THOMSON REUTERS STREETEVENTS

EDITED TRANSCRIPT

PFE - Pfizer Inc To Discuss Data From An Ongoing Phase 1/2 Study Of mRNA-Based Vaccine Candidate Against SARS-CoV-2 Call

EVENT DATE/TIME: JULY 01, 2020 / 6:00PM GMT

THOMSON REUTERS

CORPORATE PARTICIPANTS

Charles E. Triano *Pfizer Inc. - SVP of IR*

Kathrin U. Jansen *Pfizer Inc. - SVP & Head of Vaccine Research & Development*

Mikael Dolsten *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development and Medical*

CONFERENCE CALL PARTICIPANTS

David Reed Risinger *Morgan Stanley, Research Division - MD in Equity Research and United States Pharmaceuticals Analyst*

Geoffrey Craig Porges *SVB Leerink LLC, Research Division - Director of Therapeutics Research & Diversified Biopharma and Senior Research Analyst*

Louise Alesandra Chen *Cantor Fitzgerald & Co., Research Division - Senior Research Analyst & MD*

Navin Cyriac Jacob *UBS Investment Bank, Research Division - Equity Research Analyst of Specialty Pharmaceuticals and Large Cap Pharmaceutic*

Scott Daniel Puckhaber *BofA Merrill Lynch, Research Division - VP*

Seamus Christopher Fernandez *Guggenheim Securities, LLC, Research Division - Senior Analyst of Global Pharmaceuticals*

Terence C. Flynn *Goldman Sachs Group Inc., Research Division - MD*

Umer Raffat *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Vamil Kishore Divan *Mizuho Securities USA LLC, Research Division - MD*

PRESENTATION

Operator

Good day, everyone, and welcome to Pfizer's Analyst and Investor Call to discuss data from an ongoing Phase 1/2 study of mRNA-based vaccine candidate against SARS-CoV-2. Today's call is being recorded.

At this time, I would like to turn the call over to Mr. Chuck Triano, Senior Vice President of Investor Relations. Please go ahead, sir.

Charles E. Triano - *Pfizer Inc. - SVP of IR*

Thank you, operator. Good afternoon, everyone, and thanks for joining us today on short notice to review initial clinical data from our U.S. Phase 1/2 study for our most advanced COVID-19 vaccine candidate.

I'm joined this afternoon by Mikael Dolsten, Chief Scientific Officer and President of Pfizer Worldwide Research and Development; and Kathrin Jansen, our Senior Vice President and Head of Vaccine Research and Development.

Before we start, I want to remind everybody that we will be making forward-looking statements on today's call, and actual results may differ from those statements. The forward-looking statements speak only as of the original date of this presentation, and we undertake no obligation to update or revise any of these statements.

So for the flow of the call, Mikael and Kathrin will make opening remarks, and then we will move into a Q&A session. I'll now turn the call over to Mikael Dolsten. Mikael?

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development and Medical*

Thank you, Chuck. Good afternoon, everyone. I'm pleased to be talking to you today about Pfizer and BioNTech's early positive data from the most advanced of our 4 investigational vaccine candidates from our BNT162 mRNA-based vaccine program against SARS-CoV-2.

Before, we go into the data deeper, a brief mention that Pfizer has a rich vaccine history with 6 approved vaccines currently in over 160 countries. We have committed our experience and knowledge to the fight against COVID-19. Beyond the vaccine that we're discussing today, Pfizer has identified antiviral protease inhibitor compounds that may have potential to address COVID-19, one of which we hope to have in the clinic by August or September. We're also exploring the potential utility of certain existing Pfizer pipeline assets, none of which are currently approved for COVID-19.

So now going back to our vaccine and today's discussion. Next slide, please.

The data we are presenting today was gathered from the U.S. Phase 1/2 placebo-controlled observer-blinded clinical trial we initiated in May, and from 1 of the vaccine candidates under investigation, specifically, the nucleoside-modified messenger RNA vaccine candidate, BNT162b1 expressing the SARS-CoV-2 receptor binding domain in short, RBD, that's being evaluated in 45 subjects. It's important to note that the preliminary clinical data from this ongoing study is available on an online preprint manuscript server, medRxiv, and have been submitted for potential publication in a peer-reviewed journal.

The data we're sharing today is in collaboration with our partner, BioNTech. Pfizer and BioNTech started working together in 2018, exploring a potential influenza vaccine using BioNTech's proprietary mRNA vaccine platform. By combining BioNTech's leading mRNA platform with Pfizer's proven expertise across vaccine research and development, regulatory affairs, global manufacturing and distribution, we hope to make an important contribution to help combat this pandemic.

Slide, please. I think it's important to briefly explain why we believe that an mRNA platform could help us deliver a vaccine against COVID-19. We are guided by a sense of urgency to deliver a safe and effective vaccine as quickly as possible. Our BNT162 program is based on BioNTech's proprietary mRNA-based technology, a novel tech platform that provides efficiency and flexibility which is apparent by the pace of vaccine development and the unprecedented trial design that it supports.

The mRNA platform has several key advantages uniquely suited to this crisis. First, mRNA vaccine technology uses the cell's own machinery tamed to stimulating immune response, including the production of T cells and neutralizing antibodies. If shown to be safe and effective, mRNA vaccines have the potential to help prevent SARS-CoV-2 infection and its associated COVID-19, hence it's a fast platform. mRNA-based vaccines have shown the potential to elicit neutralizing antibody responses and T-cell responses with a T helper cell 1 phenotype. And this is a combination of immune characteristics believed to potentially maximize the probability of protection and minimize potential for disease enhancement.

