President

Thank you, Stéphane, and thank you all for joining. What I'd like to provide a bit of an update on today that was covered in the preprint posted online, is some of our more recent data, looking at the range of new spike protein variants that have been described in the public health community globally as we continue to follow the pandemic.

This is an ongoing collaboration that we've had with the vaccines research center at NIH and other collaborators to continually look at what's happening out there as the virus starts to evolve and importantly, test the sera of people who've been vaccinated with our vaccine, mRNA-1273 and make sure that it is protective still against those variant spike proteins.

As you would see in the preprint that we posted online today and on the slide in front of you, there's a large number of variants we've been following over time. In fact, this is activity that's really been ongoing continuously since we first started developing our vaccine.

At least 5 of these variants involve multiple mutations and are highlighted on Slide 5. And against all of these, what we've done is we've tested the blood from peer of people who were in our Phase I study as well as primates across a wider range of doses to see whether or not that serum is able to neutralize these variant viruses or these variant forms of the spike protein.

Now there are large number of ongoing variants that have been described, including, as you'll see at the bottom of the slide, P.1, which is also known as the Brazilian variant, and more recently, a California variant.

Importantly, many of the mutations are going to be common between these variants over time, and I'll try and cover that a little bit over the next couple of slides before getting into the data.

So on Slide 6. What I want to highlight here are the 3 primary variants that seem to be getting a lot of attention right now. On the left is B.1.1.7. This is also known as the U.K. variant, whereas first described. In the middle, B.1.351, also known as the South African variant. And on the far right-hand side, P.1, which is sometimes called the Brazilian variant, sometimes called the Japanese variant.

In all 3 cases, what we're showing you is the spike protein that is the key protein that we make in our vaccine and that has been -- that had allowed us to show 95% efficacy or approximately 95% efficacy in protection against COVID-19 disease.

If you look across these different pictures, what you'll see is the trimer, the 3 different colored pieces, a light purple, a more tan color and a pinkish color are the 3 pieces of the trimer. And then highlighted in red are the mutations, the new variants that are starting to emerge.

Now the virus will bind onto its host, bind onto cells, using the top end, which is denoted here as the receptor binding domain, or RBD, or the end terminal domain, NTD. That's the place where the virus really interacts with its human target.

And as you can see, the U.K. strain and all 3 of these strains, in fact, include many mutations across the protein. Many of these we've actually already described and tested before. In fact, you'll note in the middle something called D614G, which is a variant of the spike protein that was described extensively this summer as it was circulating.

Over time, these strains have also developed a large number of other mutations. And as you can see, a decent number of them are now on the top of the molecule near the RBD and NTD. And these are a particular concern because when we develop antibodies that neutralize and protect against the coronavirus, we really find that the antibodies that bind at the top of the spike protein are particularly affected.

Now the good news is we get antibodies that are effective all over the spike protein, but we really want to focus on the following, Slide 7, on the receptor binding the domain at the top of that molecule.

Now if we zoom in there and look at the mutations that were on the prior slide, I want to highlight what that receptor binding domain looks like, what that part of the molecule looks like and how it might affect -- how mutations there might affect how it interacts with people as it tries to infect them.

So on the left-hand side, with the U.K. strain, also known as 1.1.7, what you can see here, as denoted in yellow in the picture, is the ACE2 receptor. This is the receptor that the virus tries to bind to. And underneath it, now we're looking down on it, you can see the receptor binding domain of the spike protein in the U.K. strain.

And specifically, what we're highlighting in 501Y, the N501Y, is one amino acid change, just one of the amino acids in the protein that changed in that receptor binding domain that's been described in that 1.1.7 variant. That is the one that's on the receptor binding domain. But if you contrast that with the Brazilian strain in the middle, the 1.351, what you'll note is there have been a few more mutations. In fact, 3 versus the wild-type virus that are described in the Brazilian strain.

