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EDITED TRANSCRIPT

MRNA.OQ - Moderna Inc to Discuss New Interim Clinical Data About mRNA Vaccine Against COVID-19 - Conference Call

EVENT DATE/TIME: AUGUST 26, 2020 / 8:30PM GMT

OVERVIEW:

Co. provided an update on Phase 1 study of mRNA-1273 vaccine.

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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. - Head of IR*

Thank you, Gigi. Hello, everyone. Hope you are all well, and thank you for joining us this afternoon or late night, depending on where you're dialing in from. On today's conference call, we will discuss our Phase I interim results from the older adult cohorts for mRNA-1273, our vaccine against COVID-19. 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.

Speaking on today's call are Stéphane Bancel, our Chief Executive Officer; Tal Zaks, our Chief Medical Officer; Juan Andres, our Chief Technical and Manufacturing Officer; and David Meline, our Chief Financial Officer.

Before we begin, note that this conference call will include forward-looking statements. Please see Slide 2 of the accompanying presentation and our SEC filings for important risk factors that can cause our 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.

With that, let me 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 on this call. This morning, Moderna had the opportunity to present at the Advisory Committee on Immunization Practices, ACIP, meeting where we shared some very exciting interim results in the older adult cohorts from our COVID-19 vaccine Phase I clinical trial. For those of you who are not familiar, the Advisory Committee on Immunization Practices, ACIP, comprises medical and public health experts who develop recommendations on the use of vaccine in the civilian population of United States. ACIP is under the umbrella of the U.S. Center for Disease Control or CDC.

I'm going to focus my comments on the 100-microgram dose as this is the dose selected for the ongoing Phase III clinical trial. At the 100-microgram dose, mRNA-1273 was generally safe and well tolerated in all age cohorts. Induced consistently high level of neutralizing antibodies titers in all participants in the 56 to 70 age cohort and the 71-and-above age cohort, the titers for which were two to threefold higher than those seen in convalescent sera. Our vaccine elicited Th1-biased CD4 T cell responses in the 56-to-70 and 71-and-above age cohorts. And importantly, the neutralizing antibody titers and T cell responses in these 2 cohorts were consistent with those reported in the younger adults age 18 to 55.

Given the COVID-19 disease burden in the elderly and the mortality rate in that older population, we believe that this new data presented today are very important. Based on the elderly data presented by other vaccines to date, we believe that mRNA-1273 could be best-in-class vaccine.

With that overview, I will now turn over to Tal.

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

Thank you, Stéphane. Let me start with a reminder on the trial design for the Phase I trial, which was led by -- being led by NIH. As with all Phase I vaccine studies, the key objectives are to assess safety, reactogenicity and immunogenicity. The study originally enrolled adult participants aged 18 to 55 across 3 dose cohorts: the 25, 100 and 250 microgram. And the interim data for those cohorts were published last month in The New England Journal of Medicine. 2 additional age cohorts aged 56 to 70 and 71 and above, started enrolling in the 25- and 100-microgram dose cohorts in April of this year, a month after the start of the trial. The data from those age cohorts are now mature and have been submitted for peer review by the study authors.

In today's presentation, I will review the data from the 100-microgram dose, the selected Phase III dose for the 2 older adult cohorts, as this is the data that we shared today at the ACIP meeting.

Starting with safety at the 100-microgram dose, mRNA-1273 was generally safe and well tolerated. There were no vaccine-related serious adverse events. And the most common solicited adverse events were headache, fatigue, myalgia, chills and injection site pain, the majority of which were mild to moderate in severity and self-limited. Local and systemic reactogenicity were more common and more frequently moderate in severity after the second dose. One severe solicited systemic adverse event occurred after the second dose, and that was fatigue in the above 71-age cohort, who received the 100-microgram dose.

The study evaluated clinical laboratory values of Grade 2 or higher, and this assessment revealed no patterns of concern. So while these numbers are still small, we do not see a difference in the safety or reactogenicity profile between younger and older adults.

Turning now to immunogenicity, and let me start with the binding antibody titers. I'm very happy to report that binding antibodies were comparable across age groups. We did not observe a loss of an immune response related to older ages as can be seen with other vaccines. All participants seroconverted after the first vaccination in all age cohorts. And after the first vaccination binding antibody titer levels exceeded the median level seen in convalescent sera, again, across all age groups.

Now on Slide 7, (technical difficulty) titers in the pseudovirus neutralization assay and you will see that each group age shows consistently high levels of binding titers that were all comparable to each other. Again, we show consistence of effect here across the different age groups. After the second vaccination, neutralizing antibody titers were detected in all participants. And at day 57, neutralizing antibody titers for both the 56 to 70 and above 71 age are above the median levels that you see in convalescent sera.