Disease enhancement is a phenomenon in which a T helper cell 2 phenotype response leads to an accelerated inflammatory response to infection or the binding of antibodies to a virus enhances its entry into the host cell and sometimes also its replication, infectivity, and virulence. Hence, our platform has a favorable characteristic for protective versus any possible negative immune response.

The potential mRNA vaccine delivered RNA to the cell by protein-free lipid nanoparticles, in short, LNPs. BioNTech's mRNA-based vaccine candidates have elicited immune response in multiple preclinical and ongoing clinical studies for vaccination against cancer. BioNTech's mRNA vaccine technology is expected to enable rapid development and quick production scaling, which is critical for bringing a COVID-19 vaccine to market to address the urgent medical need brought by this pandemic.

The novel design of our vaccine trial allows Pfizer and BioNTech to evaluate 4 different potential vaccine candidates with a combination of 2 different antigens and 3 different types of mRNA, unmodified mRNA, nucleoside-modified mRNA and self-amplifying RNA. The largest spike sequence is included in 2 of the vaccine candidates as antigen and a smaller portion, the active component of spike, the optimized receptor binding domain of the spike protein is included in the other 2 candidates active for receptor binding. The RBD-based candidates contain the piece of the spike that we think is most important for eliciting neutralizing antibodies for inactivation of the virus. The flexible and rapid design of our Phase 1/2 trial permits decisions to add or subtract vaccine candidates, doses or regimens based on early clinical data. This highly streamlined study

design is expected to generate safety, tolerability, immunogenicity and potentially efficacy data and allow us to select the most promising vaccine candidate for further development based on both preclinical and clinical data rather than committing early to a specific candidate based only on preclinical information.

As I mentioned, the preliminary clinical data we're discussing today is from the nucleoside-modified messenger RNA, (modRNA) BNT162b1 which encodes an optimized SARS-CoV-2 receptor binding domain, the RBD antigen.

Let me now transition to Kathrin Jansen to discuss the clinical plan and share more details around the important, early, preliminary and encouraging clinical data we share today. Kathrin?

Kathrin U. Jansen - *Pfizer Inc. - SVP & Head of Vaccine Research & Development*

Thank you very much, Mikael. It's a pleasure to be here today discussing our initial clinical data. Could I have the next slide, please?

As you can see, we have made an enormous progress in our quest to develop the COVID-19 vaccine. We are working with regulatory authorities in an effort to compress stages that have historically taken years or months into much shorter time frame in a safe but -- ensuring a safe and responsible way of conducting our development program.

Safety is our #1 priority in all human clinical trials, no matter how fast we are trying to progress our COVID-19 vaccine. As you can see, the genetic sequence of the SARS-CoV-2 virus was made available only in January, and we were able to start our human trials for this vaccine candidate in only 5 short months. Pending agreement with regulatory authorities, we hope to start our pivotal Phase 2b/3 study as early as July, expanding our trials to enroll up to 30,000 healthy participants. Could I please have the next slide?

So we are sharing with you now the preliminary data of our U.S. Phase 1/2 study with the vaccine candidate, BNT162b1. Could I have the next slide, please?

Shown here is the enrollment in our Phase 1/2 study. So what you see is that we have interim data from an ongoing placebo-controlled observer-blinded dose escalated study among healthy adults 18 to 55 years of age. What you see here that 76 participants were screened and 45 healthy adults were enrolled in our Phase 1/2 study. There were 15 participants in each dose level cohort. 12 received vaccine and 3 received placebo in each cohort. The 12 participants in each cohort were either immunized with 30, 10, 30 microgram of BNT162b1 on days 1 and 21, so that was the 2-dose series, and 12 participants received 100-microgram dose on Day 1.

The study began on May 4, 2020, and by June 19, 2020, as I said, 76 subjects were screened and 45 participants were randomized and vaccinated. What you will see in the following that overall, the initial data demonstrated that BNT162b1 could be administered at a dose level that was well tolerated and generated dose level dependent and dose-dependent immunogenicity as measured by a receptor binding domain, binding IgG antibody assay and by an authentic SARS-CoV-2 neutralizing antibody assay. Both of those assays are our go-forward clinical assays, and they have been qualified. Could I have the next slide, please?

So let me first lay out the slide for you. Here, we show our receptor binding domain IgG antibody data. So what you have on the y-axis, which, by the way, is a logarithmic scale, it shows the RBD IgG antibody concentrations. What you see on the x-axis is the days of immunization. You see in the color codes, placebo recipients in gray. You see the 30 micrograms in light green. The 10-microgram in light green, 30 micrograms in darker green and in the much darker green, you see the 100-microgram dose level. This data illustrates the significant elevated RBD-binding IgG antibody concentration observed in all 24 subjects who received 2 vaccinations at 10-microgram and 30-microgram dose levels of the BNT162b1 candidate.

At Day 28, which is 7 days after the second immunization, the geometric mean concentrations, or GMCs observed approximately eightfold and 50 -- I'm sorry, approximate 8x and 50x the GMCs of the 602 units per ml of a panel of serum from 38 subjects who had contracted SARS-CoV-2. So the relevance of the human convalescent panel is at as follows: there is evidence that individuals who contract SARS-CoV-2 are immune from disease, at least, for a short period of time. So we believe that it's a good guidepost to compare our vaccine-induced antibody responses to the human convalescent serum panel.

So I'd like to just summarize 3 points to make here. Number one, we see already substantial RBD-binding antibodies after a single dose that then is substantially boosted after the second dose.

The responses, also, if you look at the individual dots in the bars, you see that the responses of the vaccine needs are very consistent and the overall responses are very tight. The antibodies are consistently higher 2 weeks after the second dose.

