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EDITED TRANSCRIPT

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CORPORATE PARTICIPANTS

Christopher J. Stevo *Pfizer Inc. - Senior VP & Chief IR Officer*

Robert Smith *Pfizer Inc. - SVP of Global Gene Therapy Business, Pfizer Rare Disease*

CONFERENCE CALL PARTICIPANTS

Jessica Hui *Evercore ISI Institutional Equities, Research Division - Equity Research Associate*

Jonathan Miller *Evercore ISI Institutional Equities, Research Division - VP*

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

PRESENTATION

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

Hello, everyone. Thank you for joining us. Pleasure to have Pfizer management join us. There's a lot to talk about, but at the outset, I do want to say that when we were first scheduling this event, there was a lot of interest at Pfizer at the time. And this was -- we were doing this in the -- in -- during the summer, and there was a lot of interest at Pfizer at the time to talk about some of the innovation areas that aren't getting necessarily much Street focus, which included obviously an emerging gene therapy pipeline. And one of the goals at this fireside when we were first setting it up was to have Bob Smith, who's -- who could really take us through the gene therapy business in a lot of detail. But of course, we couldn't have predicted that 3 days before this fireside chat, there would obviously be a new and crazy variant.

So in light of that, we're going to start off with a few variant questions, if that's okay. But let me first turn it over to Chris, who's the new head of Investor Relations and also an old-time friend from buy side, who never gave us a hard time because nobody ever does.

Christopher J. Stevo - *Pfizer Inc. - Senior VP & Chief IR Officer*

Umer, I feel your pain, so thank you for the kind introduction to both of us. And I just want to say very briefly during this talk, we're going to be making forward-looking statements. And if you have any questions about the forward-looking statements, which we make no -- which we may undertake no obligation to update, you can see our SEC filings under Forms 10-Q and 10-K for more details. Thank you.

QUESTIONS AND ANSWERS

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

Outstanding. Well, maybe just to kick things off, Chris, I guess the first and the most obvious question a lot of investors are focused on is when will we get the antibody titer full reduction data for the Pfizer vaccine, the existing vaccine versus Omicron variant?

Christopher J. Stevo - *Pfizer Inc. - Senior VP & Chief IR Officer*

Yes. So we will have that within the next couple of weeks, and then we will have a better sense of whether the vaccines seem to preserve their efficacy or not. I think also in the last few days, you might have seen some media from some countries, which suggests that in some of their data sets -- again, real-world evidence, not laboratory tests, not clinical data, that suggests that the existing vaccines do retain their efficacy versus the Omicron variant.

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

Got it. Is that Pfizer's expectation that the vaccine should retain efficacy at least for the first 3 or so months post-booster?

Christopher J. Stevo - *Pfizer Inc. - Senior VP & Chief IR Officer*

That's entirely possible, Umer. But to be perfectly honest, we just don't know. So that's why we've always been committed to having new variant of concern vaccines available as we did for Beta, as we did for Delta. Again, those turned out not to be necessary, but we thought it was very important as part of our commitment to society that we have those variant versions ready to go if need be. So that's exactly what we're doing here as well.

So we have a DNA template for the vaccine and we started the process to produce it. And again, as we said before, our expectation is for any new variant and in less than 100 days, based on immunogenicity, not vaccine efficacy, but based on immunogenicity, that we can have it ready for EUA filing within 100 days.

Jonathan Miller - *Evercore ISI Institutional Equities, Research Division - VP*

And that assumes that the accelerated approval pathway is ready and intact, and the FDA is accepting correlative protection based on immunogenicity. Do you have an expectation of when that pathway will be a little more firmed up?

Christopher J. Stevo - *Pfizer Inc. - Senior VP & Chief IR Officer*

No, not precisely. But again, we developed this pathway, an informal pathway. I don't want to use the word pathway. I'd say pathway in quotes, in consultation with regulatory authorities. So we're pretty comfortable this will be an acceptable paradigm to them.