So what we see here is that mRNA-1273, to our knowledge, is unique in its ability to elicit generally the same level of neutralizing antibodies in older adults as in younger adults, levels that clearly exceed the level seen in convalescent sera. Now it may be that the levels of neutralizing antibody and the range that you see in convalescent sera could be enough to provide protection from disease. But we always believe that the higher levels that we are able to elicit with the vaccine, the higher the likelihood of protection and the longer we should expect the duration of that protection.

So for us, rather than choose a dose of 25 microgram that would have reached the level of convalescent sera, we've been very -- we have been able with our platform to safely dose at 100 microgram and consistently exceed the levels of convalescent plasma. And I think this is particularly important for those most vulnerable to disease. And as we've also heard today at one of the ACIP meeting, the age is the most important risk factor for both morbidity and mortality from COVID-19.

Finally, on T cell responses. Our vaccine is used as a Th1-biased CD4-positive T cell response in all participants. And again, we see a consistent picture across the different age groups.

So before I hand it over to Juan, let me just reiterate how pleased I am with the data. The consistency of the results on every metric, safety, tolerability and immunogenicity with both binding and neutralizing titers and the T cell response make me optimistic about the potential of this level of immunogenicity to translate into significant protection from COVID-19 disease across all age groups.

With that, let me hand it over to Juan for a manufacturing update.

Juan Andres - *Moderna, Inc. - Chief Technical Operations & Quality Officer*

Thank you, Tal. Good afternoon, everyone. On today's call, I wanted to give you all a quick manufacturing update. As you may already know, we are manufacturing commercial product with our partners, Lonza, Catalent and ROVI. The diagram on this slide shows how we organize our manufacturing supply chain geographically with our partners. We remain on track to supply 500 million to 1 billion doses annually at the Phase III selected dose of 100 micrograms. And we are already manufacturing product towards this goal today.

As we plan for commercialization of mRNA-1273, we are drawing on our mRNA platform and vaccine experience. The vaccines we have taken to date in the clinical trials were stored at minus 20 degrees Celsius. When we started with mRNA-1273 earlier this year, storage conditions were at minus 70 degrees Celsius. This is an ultra-cold storage and requires a special infrastructure and handling or frequent changes of special dry ice. Because of our experience and know-how, we were able to bring storage conditions to negative 20 degrees Celsius and point-of-care temperatures of normal refrigeration of 2 to 8 degrees Celsius.

It is important to note, minus 20 degrees Celsius is a very normal storage condition. That is the regular freezer temperature that we all use for food at home. Of course, industrial, well-monitored freezers for pharmaceuticals will be used for storage and shipment. The point here is that the infrastructure is widely available, and we do not need a special equipment to use our vaccine.

Another important point is that mRNA-1273 doesn't require any on-site dilution or special handling. That means there's lower risk of variability from vial to vial, vaccine to vaccine, just draw 0.5 ml from the vial -- from the multidose vial and inject.

Finally, the temperature conditions and no on-site dilution allow us to ship smaller quantities if needed to sites that only require dose smaller quantities, especially important at the beginning, and that allows us flexibility on shipment quantities and to reach more sites. We can ship, for instance, in standard cartons of 10 vials for 100 doses of vaccine. We will provide more details and additional updates on our R&D Day in September.

With that quick review, I will now hand it over to Stéphane to close.

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

Thank you, Juan. Let me take a minute to review the body of data we have on mRNA-1273 so far. I think with Phase I study, we have now reported neutralizing antibody titers were observed in 100% of evaluated participants across all age groups. In a pseudovirus ID50 neutralization assay, at the 100-microgram dose, mRNA-1273 induced consistently high level of neutralizing antibody titers in all participants in the young adults and older adult cohorts. In the live SARS-CoV-2 PRNT80 neutralizing assay in the younger adult court, 18 to 55 years old, the day 43 GMT titer levels at the Phase III selected dose of 100 microgram were above those seen in convalescent sera. Data from the live virus assay for the older age cohorts will be forthcoming with a peer-reviewed publication.

We have also shown that 2-dose vaccination schedule, our vaccine protection against SARS-CoV-2 infection in both the lungs and the nose of nonhuman primates, and that data was also peer reviewed and published in the New England Journal.

Our Phase III COVE study is recruiting on track to our plan. As of the close of business yesterday, Tuesday, August 25, we had enrolled 15,239 participants. We continue to believe that the COVE study should be fully enrolled in September. Our teams and the clinical sites are working with local communities to enroll a diverse population.

Turning to Slide 11. We often get the question are all mRNA medicines the same? The short answer is no. And today's data in the elderly confirm it. This data confirm what our platform is capable of delivering predictable and consistent results. We are now seeing that consistency in the safety and immunogenicity data with mRNA-1273 program across age groups 18 to 55, 56 to 70 and 71 and older. This performance of mRNA-1273 is not a surprise to us. We have invested hundreds of millions of dollars over the past 9 years in basic mRNA and formulation science as well as manufacturing process development. These have created valuable IP and important know-how.