I also would like to say a few words about the human convalescent serum panel. There were 38 subjects in the panel and each of the individuals had PCR-confirmed SARS-CoV-2 infection, 34 had symptomatic COVID-19 disease and 1 individual was hospitalized. So this distribution is clearly between the less severe disease that we see in young people and the more severe distribution that we see for older adults. If I could have the next slide, please?

So this panel describes our virus neutralizing antibody responses. And again, I'd like to stress that what we are measuring here is real authentic SARS-CoV-2 virus neutralization. So again, the slide is set up in a similar way. On the y-axis, you do see the 50% neutralization data, which is a common way of how neutralization is -- viral neutralization is measured. And again, it is a log scale. On the x-axis, you see the days of immunizations. Again, the green bar reflects the various dose levels and the black bar is representative of this human convalescent serum panel that I just described.

So after a single dose of BNT162b1, we see already modest virus-neutralizing antibody titers. The important point is though that after a second dose, we see 13x and 10x higher neutralizing titers observed compared to the first dose. Why is it important? These increases are very important given that higher neutralizing -- virus neutralizing antibody titers ensure longer persistence of that neutralizing antibody. This also highlights an advantage of our technology that Mikael Dolsten described earlier. With the RNA technology, we have the opportunity to boost our immune response so that the antibody responses, as you saw, both for RBG-binding antibody as well as neutralizing antibody can be enhanced, in this case, as I just said, 13x and 10x. Without an issue of an attenuation of the immune response that we often see using other technologies, such as viral vectors that actually do induce an anti-vector response, even after first dose, which then limits or attenuate subsequent booster responses.

So in summary, what you see here is that the virus-neutralizing geometric mean titers induced by the BNT162b1 after 10 and 30 microgram dose level after 2 doses are actually 1.8- to 2.8-fold higher than the GMTs of the convalescent serum panel. It is also noteworthy that the 100 microgram dose level, those individuals received only a single immunization was not better than the 30-microgram dose level. So we believe that based on those data, the dose level that will likely move forward will be somewhere between 10 to 30 microgram. Could I have the next slide, please?

Now I'd like to summarize our tolerability -- safety and tolerability data from this first cohort. Individuals were reporting local reactions for 7 days after each immunization. So what you see here on this graph is the most commonly reported local reactions was injection site pain, which was generally mild to moderate, except in 1 of the 12 subjects who received a 100-microgram dose level, where we saw a one severe event of pain. Reactions, including fever, were more common after the second dose than the first dose. Following dose 2, about 8 percent of participants who received the 10-microgram dose and 75% of participants who received the 30-microgram dose reported fever, but fever is generally resolved within 1 day of onset. There were no serious adverse events reported.

Let me now go to the systemic events. So here displayed are systemic events, 7 days after vaccination 1. What you see in general is that the systemic events after the first dose, the highest ones were really, chills, fatigue and headache. Again, you see a dose level dependency. But, in general, we saw mild to moderate reactogenicity. If I go -- if you could go back to the -- go forward to the next slide, please.

So this now shows the systemic events after the second immunization. Here, you only see the individuals that received the 10 and 30-microgram dose level. The reason for this is that because of the immunogenicity data that I showed you earlier, looking particularly at the neutralizing antibody titers, we didn't see an advantage of the 100-microgram dose. In addition, as you saw from the local tolerability as well as a systemic event for the 100-microgram dose level, they -- we saw more reactogenicity associated with the 100-microgram dose level. And therefore, based on immunogenicity and the tolerability profile, we made the decision not to immunize the 100-microgram dose level and give those individuals a second dose.

Again, in summary, you see that we have a mild to moderate systemic tolerability profile after administration of 10 and 30 microgram, both after the first as well as the second dose with our BNT162b1 candidate. Could I have the next slide, please?

And I think here, I bridge over back to, I think, Mikael.

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development and Medical*

Thank you very much, Kathrin. Now I want to briefly mention how we are ramping up manufacturing capacity and investing hundreds of millions of dollars at risk in preparation for potential COVID-19 vaccine supply. We are planning for a cumulative vaccine supply goal of up to 100 million doses in 2020 and more than 1 billion doses in 2021. We are jointly leveraging our extensive global infrastructure across this partnership. Pfizer is a proven, reliable global vaccine producer, supplying vaccines to over 165 countries. We have distributed over 1 billion doses of Prevnar 13, our pneumococcal conjugate vaccine, with unprecedented reliability since 2012. This is one of the largest scaled sterile manufacturing operations in the industry, producing 1.5 billion sterile units per year.

Next slide, please. In closing, I wanted to share a few key takeaways. Preliminary data demonstrated that BNT162b1 could be administrated in a dose that was well tolerated and generated dose-dependent immunogenicity as measured by already binding IgG concentration and SARS-CoV-2 neutralizing antibody titers, as Kathrin discussed with you thoroughly.

Early positive data shows that BNT162b1 can be administrated at a low effective dose of 10 micrograms and provide neutralizing titers at/or above human convalescent plasma as early as 4 weeks after vaccination. Local reaction and systemic events optimization with 10 and 30 micrograms of BNT162b1 were dose dependent, generally mild to moderate and transient. No serious adverse events were reported. Data from the ongoing Phase 1/2 clinical trial are expected to enable selection of a single lead candidate and dose level for a potential large, global Phase 2b/3 safety and efficacy study that may begin as early as July 2020, subject to regulatory approval.

Efforts to manufacture the leading candidates, at risk, are gearing up. If the safety and efficacy study is successful and the vaccine receives regulatory approval, the companies are currently expecting to manufacture up to 100 million doses by the end of this year, 2020, and potentially more than 1.2 billion doses by the end of 2021.