So in addition to the N501Y, you'll see a mutation called E484K. Now that is a second amino acid that's changed. And then a third in K417N. And what starts to happen as a virus evolves is it will acquire mutations, as you can see in that middle picture, that changed the face of how that receptor or that virus will bind with its receptor and also its appearance. And as the virus changes its stripes, as it changes its appearance, one of the effects of that can be that you could see a decrease in immunity, that's either as a result of the vaccine or a prior natural infection. And that's the thing that we most actively want to monitor for as a part of our ongoing monitoring about the efficacy of our vaccine and the evolution of this pandemic.

I will note on the right-hand side before moving to the next slide that the Brazilian strain does have some similar mutations, but in a couple of places or specifically in K417, different amino acids. In this case, K417T versus K417N. But on balance, it looks more similar to the South African strain. And we'll come back to that as we talk about why we think the South African strain is the right candidate for any booster activity.

So on the next slide, Slide 8, what I'd like to start to walk you through given that overview, is some of the data on how is our current vaccine, how effective is it at neutralizing all of these variant viruses. And the first thing I'll show on Slide 8 is just a wide range of mutants that we've looked at for which there has been no decrease in protection.

And so quickly, these assays are assays where we take the blood of somebody who's been vaccinated with our vaccine, and we determine whether or not that their blood can fully neutralize the virus when it expresses the variant spike protein. These are pseudo viral neutralization assays. So

we're not using the live virus, but we're using a virus that's been engineered as we do in all of our other publications and clinical studies, to express the spike protein from the mutant virus.

And whether we look in panel A at the nonhuman primate serum or on panel B in our Phase I human serum, what I think you can appreciate is compared to the benchmark variant that we've been following for a while, which is D614 or D614G on the right -- left-hand side, the gray bars, we see essentially the same sorts of neutralization in terms of titers of protection. This is nearly well over 1,000, about 1,800 across all of these samples. That's good news, including the previously concerning mink cluster variant that had broken out in Europe. So initial data across all of these is very encouraging.

If I move to Slide 9. We conducted a similar analysis on the human sera. And here, I'm going to focus just on the human sera, but the primate data showed a similar result as you saw in the preprint.

So looking at the human sera against the U.K. strain, also called B.1.1.7, what you can see is on the panel A, the level of protection, the amount of neutralizing titers that we saw in the pseudovirus neutralization assay, was as high for the 1.1.7 variant as for the control, also denoted G here.

And importantly, as we look at individual groups of mutations, including the 501Y, which I showed on that picture before as a stand-alone or any of the others, we didn't see any substantial decrease in the levels of neutralizing titers. The panel C, which shows that compared for the 8 individuals, shows that all 8 individuals had essentially similar levels of protection between the wild-type virus for which we previously developed the vaccine and the U.K. strain. This is, obviously, very good news because it suggests that the U.K. strain should be well protected or well covered by the neutralizing antibodies and responses that we've been developing with our Moderna COVID-19 vaccine.

Now as we move to Slide 10, we'll look at the Brazilian strain -- or sorry, South Africa strain I should say, also known as 351. And in this case, again, the good news is we were able to demonstrate that the blood from people who've been vaccinated with the Moderna COVID-19 vaccine was able to completely neutralize the virus.

But as you'll note on the panel on the left, in B, with the 351 strain, the level of neutralizing titers had declined about sixfold, and that's also visible on the panel in the middle with D. And that sixfold reduction happened in all of the subjects in a fairly consistent way.

Now the good news, again, is that the level of neutralizing titers that we saw in this assay suggest to us that we are still effective in being able to protect against the South African strain, the 351 strain of the virus that is now circulating. And importantly, as you can see on panel B, if we go look at just those mutations, 501Y, 484K and 417N that I had referenced before that are also related to what's happened with the Brazilian strain, again, we saw good protection in these neutralization assays.

However, it's obvious also that we saw a sixfold decrease. And so while we think we -- the vaccine is likely to continue to be effective, it just highlights the importance for continuing to be vigilant and screening against strains.