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

Got it. By the way, Chris, just going back to something you said, emerging reports suggesting vaccines retain efficacy, were you referring to efficacy on catching COVID or efficacy on COVID hospitalizations?

Christopher J. Stevo - *Pfizer Inc. - Senior VP & Chief IR Officer*

More so for hospitalizations and severe disease, but also to a decent extent, from catching the Omicron variant. But again, this is still early days and just based on real-world evidence.

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

Got it. Okay. Excellent. Jessica, any -- Jessica, Jon, anything else on COVID vaccine? I just want to be respectful of the fact that there was only so much we could ask on the COVID vaccine side.

Jonathan Miller - *Evercore ISI Institutional Equities, Research Division - VP*

We've got Bob here. I think we should talk about gene therapy as much as we can. I think obviously, there's an infinite number of questions about the COVID situation currently, but we've spent...

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

We can do a full webinar. In fact, Chris, maybe we should do a full webinar. But we'll come back to you on that on the COVID side, but I want to be respectful of sort of the mandate you guys set out, so we'll switch to sort of gene therapy specifically from here.

Christopher J. Stevo - *Pfizer Inc. - Senior VP & Chief IR Officer*

Umer, we'll consider that, but you or one of your team will need to wear a blond wig while doing the webinar. Sorry, just remembering Mark.

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

No, it sounds good. Yes. No, no, likewise. Okay. Excellent. So maybe at a high level, Bob, first turning to you, could you lay out for us sort of the top priorities for you from the gene therapy business unit at Pfizer? What's on top of your mind as we are thinking about 2022 and 2023?

Robert Smith - *Pfizer Inc. - SVP of Global Gene Therapy Business, Pfizer Rare Disease*

Sure. Umer, happy to, and thanks for your interest in learning more about our gene therapy business. And just to give you a little bit of a background, we started investing in the space in 2014 with the view that we were looking for areas of potential scientific disruption that go beyond or, at that time, 3 core scientific platforms of small molecules, biologics and vaccines. And we did a pretty thorough strategic assessment and landed on the area of in vivo recombinant, AAV gene therapy as an area that would fit well with our Rare Disease franchise, our existing businesses with leading positions in hemophilia as an example.

So one of the objectives of our investment plan in this area was to follow a 3-pronged approach of build internal capabilities, complement it with selected acquisitions and an extensive network of partnerships with both leading academic centers and leading biotech in the space. We've also made significant investments in building out an end-to-end capability from early vector biology, preclinical research, preclinical translational research, clinical development, manufacturing, regulatory science, biologics pharma sci. And now we're getting to the point as our portfolio is maturing, getting closer to the completion of a number of pivotal studies. We're also looking to leverage our existing Rare Disease business infrastructure on a global basis to be able to efficiently deliver these medicines.

So it's a really exciting progression over a 7-year period where we basically started with de facto nothing in the space to now having a pretty robust portfolio of clinical programs, an expansive preclinical portfolio and these extensive capabilities on an end-to-end basis to be -- to effectively research, develop, manufacture and ultimately, deliver on a commercial basis.

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

Got it. And maybe just for investors that are new to the Pfizer gene therapy business, can you characterize for us how much of it was sort of in-house versus from the Bamboo acquisition?

Robert Smith - *Pfizer Inc. - SVP of Global Gene Therapy Business, Pfizer Rare Disease*

Yes. We started with that 3-pronged strategy of building internal capabilities, and that was off of the backbone of extensive investments that we have made and in both the development, the process development and the manufacturing of complex biologics on both recombinant proteins and vaccines. And so the view was to use this 3-pronged strategy where we can selectively put the pieces of the puzzle, so to speak, by partnering with these leading companies.

So for example, our first few partnerships with -- were with Spark Therapeutics for the now Phase 3 hemophilia B program, with Sangamo Therapeutics for the now Phase 3 hemophilia A program. At the time we did those partnerships, both of those programs were in the pre-IND or peri-IND period.