Now we look forward to answering your questions.

Charles E. Triano - *Pfizer Inc. - SVP of IR*

Right. Thanks, Mikael and Kathrin, for those remarks. Operator, can we please poll for questions at this time?

QUESTIONS AND ANSWERS

Operator

(Operator Instructions) Your first question comes from the line of Umer Raffat of Evercore.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

First of all, I just want to say congratulations on the data. And I have 3 questions, if I may. Perhaps, first, Mikael, I want to hear your thoughts on whether the other constructs for the Pfizer-BioNTech collaboration, perhaps in particular, your B2 construct, which is the Moderna against full spike? Or the C2 construct, which is a self-amplifying mRNA, will outperform the data reported today? I'm curious what your take is on that.

Secondly, on neutralizing antibody titers, one of things I'm very confused about is that the sampling of those 38 patients you guys showed us appears to be low or materially lower than similar samplings for neutralizing antibody titers we've seen in convalescent patients in other studies. And I'm curious your take on that.

And finally, on lymphocyte count reductions, one thing I noticed was the baseline lymphocyte counts were about 1.5 to 2. And I totally acknowledge it was transient, but in older COVID patients, they often have baseline lymphocyte counts of 0.5 to 1 to begin with. So if we're going to have a lot of reduction in lymphocytes early on, could they end up in more like Grade 4 lymphocyte count reductions in older patients? Maybe you could speak to your early observations in older patients.

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development and Medical*

Yes. Let me say a few words about the first and I'll ask Kathrin to speak about the neutralizing antibody titers in our convalescent plasma. We are very excited by the data we have shared today on RBD that we think show a very promising profile for a vaccine with the potential to be protective. And we still have an opportunity, as we say, to have -- compare over the next days to a couple of weeks or so to a second candidate, as was alluded in our transcript. And this includes a spike. So this gives us an unprecedented opportunity to really cherry pick dose and construct. But clearly, today, we think we have very encouraging data for a promising vaccine to act against SARS-CoV-2 to prevent potential disease.

When you alluded to lymphocytes and how that may be depleted in patients as part of the disease, of course, we are particularly here focusing on vaccinating participants and in the future that are not infected with SARS-CoV-2. We are not thinking about vaccinating during an active infection. So normal participants, in general, do have an immune response that can give both B and the T cell response and be protected from getting severe depletion, as you alluded to. And that includes, of course, us having older patients with comorbidities continuing now in our study. So I hope I got your question right, but my answer was related to that we will prevent -- we hope that the aspiration of vaccine development of low lymphocyte counts. I'll ask Kathrin to specifically address the second question. And if you have anything to fill in on my other comments, please be welcome.

Kathrin U. Jansen - *Pfizer Inc. - SVP & Head of Vaccine Research & Development*

Yes. Thank you, Mikael. I think the one point that I want to make that was very important for us to assess multiple RNA platform as constructs as Mikael alluded to. And the trial, the Phase 1/2 trial was designed to, as I call it, quickly read out the candidates that did not give us the desired profile. We were aiming for high neutralizing antibody, the lowest possible dose and the most benign tolerability profile.

I'd now like to speak about the neutralization question that you had. One of the problems that we have in comparing multiple candidates in what -- that have been evaluated in with multiple assays, and there's a number of different assays that are being run currently in the scientific arena, it is actually not possible to compare the results from one study run in 1 assay with the results from another study run in another assay. And this is why we put that convalescent serum panel together to have a guidepost that would allow us to see which of our constructs and dose levels would give us the better and higher neutralizing antibody responses.

I'd like to also note that we do use an authentic neutralization assay, not a pseudo neutralization assay, in which the serum from immunized participants is diluted and mixed with authentic infections, SARS-CoV-2. And using this authentic assay makes actually interpretation of the results also more certain. And I think all of this is important to take into consideration when one looks at the data that are being described or published by others.

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development and Medical*

Thank you, Kathrin. And I just wanted to add, since you also asked about the self-amplifying. With the goal of progressing rapidly to have the potential for a vaccine available this fall, we -- after some initial experiences felt modified mRNA with these 2 options RBD and spike are best fit for that aggressive timeline. We do continue to learn from additional constructs such as self-amplifying that could enable after the pandemic phase to offer unique life cycle management opportunities, but not with the speed of the current formats that we think also demonstrate very promising profile by themselves. And as you have noted, a dose that is encouraging low 10 to 30 micrograms. Thank you.

Operator

Your next question comes from the line of Vamil Divan of Mizuho Securities.

Vamil Kishore Divan - *Mizuho Securities USA LLC, Research Division - MD*

So one question, just in terms of the patient population in this trial. I'm trying to get a better sense of what you're doing to ensure maybe an older population, a more diverse population in the other trials, just the mean age was fairly young here and 82% of the patients were listed as being white. So given older patients and African-American, Hispanic patients seem to be disproportionately affected by COVID-19. Curious what you're doing there. And then one other question, just more, again, sort of looking forward in terms of commercializing -- potentially commercializing a vaccine in this environment, I think, there's a lot of discussion about since these vaccines are moving quickly relative to what historically what we've seen. Is there more you think you would need to do to kind of convince people that you've gone through the proper steps to show that it's safe and effective in order for people to be comfortable taking the product, assuming that gets approved down on the road?

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development and Medical*

Thank you for the 2 questions. Kathrin, if you respond to the first one related to the initial patient population versus additional population studies, I can comment on the vaccine, the standards.