So with that, on Slide 11, we did announce today a clarification in our strategy, proactively, to continue to maintain high degrees of efficacy against SARS-CoV-2 as it continues to evolve. And the virus isn't going to standstill. And while the current strain appear to be well protected by our COVID-19 vaccine, as we continue to follow the story in the weeks, months and perhaps the years ahead, it's important that we remain vigilant and develop potential tools and countermeasures that would allow us to continue to beat back the pandemic.

And today, we announced 2 parts of that strategy. The first is testing an additional booster of Moderna's COVID-19 vaccine, mRNA-1273, to further increase titers against the emerging strains. As we've published in the past, our vaccine is very good at developing and boosting those titers, and we believe an mRNA vaccine or potentially a third dose of an mRNA vaccine is a way that if it becomes necessary in the future, we can raise those titers again. And that's particularly important as we think about, over time, waning or decreasing immunity, specifically to some of these new emerging strains if it were to pass.

And the second strategy that we announced today is advancing an emerging strain booster candidate, which we've called 1273.351 after the South African strain variant that we just described, against those variants first identified. And we would seek to determine whether this new booster candidate can be more effective at boosting the titers specifically against this new emerging strain.

We have every reason to hope and believe that 1273, the approved -- the authorized vaccine will be able to do it, but if possible to increase those titers even further with adaptation of 1273.351, the strain-specific booster, we think it's prudent to plan to do that and evaluate that today as it will give us more tools in the future.

So we're excited to announce today, as I said, the key messages are that the vaccine appears to be fully effective against all strains we've tested. But importantly, as we continue to monitor strains and where we identify the potential emergence of decreasing neutralizing protection as we did with the 351 strain from South Africa, we will develop a strategy both boosting with our 1273 Moderna COVID-19 vaccine, and moving forward, if appropriate, with strain-specific boosters.

Now with that, we'd like to open it up to the operator for any questions.

QUESTIONS AND ANSWERS

Operator

(Operator Instructions) Our first question comes from the line of Matthew Harrison from Morgan Stanley.

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

Great. Stephen, I guess I have 2 that I wanted to ask. First, can you just address, would you expect any differences if you run these experiments in the live virus assays versus the pseudovirus assay here?

And I guess second question is just around as we think about core list of protection and we think about what you guys view as the lowest level of antibodies that could be protected, what [percent do you think are the] lowest level of protection? And how are you defining that?

Stephen Hoge - *Moderna, Inc. - President*

Matt, thanks for the question. So let me try and do the first one, which is would we expect a difference in live virus assay? Not at present, but we ultimately -- the prudent thing to do is get a hold of, particularly the South Africa strain, 351, and run live virus assays and confirm that result.

I think we wouldn't expect a priority that we would see that all of a sudden as a result of the live virus that you'd see breakthrough. If anything, I would hope that the live virus might have an even more reassuring results. But we'll ultimately have to run that experiment to confirm, and those experiments are ongoing.

The second -- I would just -- a final point on that is that I would note that we have seen, in general, very good concordance across all of the live virus assays and the pseudovirus assays across all of our prior publications, including Phase I, Phase II and Phase III where we've done live and pseudovirus and neutralization assays. And so I think we have reasons for confidence there.

The second question, which is what's the level of protection? Look, I think that is the \$64,000 question. We -- I think we have confidence right now, and I would say, based on a few things. The first is, it's clear that we saw with the vaccines at 95% efficacy, a very high level of efficacy, sufficiently high that we don't know whether we would lose very much even with a titer that fell sixfold as we're seeing here in the 351 strain. And so it's quite plausible with that level of efficacy you've got a lot of room to give.

But if you ask the question from another direction, say but what can we develop as correlates prior to we have them? We don't have clinical correlates of protection, but we do have animal model surrogates. And as we develop more data over the last -- developed data over the last year, I think we've all begun to believe that some of the challenged models, including, for instance, the primate challenge models, are reasonably predictive of what we ultimately were able to demonstrate in the clinical experience.