And we structured them. We were able to leverage the best expertise and capabilities of our partners. So both of those companies were responsible for the production of clinical trial material, for the preparation of the IND to the support and conduct of the Phase 1/2 studies.

And then we've had a gradual transition, as we built up our areas of expertise, to take those programs over into global pivotal studies. We then complemented that with a number of other partnerships. And most recently, we have done both equity investments with an option to acquire Vivet for -- on the completion of their Phase 1 study for Wilson's disease. We also, last year, made an equity investment and have a right of first refusal to 2 programs in both gene addition for PKU with homology medicines and also for their second product, which is soon to be in the clinic, it's a genetic approach for PKU.

So we've kind of used this network of both the internal programs and the partnerships to build out a portfolio where we feel confident now with the investments we've made, that we could sustainably put 1 to new -- 1 to 2 new gene therapy programs into the clinic every year for a sustainable period of time. And that's kind of on the capabilities that we've built across a network of manufacturing facilities.

So we have 3 dedicated gene therapy manufacturing facilities starting in Morrisville, North Carolina, which is essentially research-scale and research-grade. Then we have a clinical facility in Durham, which is GMP-grade where we would produce for early clinical trials, and that's a multiproduct facility. And then in Sanford, North Carolina, which was a biologics campus for manufacturing, we have 2 facilities. One is we call Stage 1, which is both for late-stage clinical and commercial manufacturing. And then we have a second, more expansive facility we call Sanford Stage 2, which is coming online with GMP production actually this month.

So we feel really confident that with the portfolio that we built, the capabilities that we've built that we'll be able to efficiently advance these programs into the clinic and potentially onto the market.

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

Outstanding. Excellent. So maybe let's turn to the highest profile gene therapy program you guys are working on, the DMD gene therapy. There's a lot to discuss on this. Jessica and I are going to tag team on this and so is Jon. But maybe just to kick things off, where are we with U.S. patient enrollment? And maybe let's start there. And why was -- like my sense is the Phase 3 was supposed to start with the U.S., but it seems like it started -- ended up starting with ex U.S. Like how did that happen?

Robert Smith - *Pfizer Inc. - SVP of Global Gene Therapy Business, Pfizer Rare Disease*

Yes, I can give you a little bit of background on that, Umer. We obviously started the study where we were able to with regulatory authority clearance and site activation in 9 countries outside the United States. We definitely have been planning all along to have the U.S. as one of the key countries within the Phase 3 program. And as we were going through the progression of required steps, particularly around the potency assay, which is a relatively complicated assay, we got additional questions from the FDA on some of the technical and detailed scientific aspects of the assay that required us to do additional work.

So we need to clear the approval of that assay by the FDA. We've now submitted a complete package of information that we think adequately addresses the questions and the concerns that they have. Right now, that package is under review and we're waiting for them to clear it. We're optimistic, as we have now continued to dose patients outside the U.S., that there's a window of time where we will also be able to dose patients in the U.S. But this is a competitive enrollment program. So if the trial fills up with the ex U.S. sites, there may not be an opportunity to have U.S. sites within the ongoing trial.

But with that said, we have dosed 19 patients in the U.S. in the Phase 1b study. So I think right now, it's really we're in a conditional mode, optimistically expecting that the package that we presented to the FDA will be satisfactory for their needs. And hopefully, we'll be able to get patients dosed in the U.S. within the next couple of months.

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

I guess at a very basic level, Bob, what would be the issue of the potency assay?

Robert Smith - *Pfizer Inc. - SVP of Global Gene Therapy Business, Pfizer Rare Disease*

I'm sorry, Umer?

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

What would be the issue with the potency assay? Is it not validated versus the other assays?

Robert Smith - *Pfizer Inc. - SVP of Global Gene Therapy Business, Pfizer Rare Disease*

No, I think it's a question that it's a novel assay. Many of the things that we're doing in gene therapy are kind of pioneering by its nature. So this is not the type of study or assay that you can take off the shelf and any laboratory could run it. It's actually a highly complex assay because in addition to looking at the expression of the protein and its translocation within a cell assay, there's also an element of both the quantitative components of it. And without getting into too much technical detail, we just needed to provide additional information to satisfy the FDA that the assay was something that was scientifically valid.