Kathrin U. Jansen - *Pfizer Inc. - SVP & Head of Vaccine Research & Development*

Happy to do so, Mikael. So talking about the population, let me just give you a little bit of context of the choice of the population that we described to you today. When we were getting ready to start our clinical development program, and I'm speaking here in particular about the U.S. clinical trial, we had extensive discussions with the FDA how to bring forward these candidates into human clinical evaluation. And based on those discussions, we agreed that it would be most proven to first start with a younger population, 18 to 55 for the data today, before using the vaccine in an older population of 65 to 85. So that was done on purpose. We also were being asked by the regulatory agency that we make sure that the individual that would be first enrolled in this first instance into the study did not have any underlying medical conditions. So there were a lot of exclusion criteria because we wanted to be absolutely sure that we test these new vaccine candidates in an absolutely safe manner.

As we move forward in our clinical development program, it is understood and based on the safety and tolerability data that I shared with you that are mild to moderate that we know will move into a subject population that will also have common underlying medical conditions. And that was -- as I said, that was all pre-agreed with the regulatory agency. We then assumed that as we go into large-scale clinical trial to test the efficacy of our vaccine that this clinical study will be much more diverse because, as you know, we hear reports that certain populations preferentially are more afflicted by COVID-19 than other populations. And since we are running an efficacy study, by default, we will have a much more diverse demographics in our Phase 3 clinical evaluation.

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development and Medical*

Thank you. The FDA released guidelines recently outlining its condition for approving COVID-19 vaccine. We have worked based on a long tradition closely with FDA from the onset of this program, and the guidelines are very much in line with what we expect that the FDA is setting high standards and they have decided not to cut corners. This is really the way we always develop vaccines and are very agreeable to. And we think it favors experienced vaccine companies such as Pfizer. We support that approach. We need a safe and effective vaccine. So our studies include a plan of enrolling up to 30,000 participants that will now allow us in a timely manner to accumulate safety, immunogenicity and vaccine efficacy in preventing disease. And we expect that your -- should -- as a potential approval or emergency use authorization have a convincing safe and effective vaccine profile that, of course, over time, in a traditional post-approval commitment can further broaden experience as you increase the number of participants that have been exposed to vaccine. But that's the high-quality standard that Pfizer always adheres to, and we're very pleased to see the guidelines from FDA. Thank you.

Operator

Your next question comes from the line of Terence Flynn of Goldman Sachs.

Terence C. Flynn - *Goldman Sachs Group Inc., Research Division - MD*

Great. Congrats on the progress. I guess, 2 for me. Based on your preclinical and clinical data, how are you thinking about the durability of efficacy at this point or durability of antibody levels? And could you build into the pivotal trial, the ability to have a further boost down the road, if that would be needed? And then the second question I had was just, it seems to me like the message is this is kind of your go-forward candidate here. You've looked at a lot of the other data, but is there still the possibility that you could advance more than one candidate into Phase 3? Or is the right way to think about it that this is kind of the lead that you're moving forward?

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development and Medical*

Thank you. Let me address your questions. As Kathrin so well alluded to, we saw a very nice boost with a second dose and reaching very high RBD antibody levels and high neutralizing levels exceeding several fold, what was seen with convalescent plasma. We do think that high antibody levels or neutralizing character bodes well for expecting reasonable to very robust durability. The beauty of this technology compared to viral technologies, such as adenovirus is that you could tentatively, as you ask, boost on an annual every 2, every 3 years interval with this technology and expect new augmentation of the immune response. Right now, we assume that this is going to be a reasonably long-lasting immune response given the magnitude, but this technology allows you as, you follow patients, to regain strong immune responses. And again, this was one of the reasons why we embarked on this technology, given we had experience earlier using adenovirus. And I think in recent publications, you may also have seen that certain of the primate adenovirus do have cross-reactivity with human antibodies, and we spent quite a lot of time thinking through this and felt that the mRNA was uniquely positioned for a pandemic and where you need to be prepared to any outcome over years to come, whether from COVID-19 or other coronaviruses. And the beauty here with our technology is that we can move so fast. We even -- if there is another pandemic in a few years from another virus quickly readjusted.

And finally, I think on the go-forward candidate, we agree with you that the data today are compatible with that this is a go-forward candidate with a promising profile, but we will learn more of the near couple of weeks or so. And you heard Kathrin allude to, that we have an option to bring a second candidate. But in the end, within July, we'll select one candidate and move with regulatory dialogues into a large-scale Phase 2b, Phase 3 study. But this is a unique property of this trial that Pfizer and BioNTech designed. Thank you.

Operator

Your next question comes from the line of Louise Chen of Cantor.

Louise Alesandra Chen - *Cantor Fitzgerald & Co., Research Division - Senior Research Analyst & MD*

My first question for you is, what is the level of immunity do you think that's going to be required for protection in humans? And then how should we think about the T-cell response here, CD4, CD8 with respect to the data that you saw? And then last question I had is, what do you think -- or how do you think vaccines will be used? Is it going to be one size fits all? Or is there going to be certain vaccines for certain subpopulations or subgroups?

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development and Medical*

Thank you. Kathrin, please discuss the level of immunity with protection, your view on the T-cell responses, and I can comment on how will vaccines be used for various populations.

Kathrin U. Jansen - *Pfizer Inc. - SVP & Head of Vaccine Research & Development*

Yes. Happy to, Mikael. So the first -- the short answer to your question, Louise, is that it is not yet known what level of immunity is sufficient for protection against SARS-CoV-2 infection or COVID-19 disease. But what we do know is, and that's why we used in our evaluation, this panel of convalescent serum is that individuals that contracted SARS-CoV-2 appear, at least in the short term, to be resistant from a secondary infection. So while we do not know what the final levels will be, what we do know is that it's the immune response that we induced through vaccination with our vaccine candidate, they are very strong and mirror those that we see in individuals that have recovered from COVID-19.