I shift to Slide 11. Over the last few years in my introduction to our Annual Science Day in the spring, we have invested in mRNA science, chemistry, bioinformatic, [beauty or] design. We have invested in novel formulation focused on vaccine. Our team has optimized and invented new chemical matter for new lipid formulation. The lipid that is used in mRNA-1273 has been developed to formulate an mRNA made of several thousand nucleotides, not an RNAi of 20 nucleotides. Our lipid has been developed and optimized to be delivered as a intramuscular injection, not an IV injection.

As a result of this and other investment over time, the tolerability of our platform allows us to dose higher. Dose is important for a high level of neutralizing antibody in all age group. The young adults, 18 to 55; the older adults, 56 to 70; and the elderly, 71 and above.

We have invested in our manufacturing process. Our teams have invented new enzymes to improve our mRNA manufacturing process purity. Our process development teams are now at the sixth generation of formulation manufacturing process.

As Juan just shared with you, thanks to our investment in process development, we are able to store mRNA-1273 at minus 20 Celsius, not at minus 70 Celsius. Juan also shared with you that unlike other vaccine, we do not need on-site dilution.

And we are not stopping. Our teams continue to invent and push the boundaries of mRNA science every day. Today's strong data in the elderly are the proof in the pudding that our strategy to invest large amount of capital in science each year paid the big dividend.

I would like to recognize and thank the participants in our clinical trials and the clinical trial site investigators and nurses for their help and dedication. You are all true heroes in this fight against this virus. I would also like to thank the Moderna team and our collaborators at NIH and NIAID for their efforts and commitment to our mission.

With that, operator, we are ready to now take 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*

I guess 2 for me. One, can you just talk a little bit in more detail about the Phase III program and how you're dealing with the older population? Is there any stratification of that population? And I guess, what's your view on how the potentially differential clinical legacy in that population may play out in terms of the overall efficacy of the vaccine versus some of your peers?

And then I guess the second one is, maybe if you could just describe in a little bit more detail -- obviously, some of the other mRNA candidates in terms of their supply chain and cold storage look different than yours. Is this purely related to formulation? Or is there something else that allows you to have these different requirements? And then as part of that, maybe just comment if you're planning to develop a lyophilized formulation for maybe post the pandemic period?

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

So Matthew, this is Tal. Let me start with the Phase III question, then I'll hand it over to Stéphane or Juan for the formulation. The older adults are part of a strata of people who are at higher risk of disease should they get infected, and that includes for us both older individuals as well -- above 65 now as well as people with relevant comorbid conditions as defined by the CDC. So things like respiratory disease, cardiac disease, obesity, diabetes. They will be dealt as a strata. We expect that they will be somewhere between 25% to 40% of the trial. And to the degree that the higher neutralizing antibody levels will provide better protection, that is the population where you expect to see more cases as a proportion of infection relative to asymptomatic cases. And when you see cases, they are likely to be more severe.

So I think there's a reasonable chance that indeed the higher levels will translate into better performance and more protection to these vulnerable people. But of course, the truth is we don't know what level of antibody protection is enough. And I think another truism here, if you look at the long term, I think one of the benefits here will remain a little bit hidden until we have more data, which is what is the durability of protection and how does an initial higher level of response translate into a longer duration, which I think may get tricky to discern if trials read out very, very quickly.

Juan Andres - *Moderna, Inc. - Chief Technical Operations & Quality Officer*

So thank you, Matthew. I will take the second question. And we have covered a few of these things. I think it is the experience that we have had with a number of different vaccines. It is the formulation and how we have made the process improvement over a period of time. I think it is the lipid system. All of that are contributing to the better storage conditions.

And it has been an obsession for us to get into the storage, transportation and point-of-use conditions that would allow to easily dose these to millions and millions of people. And so the 2 things together are helping or creating this minus 20 and then refrigerated conditions, and of course, that last mile being able to go and dose at room temperature.

For post pandemic, we are not giving up in a previous range. You know that we have other vaccines in lyophilized forms, and that is very advanced. We have them in the clinical trials. And -- but for these type of vaccines, we are thinking to get into a prefilled syringe post pandemic. Let's see if we can do it. We are not there yet.

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*

Congrats on the data. Two quick questions for me, if I can. How did the AEs look between the elderly and the younger patients, especially on the second vaccination? And then secondly, you mentioned your current treatment group. Are you considering going into below 18 at a certain point?

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

Ted, it's Tal. Thanks for those questions. The AEs are, to me, to my eye, look really indistinguishable. I mean -- but I have to admit you're talking about 10 patients or 10 subjects or 10 participants per arm in each age strata on the older cohorts. So I think it's very hard to make definitive statements when the numbers are that small. But by and large, you get what you expect and you seem to get it to the same frequency. And it seems to also, in the older adults, happen more frequently after the second dose, which is sort of reassuring because for me, that systemic toxicity, as we've discussed in the past, those flu-like symptoms are what we expect when you're waking up somebody's immune system to recognize a specific protein.