And in that sense, the levels of titers that we have shown and published to be protective against viral challenge and primates is usually just above the level of detection in our pseudovirus neutralization assay, down slightly below 100 is sufficient to modify disease. And in fact, the levels that we published in the New England Journal in primates where we give primates a 10-microgram prime induced, the level of titers they had were even below the levels that you see against the pseudovirus assay for 351 strain. And even there, we're able to protect against disease.

And so as we build more confidence in those surrogates, and obviously, we have more work to do and confirm that against the new strains, as we build more confidence in the surrogate, I think it continues to give us reasons to believe that we're still well above what we need from a protection perspective. But ultimately, we'll have to run those challenged models and primates again with the new strain and confirm it just like we will with the live virus assay.

Operator

Our next question comes from the line of Ted Tenthoff from Piper Sandler.

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

I think it goes without saying, but it's just very reassuring all of this work that you're doing and not just hanging up gates and claiming victory on the success of 1273, but I think this is really important work.

I wanted to get a sense for this prime -- or this boosting strategy. And obviously, there's still a lot of work to do on the preclinical side and the early clinical side, but can you give us a sense from the antibody data that you have today what that schedule might look like?

Are we talking 3 months after, the same 4 weeks after? Would it be even further out? Any just early ideas of what that might look like could be really helpful.

Tal Zaks - Moderna, Inc. - Chief Medical Officer

So Ted, this is Tal. Let me try and take that one. Look, I think the levels of neutralizing antibodies that we see after the primary series, as you'll recall, are quite high. And judging by everything that Stephen has described, I expect they're going to be protective in the near term even against the South African strain.

So our thinking at this point is to start to study a third booster shot out 12 months, maybe 6 to 12 months, but not sooner as the way to demonstrate the utility of that third dose.

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

That makes a lot of sense. And obviously, you'll be gaining more information from the antibodies as you kind of collect that. So very cool.

That's helpful to start. And again, thanks for all the hard work you're doing here and keeping us safe.

Tal Zaks - Moderna, Inc. - Chief Medical Officer

Thank you, Ted.

Operator

Our next question comes from the line of Salveen Richter from Goldman Sachs.

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

With regard to the work that was done here, did you look at any higher doses, including the prior 250-microgram dose? And then, secondly, as you think about the vaccine on the forward here, how are you -- or where is your updated thinking with regard to durability of protection as well as this lever of novel strains that are coming out and how you might think about creating a new vaccine and over what period?

I just -- and I guess, if I could add another layer into that, how you would think about younger population versus older population and how this might play out?

Tal Zaks - Moderna, Inc. - Chief Medical Officer

Salveen, let me try and take those. So 250, we don't have, I don't think, data on the small cohort that got the 250, but I think the extrapolation here should be pretty clear. I should say that the data between the different assays correlate pretty well. So I think you can extrapolate there.

But in my mind, from what I see -- what I've seen to date, the most straightforward way to raise somebody's neutralizing titers is to just give another booster shot. That immunologically makes more sense to me than increase any given dose.

In terms of durability, our sense is -- the 3 months data have been out there. I think the 6 months data should be out shortly. I anticipate that the decay of antibody levels should be relatively consistent with other antibody responses consistent with having a very strong T cell response that boost immunity to begin with. So I continue to maintain that I expect the durability of the primary series to be out to a year, if not longer, based on the kinetics so far.

There is the concern that these data raise that if there's a higher sensitivity to this strain because -- or the 351 strain because, potentially, the levels required are higher because you generate relatively less neutralizing anybody to them, does that mean that protection against that specific strain may wane sooner? That could be. I think time will tell. And this will require an ongoing evaluation both of the antibodies in people, but frankly, also of the clinical reality of what happens in the real world. I.e., do people previously immunized or infected with prior variants actually get reinfected with this variant? So I think that's to be determined.