Now you also asked about the T-cell responses, and that is very important. The reason we chose the mRNA technology in contrast to other technology was in part our experience that came out of the oncology field. You may know that BioNTech has started their work in oncology patients. And from there, we saw the power of the mRNA platform to really induce the very broad CD4 and CD8 T-cell response as well as innate responses. And because we did not know and still actually do not know which arms of the immunity will ultimately be needed for protection, will they all be needed, will antibodies be sufficient? Is T-cells -- or T cells be sufficient, it was important to us to select a vaccine platform that gives us the broadest possible immune response that we then hope will be sufficient to protect against COVID-19.

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development and Medical*

Thank you, Kathrin. That was an excellent overview. And of course, when we compare to convalescent plasma with our immune response and we shared today that for neutralizing antibodies, we are about 2 to threefold higher with the 2 doses, as you heard from Kathrin, in addition to that, what you do not accomplish with convalescent plasma transfusion is activation of T cells. And the learning from this platform in numerous studies is that you see a favorable CD4 and CD8 cell response. We're working with our German colleagues to study that and hope to shortly report back to you. And we also have seen that within the CD4, it's a favorable Th1 response.

Now how will this vaccine be used in various populations? Well, as Kathrin alluded to, regulatory dialogues ask you to start with adult healthy population, hence, 18 to 55 years of age. And we have generated a promising profile of the vaccine. We are now dosing 65 to 85. We are fortunate that right now the dose, as indicated, may be in the 10 to the 30 microgram interval and that gives us an opportunity to select one dose that potentially works very well in older or younger adults. And that's our preliminary plan that it will be one dose, one format given the potency we have seen of this vaccine, the antibody and the T-cell responsiveness and those responses at acceptable mild to moderate local and systemic events. So we remain optimistic that it will be a simple dose and format for all patients, whether younger or older, whether with or without comorbidities.

Operator

Your next question comes from the line of Geoffrey Porges of SVB Leerink.

Geoffrey Craig Porges - *SVB Leerink LLC, Research Division - Director of Therapeutics Research & Diversified Biopharma and Senior Research Analyst*

Congratulations on this really interesting result. Kathrin, a few questions for you, if I may. First, could you talk about how you plan to establish that there isn't any risk of vaccine-related disease enhancement? And then could you talk a little bit more about the clinical trial plan? It sounds as though you have a couple of phases. And in the FDA's guidance document, they suggested Phase 2 should be several hundred patients. So in the 30,000, is there a several hundred patients Phase 2 component, after which you would proceed to expand enrollment? And then lastly, assuming it is 30,000 patients, how long do you think, realistically, it would take to enroll those patients or vaccine subjects, given all the competing trials that are now going to be going on around the world?

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development and Medical*

Thank you. Kathrin, please respond, and I'm happy to fill in.

Kathrin U. Jansen - *Pfizer Inc. - SVP & Head of Vaccine Research & Development*

Yes. Geoff, good to hear your voice again. Yes. So let me first -- take your first question and talk about the theoretical concern about enhanced disease. So first of all, we have done an extensive evaluation of all the available data and literature and finding pertaining to a theoretical concern of enhanced disease. And we through this assessment, which by the way we also did not just internally but we also had support from ACTIV which is the NIAID private-public partnership where the vaccine working group was also tasked to do an evaluation that was done by mostly academic participants in this working group. And both we, ourselves, through the study of the literature and available information as well as the academic consortium that was tasked with doing an assessment, we both came to the conclusion that indeed antibody-enhanced disease, in this particular case is really only a theoretical concern. That said, and as I mentioned earlier, safety for us is of the utmost importance. So we have discussed with regulatory -- with the FDA that we would put into our Phase 2B/3 clinical trial, what we call a potential stopping rule if there would be any evidence about a certain threshold that would indicate that we may have such a finding. And so that secures that as we enroll large numbers of subjects in our clinical trials that we continue to ensure the safety of our participants, no matter what the findings are.

You also asked about the Phase 2b/3 clinical trial and to get a little bit more information about this. Here, I just want to share that we -- it is a 20,000 to 30,000 study. We plan to randomize a subject 1:1 to receive placebo and vaccine. It is an endpoint-driven study. Now we have, as mentioned earlier, an enormous expertise in performing large-scale vaccine clinical studies. I mean, you may remember our capital study, where we enrolled over 80,000 participants in a relatively short period of time. And here, given the urgency, we set up to enroll those 30,000 participants, again, in a very short period of time. It could be as short as about 4 weeks or so. That is the plan.

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development and Medical*

Thank you, Kathrin. I just wanted to punctuate a couple of things on this really good question. Now this particular vaccine format we reported today contains the smallest binding element to the human H2 receptor, the human receptor for SARS-CoV-2. And as you may have noted from reports of our German colleagues, our RBD fragment binds potently to H2. So that was selected to optimize for binding neutralizing antibodies versus just binding. And that's one favorable aspect of improving chances of good efficacy versus limiting theoretical risk of adversity that you spoke to.