Your question on pediatrics is a very astute one and, indeed, one that we're looking at carefully. There was an active meeting between NIH and various sponsors yesterday on this very topic. I think we believe that like the scientific community, the unmet need in pediatrics is quite significant. It has taken a little bit of backseat within the world of COVID because relative to adults, the pediatric burden of disease is less. That being said, relative to other pediatric diseases, the burden of disease is very significant. And I think that's the appropriate yardstick to measure the unmet need here. And so we absolutely need to develop this for the pediatric population as well because of the unmet need there and the disease, both the immediate and the long-term sequela, that people have started to describe.

We're working closely with FDA on this topic. Ultimately, it will be up to the agency how fast we can go into younger age strata, if you will, to demonstrate the immunogenicity. I expect from a practical standpoint that we will be doing immunobridging studies. That is we will first define the immunology that appears when one protects from disease in an older adult cohort, we will use that to justify the right dose in the younger age groups because I don't think it's going to be feasible to do efficacy trials in pediatric populations.

But with that in mind, you can anticipate that as soon as we get started with pediatric studies, they should move relatively quickly. And given the readouts are going to be immunology, their size should be reasonable, sufficient to define safety and demonstrate bridging immunology so that we are able relatively quickly to define the right dose. And anticipating a benefit to adults, we would anticipate a similar benefit to the pediatric population.

Operator

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

Andrea R. Tan - *Goldman Sachs Group, Inc., Research Division - Research Analyst*

This is Andrea on for Salveen. Maybe, Tal, first question for you, could you comment on why you think the immunogenicity profile is comparable across the age groups, particularly given that immune responses typically diminish with increasing age? And then maybe if you could comment on whether or not you think there's a specific aspect to the construct that may contribute to this?

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

Andrea, it's a great question. I think Stéphane alluded to it when he said we weren't surprised, and we expected that. I think if you look at the immune response of older people, in some aspects, they wane; in others, they remain robust. Certainly, if you look vaccinated, there are vaccines that continue to be very potent in the adult population.

So I don't think it -- let me rephrase it (technical difficulty) is a must that vaccines lose potency. I've never believed that in older individuals. I think it deals with a more nuanced understanding of the immune system and what your vaccine is achieving. And I believe that sort of the totality of the investment and inventions that we've brought to bear, and it has to do with the mRNA and has to do with the process and has to do with the chemistry and it has to do the L&P and it has to do the way everything is put together. But the proof is in the pudding here and that -- and I think what's important is that it solidifies our optimism that we should be able to prevent disease across all age groups with this vaccine.

Andrea R. Tan - *Goldman Sachs Group, Inc., Research Division - Research Analyst*

Great. And then maybe just can you remind us on the time lines for the final efficacy data?

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

Yes. That depends on what the final efficacy will be, which depend on how efficacious the vaccine is. So as a reminder, the primary analysis here was always meant to occur at 150-some cases, but that's based on the original assumption of what the point estimate for the vaccine is that's how you power a trial. We do have 2 earlier interim analyses, one that will be a 53 cases and the other one that will be at 106, if I remember correctly.

And so these 2 -- we may cross the boundary for efficacy of the vaccine is very efficacious already in those. And so it's a case-driven design, and it will depend on when we have enough cases and what the vaccine efficacy is so that the DSMB can look at the unblinded data and sort of call it, if you will.

We do have an intent to follow everybody out for 2 years so that we continue to collect safety information as appropriate in the trial of this size and design. But I think your question was more about the primary efficacy here.

Operator

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

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

I guess following up on the process of the Phase III, 2 questions. Your competitor has announced that they think that they could have emergency authorization filing by October. You guys have a similar design, similar enrollment numbers. Maybe you could just comment about the timing of others and whether you think those things are generally similar to your events and what you're seeing?

And then the second part of that is assuming something is positive, do you expect that everything actually would stop at interims? How do you think about getting everybody with longer-term follow-up, unblinding people and the distribution of the next steps, I guess, is really a question? How do you foresee the next few months?

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

Michael, let me take these one at a time. You're going to have to ask our competitors as to what they believe is the basis for their Emergency Use Authorization, I can't really answer that. I do think there is an expectation of an advisory committee in October that the FDA is requesting. And I suspect that the topic there will be what is the appropriate basis for an Emergency Use Authorization.

Our current understanding is what the FDA put out in guidance and has referenced repeatedly in public, which is that they expect there to be efficacy data as a basis for an Emergency Use Authorization. And they further were very clear that they expect those efficacy data will be substantial, i.e. efficacy data that would be required for a BLA, which is the way our trial is designed. And I've already mentioned what -- I expect the time line for that or the event-driven nature of that to be.