We always have had the view that on a fundamental science and technical perspective, it's an appropriate assay. And in fact, in the other 9 countries where we went through the review process to start the pivotal study, none of those other regulatory or health authorities had a concern about the assay. So this is a very specific technical aspect, and we've done all of the work that we believe is required to have the FDA review and clear it. And once we get through that hurdle, we'll be able to dose patients in the U.S.

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

Got it. Jessica, Jon, did one of you guys want to touch up on the muscle weakness or should I?

Jonathan Miller - *Evercore ISI Institutional Equities, Research Division - VP*

Sure. I think, obviously, the appearance of a muscle weakness tox in DMD especially is particularly worrisome. The -- I feel like there has been some speculation that this might be caused by immune reaction to the dystrophin itself or to the construct that you're using. Have you been able to characterize immune response to your dystrophin construct or be able to nail down what the ideology of that tox is in particular?

Robert Smith - *Pfizer Inc. - SVP of Global Gene Therapy Business, Pfizer Rare Disease*

Yes. Jonathan, maybe just -- I mean, first of all, it's a great question. One of the challenges that we have right now is we are in the conduct of a double-blind Phase 3 trial. And the protocol is pretty robust in terms of the collection of immune response information. And obviously, as a prerequisite for entry into the study, we know the genetic sequence and the mutations of all of the study participants.

And so the protocol was designed, particularly, that we would capture a robust set of information about these potential immune responses. And it's not an unexpected finding. Potentially, this is a wide-class effect where patients would have immune responses to a gene therapy transgene protein product. So we obviously had these safeguards built into the consent form. The protocol was robust in terms of data collection.

But because we're in a double-blind situation, when the safety signals were observed, the data was collected, presented in a comprehensive way to the external data monitoring committee. They did a comprehensive analysis and through a series of evaluations, they determined that there were particular deletions. And in our program, exons 9 to 13 and 29 and 30, that we're triggering potential immune responses.

So I think the hypothesis here is that in these particular cases, they are having immune response to the mini-dystrophin protein product. So there were 3 cases of muscle weakness, 2 with myocarditis. They were all treated with increased doses of steroids. All the boys recovered or are in the stages of recovering. So I think we had all the appropriate precautions and safeguards in place.

Now with that said, what we've done is on the advice of the external data monitoring committee, the principal investigators, we put appropriate protocol changes in place to not have those boys with those particular mutations eligible for the subsequent enrollment in the study. And now that we've gone through that process, the study sites are up and running where we have the approvals to do so. And as I said, we hope to complete the enrollment within the next couple of months.

Now we also -- with all of that said, we're going to go back and do some really detailed analysis and with the advice of experts in the field, with the input from advisory boards that we've already set up, to really get down to the heart of the matter because this is going to be an area that's not going to be -- at least my estimation and this is more of my personal view, is that in the pioneering nature of gene therapy, there are going to be things that are anticipated risks that will become real risks, and we need to do the best assessment based on the science and how best to address immune responses in these cases when they do arise. So I feel confident and optimistic that we'll be able to better understand and better characterize this risk going forward and put the appropriate safeguards in place to protect patients.

Jessica Hui - *Evercore ISI Institutional Equities, Research Division - Equity Research Associate*

So Sarepta also saw muscle weakness events driven by specific mutations. So is it possible that as the trial progresses, we might see additional events of muscle weaknesses driven by other mutations that will then also need to be excluded, thus further narrowing the pool of DMD patients who are eligible for this therapy?

Robert Smith - *Pfizer Inc. - SVP of Global Gene Therapy Business, Pfizer Rare Disease*

Yes. I think it's -- just first of all, it's a complicated question to answer because we're in a double-blind Phase 3 study and these events occurred in our Phase 3 study. So we're a little bit limited in what we can see, obviously, from our side of the blind. I think the expectation is that based upon the sequences of the transgene and the expected mini- or micro-dystrophin protein that expressed, there is sequence homology across the remainder of the gene with other proteins in the body.