Your question about younger versus older, I think, by and large, it's true that it's often difficult to generate the titers you want in older people. That being said, I think at the 100-microgram dose, we've pretty conclusively shown that the levels we get are indistinguishable between younger adults and older adults. And so far, I don't have a significant concern for them waning sooner in the elderly, but they may, and we're going to have to follow that.

I still believe that the boosting strategy, whether it's 6, 12 months later, should be applicable to both younger and older adults. And based on the totality of the data that I've seen to date, I don't think we're about to develop 2 different dosing recommendations to younger and older people. At least that's my sentiment today, over.

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

Maybe with regard to the last question, I was just more wondering if the frequency of another vaccination would be different between adults and children versus different vaccines.

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

I don't think so. What -- this variant that we're putting into production is really meant to help us evaluate whether what we need to do is sort of plug an immunological gap in case that a different variant requires a slightly different immune response or just to boost the levels. And I think we just don't know the answer to that yet.

Once we have a better understanding of the relative immunogenicity of the different vaccines, I think we can be wiser about what the actual recommendation is. But I do think it's too early.

Operator

Our next question comes from the line of Michael Yee from Jefferies.

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

I think I have 2 important questions. One is, what you think the FDA or the agency or what your conversations are like around approvals for future variants and whether you think antibody titer levels could be at, what's the threshold level? Maybe make some comments on that because I think that's super important.

And then the second question is also related, which is now that you have all this capacity, how do you think about how fast you can actually ramp things? Maybe we could do some math around that. But I think those are 2 super important questions.

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

Thank you, Michael. This is Tal. I agree with you. They are important questions. Let me take the first one.

As it relates to FDA, let me preface by saying I don't know, and I've yet to have our first deep dive conversation with them around this. That being said, I think they're on record as stating that should we need a variant, the path to approvals there, while they need to be flushed out, they should not involve repeating efficacy trials. I think there is a regulatory paradigm that's been established around flu, albeit with many more years of experience.

But look, where we are in January -- at the end of January of 2021 in terms of understanding the relationship between neutralizing antibodies and antibodies in total and prevention of disease is not where we were in January of 2020. There's unmistakable, unimpeachable evidence for a very strong correlation, at least for 2 mRNA vaccines done independently, that high levels of neutralizing antibodies do correlate with protection.

So I think extrapolating that understanding into a new variant is a very different framework than establishing the initial proof of principle that indeed such a vaccine can prevent disease.

So more to come on that, but we have to have a chance to have that dialogue. And I expect FDA, like before, will be ahead of us and provide clear thinking and guidance as to what would be required.

I'll defer to Stéphane to talk about the manufacturing piece.

Stéphane Bancel - Moderna, Inc. - CEO & Director

Thanks, Tal. Indeed, manufacturing ramp is a very good question. I think there are 2 parameters to think about. One is that the potential strain booster, 1273.351, is a single dose, of course, as a boost versus 2 dose for the initial vaccination treatment with the current COVID-19 authorized vaccine. So that's already 2x right there.

And then the second dimension is the dose. It's unknown at this stage, and Tal and Stephen are going to run the clinical study to understand what dose is required. For example, if we were to try 3 doses, 25, 50, 100 micrograms. Those are just examples. No decision has been made yet.

But just as an example. If we ended up too long in the clinic that because people have been extremely well protected with the initial vaccination, the 25-microgram of the strain booster is enough. That right there an 8x more mass of product that you can do. Sorry, we say mass of product produced, which is a bottleneck. You can make 8x more doses.

As we've said, we are building the capacity for 2021 for \$1 billion of capacity. We currently have a plan to deliver at least \$600 million of supply. We're trying as hard as we can to get to \$1 billion of supply. And we've said that next year because of a ramp, we should be around 1.2 billion dose, assuming 100 micrograms. So you can do the math right there.

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

Yes. Perfect. Peter Marks, Director of CBER, made the comment that Tal was referring to. So that could be good news for you guys.