The second one is the TH1 versus TH2 profile that we are pretty knowledgeable about that this platform is preferentially TH1 with the right size and kind for preventing vaccine infection and not leading to supporting an antibody disease enhancement. And finally, that the numerous studies in various animals, exploring the risk for this with SARS-CoV-2 and while data are not always completely convergent, I think the overall picture is that there seems to be no reason to believe anything else than a vaccine can be efficacious while you always need to be prepared for unexpected things as you asked us. When it comes to the enrollment, as you know, we are planning, pending finalization with FDA dialogues, to start enrolling in July. And we have a large experience how to enroll fast. Kathrin exemplified enrolling for very large studies. And we have continuously multiple Phase 3 studies ongoing. So we learn constantly. We'll have a large number of sites. We've had good epidemiological advice from internal experts and CDC has been very collaborative in sharing their map of disease across U.S. and other regions. So we think we will be able to conclude enrollment potentially late August, early September, to allow us to have not just enough participants but also enough events to be able in October to file for potential approval based on safety, immunogenicity and vaccine efficacy. So these are our plans, and we have validated them by looking at assumption of today's environment when it comes to disease percentage in the population. And we think there is a very good probability and feasibility that our plans can materialize, and we feel optimistic about this. And we are very grateful for great advice from FDA, CDC as well as dialogues we've had with ACTIV consortium. Thank you.

Operator

Your next question comes from Navin Jacob of UBS.

Navin Cyriac Jacob - *UBS Investment Bank, Research Division - Equity Research Analyst of Specialty Pharmaceuticals and Large Cap Pharmaceutic*

It's Navin from UBS. Can you hear me okay?

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development and Medical*

Yes.

Navin Cyriac Jacob - *UBS Investment Bank, Research Division - Equity Research Analyst of Specialty Pharmaceuticals and Large Cap Pharmaceutic*

Perfect. Just some questions on the practical front. Wondering the -- obviously, COVID-19 has created an environment that's very different than traditional -- than an environment where traditional vaccine trials are conducted. Specifically, I'm wondering, is there any -- how are you thinking about mask wearing, social distancing affecting your protocol? And more importantly, the event rate that you may be seeing in the Phase 3? That's number one. And then with regard to manufacturing, you say 100 million doses by 2020, 1.2 billion doses by the end of 2021, is that assuming 30 micrograms, 100 microgram? Any kind of color around that would be helpful. And then final question is just around the storage and -- of the vaccine itself. I just want to understand, again, sort of the stability, what requirements are needed with regards to cold storage and so on and so forth? Congrats, by the way.

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development and Medical*

Navin, I'll respond to the first 2. And Kathrin, if you discuss the storage stability and our experience with that and feel welcome to add to my comments. No, of course, it's good that there are learnings how to deal with public health action cautious when it comes to spreading of the vaccine -- virus using masks, social distancing, et cetera. Unfortunately, if you look at the situation, for example, in the United States, there are many, many states where it has been either difficult to implement or insufficient and you see rising numbers of COVID-19 cases and unfortunate poor outcomes with hospitalization and death. And I think that's true also in other countries in Europe, various regions of the world, and we have seen dramatic outbreak of disease in Latin America, Brazil, Argentina, et cetera. So although we applaud the use of these actions, it seems not to easily change over the next period, including when we plan to run this trial, the need for a vaccine, and we think we will be able to enroll and get events. And in fact, recently, when we did the simulation about current events at the various parts of the United States and the world, we saw actually that we could easily have enough events in our trial planning to meet the requirement to demonstrate vaccine efficacy against disease. And since then, unfortunate, if anything, the disease incidents has worsened. The doses that we shared today assume a vaccine given at the dose of 10 to 30 microgram. And so we think these are very accurate according to the current plans in the program.

Kathrin, please.

Kathrin U. Jansen - *Pfizer Inc. - SVP & Head of Vaccine Research & Development*

Yes. Thank you, Mikael. I think the other question was about the vaccine storage. So currently, our vaccine is stored at minus 80 degrees. We have generated a shorter-term stability data that are still ongoing, where we evaluate storage, at least, short-term storage at other temperatures. When it comes to -- if you think about distribution, Pfizer has a very large distribution footprint all over the world. And so we have already looked into special shipping containers that would allow to distribute the vaccine to literally wherever it needs to go and with data associated that we can keep the storage temperature for probably about 10 days, maybe somewhat longer than that without -- with those storage containers to keep the vaccine in its frozen state. So given our distribution network and given the technology that is available to us to keep the material at the appropriate temperature, we are very encouraged that we can distribute the vaccine to wherever it needs to go.

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development and Medical*

Thank you, Kathrin. And as you said, our distribution logistics have been already carefully validated, and we feel that this should be within the experience and capabilities of what we have. But we also hope to have, as we always do in life cycle management, a new lyophilized formulated vaccine by -- within maybe a year after initial delivery such as fourth quarter 2021 and the lyophilized formulation could be stored in refrigerator. So there are multiple opportunities from the initial first year towards life cycle management with improvements in formulation, while being able to have a large amount of vaccine as soon as possible, pending conclusion of the studies with quality and consistency and then further optimizing formulations.

Operator

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

Scott Daniel Puckhaber - *BofA Merrill Lynch, Research Division - VP*

This is Scott on for Geoff. Congrats on the early progress. Just wondering if you can provide any additional details on the specific characteristics for the 11 patients that were excluded due to eligibility criteria? Just wanted to get a better understanding of the underlying conditions in these specific patients that were deemed inappropriate to include?

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development and Medical*

Kathrin, please.

Kathrin U. Jansen - *Pfizer Inc. - SVP & Head of Vaccine Research & Development*

Yes. So as I mentioned earlier, we had agreed with the FDA to ensure that -- had very strong exclusion criteria for the first round, so to speak, of immunizations in the 18 to 55 year old. And so the reason those individuals were excluded is because they did not meet the study inclusion criteria. So for example, one of the things that we looked at, we needed to make sure that individuals that were newly infected, for example, with SARS-CoV-2 would be excluded. We wanted to exclude individuals that had previously been infected with SARS-CoV-2 and already had pre-existing immune responses. So that was 2 major reasons that led us to exclude individuals. And then, of course, all of those that did have underlying medical conditions that would not meet the inclusion criteria or trigger the extrusion criteria.