So I can tell you that my current understanding from the agency is that, that is the basis of an Emergency Use Authorization. Should that basis change, of course, we will be -- and we will continue our dialogue with the agency and make sure that we're appropriate.

Your question about unblinding is, I think, on the top of everybody's mind. I think we're going to do what's right by the participants on this trial, and we're going to have to do what's right by the public. And you're going to have here potentially to competing priorities, to put it bluntly. And it will be a conversation to be had at the time with regulatory agencies in terms of how one goes about it.

Ultimately, I think it's going to be a sponsored decision. I expect it's going to be a very tough decision, but let's cross that bridge when we get there. I think the time at which this analysis is done and the amount of safety information we will have collected until that point is also going to be an important determinant.

You asked the question -- I think your final question, Michael, was about distribution and CDC. I don't have any answers yet. I think the ACIP meeting today started to have that public dialogue. I think there's a lot of work that will need to take place to better define how that happens. And of course, we'll be working closely with CDC, DoD and others in the government branches to ensure that we're able to deploy our vaccine. I think the advantage here, as Juan clearly alluded to, is that our vaccine makes it easy to distribute, makes it easy to actually even send very small amounts of vaccine to remote locations, and the handling temperatures are one that don't need any special infrastructure.

Operator

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

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

Two questions. The first one follow Michael's question on Phase III. So for the Phase III interim readout, will that be only for the overall study groups? Or will we also get a subpopulation data? And how's the alpha allocated among different groups?

My second question is regarding the new formulation. How long will be the -- will the new formulation be stable at minus 20 degree? And also how long that will be stable at the 2 to 8 degrees?

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

So let me answer the first question, then I'll hand it over to Juan. The trial design does not apportion out such a different strata, let me be clear. It looks at the overall trial glucose 1 homogenous group for the primary end point. You will have, as one usually does, sort of subgroup analysis once you cross that threshold to look at your relative performance and do the usual sort of look to see the consistency of effect across the smaller subgroup. But there's no explicit statistical powering or alpha spending for those. Your duration of formulation, I think Juan can more accurately tell you what is the data that we have today, but of course, that data continues to evolve. Juan?

Juan Andres - *Moderna, Inc. - Chief Technical Operations & Quality Officer*

Yes. Thank you. Thank you, Gena. So we are still collecting real-time stability. But one of the things that we know is that the profile -- the stability profile follows the same shape of degradation that we have with previous vaccines that have similar formulations. And therefore, we are predicting between 6 and 12 months of stability at minus 20 degrees Celsius, definitely thinking that we will start with 6 months at least. And then we are deciding to have a point-of-use of approximately a week at refrigerated conditions.

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

Okay. And what about subpopulation data during the interim readout?

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

Yes. (inaudible) I think it will be a conversation with the agency as it relates to how it wants to see the data, how we're able to report it, whether there's a blinding, whether there's a blinding to everybody. I think there's a lot of questions that are still ahead of us and will require active discussions both with our collaborators at the NIH as well as with FDA.

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 for me as well. You've been asked a lot of questions, obviously and not surprisingly, on this Phase III trial. I guess I'm curious, how high of a hurdle do you think you've set with the 2 interim looks? I mean do you think this has been designed to potentially hit at the interim? Or is your underlying assumption this goes to the end? And then acknowledging upfront that data at this point are limited, I'm curious to understand what you've seen in terms of immunogenicity from patients that have either had COVID-19 infection at baseline or ones that have preexisting reactivegenicity at baseline.

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

Yes. So on the first question, how high a hurdle have we set, I think we can pull bets on what everybody thinks. I think people have commented that they have expectations that we could be as high as 90%. I think if we -- the truth for this vaccine is that we're at 90% efficacy, then there's a good probability that we will hit it at the first interim. Its truth is that the efficacy is 60% and the trial is designed to ensure we don't miss it at 160-or-so events and everything else is in between, right? So it's a probabilistic expectation of what the vaccine actually does. What is the sort of (inaudible) distribution of outcomes in this particular sample of 30,000 subjects and how many cases you actually get distributed that will ultimately dictate whether you cross it. So I hope that answers the question. I can't -- I don't think I can be more precise because it really is a function of where you personally peg how effective you think this vaccine is.

And I'll tell you that today, watching the data on the older adults, I am optimistic that this is going to be more than 60% of the cases. I think if you can consistently get the level of antibodies that we have above that of convalescent plasma with very nice tight clustering of participants, meaning there's not that much variability that we're seeing so far. Everybody that gets this vaccine gets a pretty good level of antibodies. I think that makes me very optimistic that we'll actually see a high true effect rate here.

What have we seen in terms of baseline, et cetera? I don't think we've done those analysis yet. I don't think we really have enough data to answer that in a meaningful way. I think that will all come out once we really have an opportunity to dig into the Phase III data in due course.