Stéphane Bancel - Moderna, Inc. - CEO & Director

Correct. Peter made that comment in a public setting. And the other piece on the manufacturing ramp, maybe to add, Michael, is what could be the competitive landscape? Because as we learned recombinant protein take very long to develop will mean very long to adapt to a new strain. And then I think an open question on the adenovirus in terms of as you keep injecting people the virus, do you mount an immune response to a vaccine that will actually weigh in efficacy over time?

So I think mRNA technology, modern mRNA technology is very well positioned if that were to be used again. As we've said in our introduction and our conclusion, we are taking this new product to the clinic because we want to be prudent and to be ready if it is required to boost, especially, I would say, people at risk or the elderly, but we will figure this out in the coming months, over. Thanks, Michael.

Operator

Our next question comes from the line of Gena Wang from Barclays.

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

I have 2 questions regarding animal data. You tested 30-microgram and 100-microgram in nonhuman primates that translate to roughly 100-microgram and the 300-microgram in human. So we did see the full drop was higher and higher dose of the 100 microgram. Just wondering if you can give some explanation on that.

And then second question is, have you done the third boost in nonhuman primate to see if that can generate sufficient or improved neutralizing antibody against the new strain?

Stephen Hoge - Moderna, Inc. - President

Thanks, Gena, for the question. They're very astute. I think first on the -- I'll just take the second question first very quickly. The primates are very important for us because they give us a lens into what's going to happen perhaps as we boost humans. And those experiments are -- experiments are going to be conducted very quickly in the near term. And so we haven't done that third dose yet, but we'll be looking to do that as well as testing the new 1273.351 booster.

On the question of sort of the relative immunogenicity, it's actually expected if you're going to continue to boost with a -- an antigen, for instance, if you're boosting with the wild-type virus spike protein as we were at 1273, that you -- as you get higher in doses, you'd see more and more exaggerated responses. And so higher and higher levels of neutralizing antibody titer. And in that sense, it's not surprising that at the 100-microgram level in a primate, you saw the relative difference between what you were seeing with the wild-type virus versus what you see with the, in this case, the 351 strain would start to get a little more exaggerated. That's the effect of boosting.

I think the important point on those is that as you start to get those really high exaggerated numbers in the primate as we'd expect to see in humans, the relative importance of that comparison probably goes down in import.

When you start talking about neutralizing titers well above 300, maybe even above 500 against even the South African strain, you're starting to get to very, very high levels of neutralizing titers, and it's fine distinctions that you're chasing between them. So I wouldn't overinterpret the difference as you were pointing to it on the 100-microgram versus the 30-microgram in the primate in the paper. I'd really kind of pull back and say, the good news is, first, even at the lower doses, we're seeing neutralization against the pseudovirus for the new spike protein.

As we boost with the 1273, we see increasing titers both for the new strains, the emerging strains, and for the original strains, and that's expected. There may be a slight decrease in the rate of increase. We might see more increases in boosting in the old strain, but that's what you'd expect immunologically.

And the last thing I'd say is that these primates, preclinical systems, as Tal referenced a moment ago, they become really good systems for us to understand how to develop strain-specific boosters and evolve and hopefully even work with regulators to get approval to update to the vaccine in the time ahead because we do think they really do start to predict, or hopefully, they start to predict our prior experiences and don't require extensive clinical studies.

So I hope I answered that question. A good catch, but nothing there that's unexpected from our side.

Operator

Our next question comes from the line of Cory Kasimov from JPMorgan.

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

Two questions for me as well. First of all, I'm just curious for the patients in the Phase III study that were vaccinated and still got COVID, have you been able to sequence their virus? And did you find any of these variants there?

And then secondly, are you interested in potentially multiplexing variants? Or do you have any preclinical work that suggest that might be effective in the future if it becomes necessary?