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development and Medical*

Thank you very much, Kathrin. And as you heard, that was driven by standard FDA guidelines for this particular program, but also very much in line with typical FDA procedures for any vaccine program. Thank you.

Operator

Your next question comes from the line of David Risinger of Morgan Stanley.

David Reed Risinger - *Morgan Stanley, Research Division - MD in Equity Research and United States Pharmaceuticals Analyst*

So first, can you just discuss your view on the importance of targeting the receptor binding domain in addition to the spike protein, given that, that is differentiated versus some of your competitors, including Moderna? I think you'll be able to rule out the risk of the...

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development and Medical*

David, could you say the second question, rule out the risk...?

Operator

I'm showing his line disconnected. We'll move to the next question.

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development and Medical*

I think we can answer his first question. And I'll ask Kathrin first to share a few words. What was the view of this program targeting the receptor binding domain compared to the majority of other trials targeting spike, which is also included in our format? And please share some thoughts.

Kathrin U. Jansen - *Pfizer Inc. - SVP & Head of Vaccine Research & Development*

Yes. Thank you, Mikael. So as we discussed earlier, we tested -- or we are testing multiple constructs of the spike protein, the receptor binding protein by itself and, of course, the full-length spike protein. And the reason for this was that we wanted to see which of those constructs gives us the best immune response and also the best tolerability profile. So why we chose to look at the receptor binding domain in contrast to many others who focus on the full-length protein was that the receptor binding domain, of course, is the business end of the spike protein molecule. I mean it docks to the human receptor, h2 with high affinity. So the idea is, if one focuses the immune response to this RBD domain, in principle, one should see very powerful inhibition of the virus docking to the host cell and subsequent uptake. Now given that, we still look at those constructs, and we will make decisions, as Mikael noted earlier, in the next couple of weeks, which constructs to go forward with. And again, it's all about the safety, tolerability profile, coupled with an optimal immune response, T-cell responses, high neutralizing antibody responses and, of course, the innate responses afforded by the platform.

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development and Medical*

Thank you, Kathrin. And we are the only company, to the best of my knowledge, in the clinic with this unique RBD encoded domain. And there was some very elegant work done how to make it primaries to be highly immunogenic. And I think that's what we have seen in this study and the encouraging data reported today, but we still will have an opportunity to benchmark it versus a spike over the next couple of weeks. We feel very good about this. And I should say that our spike has also some unique features among that being code and optimize for efficient expression in humans. So the selection between good and good will result in us then sharing at a final dose construct in quite a near future here. Thank you, David. Sorry, you got cut off.

Operator

Your final question comes from the line of Seamus Fernandez of Guggenheim.

Seamus Christopher Fernandez - *Guggenheim Securities, LLC, Research Division - Senior Analyst of Global Pharmaceuticals*

So, I guess, the question that I have is actually on the self-amplifying RNA. Mikael, you mentioned, it sounded like there's some attempt to or some questions around manufacturing capabilities there as well as maybe the construct itself. But I wanted to get a better understanding, you suggested that this could be part of a second-generation opportunity. Could you talk a little bit more about what you would be looking for self-amplifying RNA construct to achieve perhaps better than the current vaccine, if you were to see that as a realistic second-generation opportunity?

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development and Medical*

Yes. Thank you, Seamus. I'll say a few words and then I'll ask Kathrin to further comment. Well, the beauty of this light speed program, and Kathrin alluded to that, is that we have the ability to look at multiple constructs, while cherry picking one that we move forward with. And given the good promising profile we have seen at this time point, we're at the stage now where we will select shortly a candidate with a very promising profile that then can be available pending clinical studies, regulatory dialogues as a potential for consideration for FDA in October. Now self-amplified, originally, we thought could lower the dose maybe -- and particularly, that would have been important. If you need doses like 100 microgram, that puts a significant constraint on the manufacturing network. Now we were pleased to see that we are in a much lower interval, 10 to 30 microgram that can allow us to move quickly with a potential vaccine from approval to millions of doses. And you heard us say we already think we can be at 1.2 billion doses or more. So of course, self-amplified as a life cycle management could make you go even further and of course, there may always be learning for second-generation vaccines. And I'll ask Kathrin to speak about that. But again, I wanted to emphasize the current data today are really encouraging. We're very excited by them, but it's always good to have opportunities to think not just about one product launch for a pandemic, potentially in a relatively near time frame but even have a platform that can help you to support pandemics over several years to come. Kathrin, please.

Kathrin U. Jansen - *Pfizer Inc. - SVP & Head of Vaccine Research & Development*

Yes. I think, Mikael, you actually highlighted all the important points that Seamus was asking about. So I really do not have anything to add at this point.

Mikael Dolsten - *Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development and Medical*

Thank you very much. We were very pleased to have all of you with these number of good questions. And we feel certainly very enthusiastic after sharing this publication in an open-source format. And we will see it later in a peer-reviewed journal. We continue to advance the program with a focus on quality, safety and efficacy. I look forward to continuing to communicate with you in relative near term about additional data as we are able to share with them concerning T-cell activity, activity on more patient numbers, et cetera. But we certainly view this as a good day for patients and for science, and thank you for interest.

Charles E. Triano - *Pfizer Inc. - SVP of IR*

Thank you, everyone. This will conclude our call.

Operator

Thank you for participating in today's conference. This concludes today's call. You may disconnect at this time. Presenters, please hold.