Operator

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

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

Just a quick question about the ACIP meeting, a follow-up from that. Is that -- what populations do you see being vaccinated? Assuming the Phase III is successful and you get to EUA, what population do you see being vaccinated first? Would it be the frontline workers, older folks and then immunocompromised? What percent of the population would that be?

And then secondly, would you need longer safety follow-up for older and immunocompromised patients before you can actually vaccinate them?

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

So Hartaj, thank you for that. I think your first question is one that many people wrestle with. I actually think that in the context of the pandemic, under the expectation that this will be an EUA that will be worked closely with the CDC, I think they're going to have the final say on how that distribution looks like. OWS is clearly involved in this. I think they've already publicly picked the distributor, and I think they're sort of waiting for a CDC guidance.

I can tell you that we internally have started to look at this. We've actually formed recently an ethics panel to help advise us sort of on the company position. But ultimately, I think our obligation is such that it will be up to CDC.

Now if you listen to the ACIP presentation, one thing that came out loud and clear is that the #1 risk factor for severe morbidity and severe mortality is age. And it's pretty clear that the older you get, the worse the outcomes, just on average in terms of going asymptomatic infection, the symptomatic infection to really severe disease to mortality. And that context seems the data [steer into any strata] in the elderly. This is just one bucket of 65-year olds. What we have here is really those between 56 and 70 and those that are above 71. Seeing that level immunogenicity hold with high level of neutralizing antibodies, I think, bodes well for that population getting a benefit.

And I think between their need and the potential benefits here and what I hope the efficacy data will display, I would personally expect that older adults are going to be some of the first to get vaccinated here. I think there is a sense of a moral obligation to the health care workers who are in the front lines of this pandemic. And I think you're going to see other populations who have a sense of a higher need and a higher urgency also be prioritized until we get enough vaccine to ultimately vaccinate everybody. At the end of the day, I want myself to get back to my family, and I think we're all going to be in line. Your question is who gets to be first in line. I think that's going to be an interesting public discourse.

Longer safety follow-up on immunocompromised. I'm not sure if there's a reason for your question. I don't anticipate a different level of adverse event profile in immunocompromised. I think that we've shown -- and now I speak as an oncologist, by and large, we've shown the ability to amount to antibody responses, even in people who get chemotherapy and even in people who are immunocompromised for other reasons. And in fact, we often vaccinate cancer patients very diligently during the best periods that we're able to. And so I don't think that you're going to see a different safety requirement for that population and I'm not sure why you would. But obviously, that will be a discussion we'll have with FDA when the time comes.

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

Great. And the reason I was asking was, let's say, there's an advisory committee meeting in October. You said that there's an expectation of significant efficacy for an EUA. Could there also be discussions, the advisory committee members, possibly seeing more safety data, especially in some of these subpopulations? The only reason I was speculating.

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

Yes. Thanks, Hartaj. Look, I think that the VRBPAC has been -- I mean, part of the difficulty is that we want to make sure that there's an open discourse that the public sees the same thing VRBPAC sees. So I don't think VRBPAC is going to see things that the public doesn't see in that context.

We will be accumulating safety. We started at the end of July. So I think the safety information in October is going to be significant by the numbers, but it's still going to be evolving in terms of the time and duration. I think we will get a pretty good sense for the sort of immediate reactogenicity because by day 35, you're a week out from the second dose. And so we will have a good sense of the reactogenicity. You never stop following for safety, and so that data will obviously continue to accumulate. And at some point, the agency and VRBPAC are going to have to decide when there's enough safety information to warrant the benefit that has been described. And I suspect that is going to be one of the topics on VRBPAC. It's hard for me to predict what the questions will be. But I like you, I'm very curious and look forward to that public dialogue.

Operator

Our next question comes from the line of Alan Carr from Needham & Company.

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

A couple of them. I wonder if you can give us an update on where things stand with respect to manufacturing. And I know you've guided about what you expect to be able to manufacture on an annual rate, but I'm curious if you can give us sense of where you stand now and maybe what sort of supply might be available in the fourth quarter.

And then other question, Tal, you had touched on this balance between maybe getting or hitting an interim end point and whether or not to unblind the data and stop the trial and you have to balance safety. I wonder if you can elaborate on that. Certainly, there's a -- I guess vaccines have a -- there's a special sensitivity to safety profile with vaccines. And I wonder if you can just comment some more on how you're going to balance that if you do hit an interim end point and whether you'd stop the trial earlier unblinded data?

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

So Alan, this is Stéphane. Let me take the manufacturing one. As Juan said during his remarks, we have started to make commercial products so we currently have stored finished vials that are ready to go. And the team is working really hard across the network, at our manufacturing plant in Massachusetts and Lonza to make as much product as we can. As we've said in the past, the output is improving -- increasing almost on a weekly basis based on process scale up and new lines coming on-site of new CapEx and so on. So the shift that Juan is putting in place.