Tal Zaks - Moderna, Inc. - Chief Medical Officer

So Cory, let me take those. Thanks for the questions. In Phase III, we don't know yet. So that work is ongoing, but I still don't have any news to share on the sequence of the breakthrough infections.

In terms of multiplexing, I think we're looking at that. For me, putting this .351 is the first one. Of course, we'll do a whole bunch of preclinical evaluation to see the utility of multiplexing versus more simply just a heterologous prime boost to, over time, close any immunological gaps that a monomeric vaccine may engender. So these are good questions, but they will require more data that we don't yet have.

Operator

Our next question comes from the line of Geoff Meacham from Bank of America.

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

This is Alec, on for Geoff. When you're thinking about the boosting study, would you expect your ability to boost to be stronger in individuals receiving a non-mRNA-based vaccine first?

And what, in your mind, could limit an individual's ability to receive a booster? Would this be maybe hypersensitivity or vaccine neutralizing antibodies? And then when you look at the structure of the spike protein, are there any other regions? I know you mentioned E484K, but any other regions where mutations that we maybe haven't seen yet could uniquely detract from the efficacy of 1273? Or do you think it's really more of a cumulative effect of maybe not 10, but maybe 15 or 20 mutations across the spike protein?

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

So let me take -- Alec, thanks for the question. Let me take the first one. I'll let Stephen comment on the structural one.

The -- I don't see necessarily a difference in the ability to boost whether somebody got a primary series of an adenovector or recombinant protein for that matter or an mRNA. I think whatever specific immunity you have, which is encompassed in memory B cells, et cetera, that's the basis upon which you're boosting. I think we do have data from our CMV vaccine showing that when you come in with a third dose, you get a further very nice increase in titers.

And since the immune system can't see the LNP specifically, our vaccine platform has the inherent advantage of -- that it should be able to boost irrespective of how you have become immune. By the way, that should also apply to boosting people who have been infected previously with the wild-type virus, whether they were symptomatic or not from that infection.

And certainly, we know on the safety side that even if you had been infected, we had 600 of those individuals in our 3,000 Phase III trial, then there's no adverse safety. So there's no problem in giving somebody from a safety perspective another boost and -- as evidenced by the fact that we had people with high levels of antibodies because of infection, and they were fine.

Along those veins, I see no reason to have any contraindication for a boost that is different than the third dose than it would be in the second dose. The only contraindication to date that we have for boosting somebody -- giving them a second dose is if they had true anaphylaxis to the first, and those are really, really rare events.

If you look at the MMWR report just last week, it seems like our event rate is -- it's not clear that it's even above background rates of the rates you see just with flu vaccine. So I think I feel very confident on that. I'll let Stephen talk to the structural elements here.

Stephen Hoge - *Moderna, Inc. - President*

Yes. Yes. Thank you for the question. I think the short answer is, yes, it's probably a totality of many acquired mutations that are going to be required. And remind you that the difference between a vaccine, especially one with a full spike protein like ours, is that you get a really broad polyclonal response against all parts of the protein. And so that ensures that there's many different places you can develop neutralizing immunity, too.

And so that's been our experience and that's the advantage of a polling spike protein. And what that means is that single mutations or maybe small handfuls are unlikely to completely abate. And I think even to this point now where we're looking at the 351 strain and seeing a large number of mutations present, we're still seeing that we have good neutralizing activity, at least in these in vitro assays. And so that's encouraging.

But it's definitely true that in a few mutations that you pointed to do start to create specific concern because they seem to be individually driving some of the difference. And I think the 484K variant as well as 501Y and 417 are things that we're all going to be watching as a public health community very closely as those play out across the strain.

So I think the good news is we're still in good shape. It does require a lot of mutations in order to create a gap. And as of right now, we don't think we have a gap with the vaccines using our spike protein. Frankly, the same may be true for others. But it does point to a place, particularly as you were referencing some of those mutations that are showing from the South African strain, where you want to get ahead of it and you want to start developing countermeasures in case they're necessary in the future. Certainly, right now, it doesn't feel like they are.

Operator

Our next question comes from the line of Hartaj Singh from Oppenheimer & Co.

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

Great. I just got 2 quick questions. One is, as there's debate between extending the duration between the first and the second vaccine of the 2 mRNA vaccines that are approved, any thoughts on what this new data gives you any additional insights there or how to go about proceeding going forward in that context?

And the other is, as we see more mutants and these variants, there's another couple of adenovirus vaccines that should be getting on the market soon, AstraZeneca, Johnson & Johnson, not too -- please don't -- I don't expect you to comment on them, but could you give any insight as to how the new mutant variations could make some drug development more complicated? Will it? You don't think so? Just any thoughts there?

Tal Zaks - Moderna, Inc. - Chief Medical Officer

Hartaj, it's Tal. Let me start with the first one. Look, I think that our data are clear and unimpeachable and only obtained with a 4-week difference on trial that was 3 to 5 weeks. You want to extend it to 6, I get it.

I think if you -- the more people extend the window between the first and the second dose is the more we're operating in land of conjecture as opposed to hard data. There's good immunological arguments to be made of why boosting 2 or 3 months later immunologically still should be as robust. But there's also a concern we have personally that during the period, people are suboptimally protected.

It's totally within the jurisdiction of any given regulatory or health care framework to make that decision for their population. Our job is to generate the data, the data to date that we have point to a 4-week window between our vaccine is the one that's been studied. In the future, I think we'll look for opportunities to study and provide data for lighter windows. But by and large, I think this is a function in the immediate future because of limited supply.

You're asking me a question about do mutants make the future of development more difficult there, every other vaccine that will be out there? Actually, in a lot of a way quite the opposite because there's been a wonderful convergence of science here. I think the science for understanding that the spike protein, the antigen of interest has been so robust that it really, if you look back at 2020, if there was one unifying themes to all these vaccines, the protein that they all encode either ex vivo or in our own body, is pretty much similar, if not even identical.

So I think many of these vaccines, as it relates to the specificity of the immune response, will be very similar and in a way that makes it quite straightforward to then conduct experiments that either have to do with heterologous prime boost with a different protein or a different platform.

We've developed assays, and we'll continue to develop assays and look at specific neutralization against these different strains as you can see from -- through those treatments.

So I think in between that concordance of what the immunity we're reaching for, what these vaccine encodes on the availability of the assay as a vaccine developer, they actually make, I think, our life more straightforward.

Stephen Hoge - Moderna, Inc. - President

Yes. Maybe, Hartaj, as I -- I'll just add one thing to that, which is -- just to draw a link between the 2 comments, I think, really.

The virus is going to evolve as long as it's infecting, and the key thing we need to do is stop it from infecting. We need to break that transmission. Secondly, to stop those infections from lasting a very long time. And I think when you get to the questions of sort of the dosing regimen, where I think we have the highest degree of confidence is the -- obviously, the dose that we studied for which there's data, which shows that 2 doses, approximately 28 days apart of 100 micrograms of our vaccine, stops that disease. And we hope is ultimately, therefore, suppressing transmission and infection.

Once we start in a world where we're, say, only giving one dose and then waiting a long period of time, we start to, as Tal said, start to experiment with that and create opportunities for the virus to continue to evolve.

Now we don't know whether that's an issue or not with missing a dose, but it doesn't seem prudent right now to be providing that kind of a fertile ground for those things to happen as opposed to doing everything we can to continue to follow public health guidelines, do everything we can to vaccinate as supported by the data and ultimately try and beat this thing back for good.

Operator

At this time, I'm showing no further questions. I would like to turn the call back over to Stéphane Bancel for closing remarks.

Stéphane Bancel - Moderna, Inc. - CEO & Director

Well, thank you very much, everybody, for jumping quickly on the call. I hope those data and the answers to the questions were helpful. We wish you a nice evening. And please, everybody stay safe. Bye.

Operator

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

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