As we said in the past, we're not guiding on Q4. We're guiding on a full year basis. And we'll communicate further in the months to come. I'm turning to Tal for the second one.

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

Thank you. So Alan, let me -- you asked to dive a little bit deeper into safety. So let me sort of go there, if you will. When we use the words to describe safety, we talk about safety and tolerability. And the reason we do that is these are 2 different concepts. As Wellington Sun, he was that the FDA, taught me day 1 on the job, he said, probably these are 2 different things. Tolerability is the expected adverse event profile that you see because the vaccine is having the desired effect. So when you get flu-like symptoms, we call it flu-like symptoms because that's what happen when you get the flu. You're activating your immune system. And so the fact is that a very potent vaccine. And you can see that here in the second dose more than in the first probably because you're waking up the immune system specifically.

You look at those cytokines that I show in the CD4 T cells, well, you see interferon gamma. Those are cytokines that make us feel wobbly. And so you got an evening of headache, some fatigue, maybe some low-grade fever. That's on target, you're waking up the immune system, by and large within the day or 2 that's gone, and that's your tolerability profile.

And then the question is, is that tolerability profile worth the benefit of avoiding COVID-19 disease? And I think the answer from everything we know about the disease is going to be yes. And we have a vaccine that has a tolerable profile, certainly relative to that risk at 100 microgram, I think that's pretty clear to us. Safety has to do with the unexpected rare things that are really worse and in the context of vaccinating a large healthy population, of course, there's a special lens to be had to look at safety.

Now if you step back and think about, we talk about this being a new platform, and therefore, you have to look at safety carefully. But while this is a new platform, it's not black magic. What do we have? We have a lipid nanoparticle, mRNA within it, and then it makes the protein in our body. Now the lipid nanoparticle per se, yes, we've invented a new lipid. The rest of it is sort of cholesterol and stuff that your body already has. That new lipid has a half-life of hours. So we would anticipate that any safety or any adversity that would be ascribed to the lipid nanoparticle would be something that you would see acutely, maybe that's responsible for some of the mild pain that we see. Okay.

The mRNA itself, it's like food for the cells. It is a modified mRNA, but that modification is naturally occurring in our own cells. You can find it in TRNA. So there's no safety signal that we have ever been able to ascribe to the mRNA per se back in the day when we do studies with mRNA that is not lipid-encapsulated. There's really no adverse events that you can ascribe to the mRNA that you see.

And so what's remaining is the protein that ourselves make in order to teach the immune response to see the virus. Well, it's the same protein [a writhe large] that the virus makes. It's the same protein that every other vaccine out there is trying to make. So if as a field we learn down on the road that there are very rare adverse events that have to do with that protein being recognized by the immune system, okay, then we're all try to assess the safety benefit.

But so far -- and we've now got studies with monoclonal antibodies against that protein, right, that are being given to patients that are also being given in prophylactic trials. There's no evidence to suggest that mounting an immune response against the spike protein is in any way detrimental to one's health. In fact, the entire literature suggests the opposite as far as I can tell, all the way from all the preclinical models through the clinical experiments that people are doing, whether it's convalescent plasma.

Look, we had a lot of debate on what is the benefit of convalescent plasma. Is it high? Is it moderate? Is it medium? Nobody has ever suggested that the convalescent plasma is bad or it has adverse events. We're all just arguing on how good is it actually. Well, think of that, that actually tells you that mounting an antibody response actually is not detrimental in the totality of experience that we've had to date. We're just arguing on shades of how beneficial it is.

Those are all sort of the connecting dots that lead me to believe that safety here, while it's something that obviously will be followed closely and monitored, there's no scientific expectation for anything strange or untoward to happen. Did that answer the question?

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

Yes. Yes.

Operator

Our next question comes from the line of George Farmer from BMO.

George Farmer - *BMO Capital Markets Equity Research - Analyst*

Wanted to know, Tal, if you can speak to the design of the Phase III protocol and how it treats individuals who may get COVID prior to receiving the booster? Do they continue on and get the booster even though they may have gone sick? Or are they just centered for efficacy and file for safety or maybe just treated some other way?

And then also, Juan, can you comment also on this formulation and the stability data that you've collected so far? I mean is there any hope that the current formulation could be stable at 2 to 8 degrees? Or do you think that definitively with this particular formulation minus 20 is going to be absolutely essential for long-term storage?

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

So George, let me take the first question. It's a great one in the sense that as you look going with the Phase III trial into regions that have a high transmission, I expect -- and this is contrary to, I think, what we thought several months ago, there may be cases accumulating in that period before we start counting them, which is 2 weeks post the boost. And so what happened if somebody hits the case in the first month? Well, I think they would probably not come in and get the booster shot. There's no point, right? They've already had a case.

I think the interesting question is, will that first shot already start to protect individuals? Now here's an interesting thought. In the non -- in the preclinical model, certainly in the monkey studies ongoing, a single shot was already enough at protecting from lung infection. And in fact, if you think about it, the booster shot, the fact that our vaccine can boost so effectively tells you that, that priming was super effective, right? And so what happens if somebody gets that first prime and the boost is actually not the vaccine, but it's an infection. So somebody got, as you suggested, they get the priming shot, the first shot. And then 2, 3 weeks later, somebody with COVID -- SARS-CoV-2 sneezes on them, and they get infected.

Well, that may actually boost their immune response, and now it becomes a race between generating the neutralizing antibodies, and you see what the levels are across all age groups now, and the ability of the virus to replicate in their lungs. And it's going to be an interesting race. I wouldn't bet against the vaccine having already a sense of some efficacy already at dose 1.

Now to be fair, it's only a secondary end point in the trial. The primary end point, we're counting cases only 2 weeks after the boost. Because as you launch a trial like this, you want to be absolutely sure you have given the vaccine the best chance to work before you call it. But we'll be looking as one of the important secondary end points here at all cases that start to occur from day 1. And given we're going into areas of high transmission, I'm super curious to see what that looks like in that secondary end point when you get it. Over to Juan.

Juan Andres - *Moderna, Inc. - Chief Technical Operations & Quality Officer*

George, let me take that one. So for the pandemic, we are planning to have this minus 20 degrees Celsius. And if you think about it, these are normal freezing conditions. You can -- or you have walk-in freezers, infrastructure that already exist to handle these to transport to a store. And in the 6 to 12 months, it's going to have ample time to have the vaccination.

And then if you think about normal refrigerated conditions for up to a week, even those small places that do not have any storage freezer that the majority already have, but those -- they could handle for a week at normal refrigerated conditions, which is also going to be enough time to do that.

If we were talking about deep frozen, ultra-cold type of conditions, that would be much harder because that would require a special infrastructure. And as I mentioned before, we continue working on formulations that would give us a prefilled range post pandemic. By that, it means that it would be 2 to 8 normal refrigerated conditions. And we hope to achieve it.

Operator

Our next question comes from the line of Mani Foroohar from SVB Leerink.

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

A couple of quick ones. First, a follow-up to Gena's question, I guess, the answer to it. You laid out that wanting 6 to 12 months of real-time stability data to go to regulators with or at least that's how I interpreted your answer. Are you saying you have -- do you expect to have that in -- sort of potential 4Q EUA? Or is that something that you'd expect to have in hand closer to next year at around the time of 1-year data? Exactly when will you have that data on this negative 20 Celsius, negative 4 Fahrenheit formulation in hand? And I have one more follow-up.

Juan Andres - *Moderna, Inc. - Chief Technical Operations & Quality Officer*

So we are collecting real-time stability. And so if you think about the time when we started this, it has not been a year. And we started to make quantities of the scale-up process. So we continue gathering the stability information, and we have several months already. And as I mentioned before, the pattern that we are seeing with these vaccines is very similar to the ones that we have seen in previous vaccines that we have had in the clinic -- and that is what makes us so optimistic about the 6 to 12 months .

So we will be updating these stability conditions as we generate that data, and we will be working with FDA to do that. Does that answer the question?

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

Yes. That makes sense. So do we -- would you expect to have that in hand by 4Q of this year? Or would that have to be something for a supplement sometime after the EUA? I'm just trying to get a sense of what formulation you guys would potentially launch with.

Juan Andres - *Moderna, Inc. - Chief Technical Operations & Quality Officer*

We will launch with the existing formulation that we have, and that is the one that we are expecting to have stability information, 6 to 12 months. And we will do amendments, and we will increase as we have that real-time stability. So depending on when we are going to be having the launch, the Emergency Use Authorization, we will go with the data that we have at hand at this time.

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

Great. And for my second question, I'm looking at Slide 10, where you lay out the results in older adults seen by the pseudovirus ID50. And then in a separate bullet, you lay out results in younger adult cohort and call out the gold standard, PRNT80. Given the importance of the older population data, which is upon promoted as proof in the pudding as it were, what was your rationale from moving away from the gold standard assay and not disclosing that today? And can you tell us what in the data led you not to do that?

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

Yes. So this is Tal. There's nothing in the data that led us to do that. There was -- this was just a practical choice because we needed to show -- we had 15 minutes with ACIP, and they had requested to see the data. All the assays correlated with each other. You're going to see several assays, I think, for the live virus, that will all come into publication shortly. I did not want to overstep the boundaries of the data that were presented at ACIP today.

Operator

Thank you. 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*

Thank you, operator. Well, thanks, everybody, for jumping on the call today with us. A quick reminder as a save the date that our Annual R&D Day will take place September 17 in the morning, U.S. time. We look forward to speaking to many of you in the following days. Stay safe, everybody, and have a nice evening. Bye.

Operator

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