So they may not be in this situation where the other sequencers are going to present themselves as a foreign epitope. Now a lot more scientific work needs to be done to address that and understand them more completely. But there are some very plausible scientific hypotheses that lead us to the conclusion that by eliminating mutations where we have seen an immune response, that we'll be able to limit the number of study participation and probably potentially limit the number of these epitopes across different types of transgene, not just in mini-dystrophin but probably in other gene therapy transgene product.

So we very much view this as a potential class effect. We're early in the investigation and evaluation of, and I think there will be a lot more scientific information that comes out over this over the coming months and quarters.

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

Bob, did you guys ever look at anti-drug antibodies?

Robert Smith - *Pfizer Inc. - SVP of Global Gene Therapy Business, Pfizer Rare Disease*

Sorry, Umer, just repeat that because...

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

Oh, sorry. Did you guys ever look at anti-drug antibodies or anti-gene therapy antibodies?

Robert Smith - *Pfizer Inc. - SVP of Global Gene Therapy Business, Pfizer Rare Disease*

Yes. In both the Phase 1b study and also in the Phase 3 study, there are a whole variety of immune response data that we've been collecting.

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

Okay. I guess the...

Jonathan Miller - *Evercore ISI Institutional Equities, Research Division - VP*

To clarify, Bob, the -- neither -- none of these potentially worrisome mutations that are now being excluded from the Phase 3 was -- did nobody in the Phase 1 -- none of the participants in the Phase 1 have those particular deficits in their dystrophin? And then I guess the follow-up is if you expect this to be a class effect not just in DMD but across all gene therapies where a patient might be missing epitopes that you've been seeking to supply, how does this limit the potential of the broader class beyond -- obviously beyond DMD? But how much extra work is this going to entail?

Robert Smith - *Pfizer Inc. - SVP of Global Gene Therapy Business, Pfizer Rare Disease*

Yes, why don't I answer the first question first, Jonathan, then I'll come back because maybe I might have miscommunicated a little bit the potential of the risk in that broader statement. So in the Phase 1b study, we did have patients with similar mutations to those that had the immune responses in the Phase 3 study. Fortunately, they did not have muscle weakness or myositis.

And when we get into the first quarter of 2022, we'll be giving a more comprehensive update on the 52-week data across all the study participants in the Phase 1b study. So more to come on those particular patients in that update.

And then kind of on your second question, maybe just to better qualify and describe my comments, one of the issues with gene therapy is you're going to be -- especially in the area of gene replacement or gene addition for a patient who has a missing gene or an older gene that doesn't produce the correct physiologic protein, there's a risk that if their body hasn't seen the transgene product protein before that they may have an immune response to it.

Now these are kind of theoretical risks. And depending upon the nature of the trial, the transgene product, the patient population, it may or may not be a risk that actually materializes. So kind of keep it in that context. And I think it shouldn't have any dampening effect on the potential utility of gene therapies. It's just a risk that is theoretical, that may or may not materialize in any given program. And that's why I think the study protocols are designed to have careful monitoring and appropriate management in the event there is an immune response. So hopefully, that's clarified.

Christopher J. Stevo - *Pfizer Inc. - Senior VP & Chief IR Officer*

Sorry, but, Jon, I'm just going to -- oh, sorry, with recombinant proteins and monoclonal antibodies, right, we've seen anti-drug antibodies or anti-protein antibodies all the time, right? And that doesn't mean they necessarily neutralize the effect of what you're trying to do. So again, this is something that's been widely seen before, and it's just something that we have to manage through and we will.

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

Right. By the way, Chris, can I just mention? There's a couple of investor questions from some very important investors that were a follow-up to some of the stuff you said at the start of the session on COVID. We'll come back to that in about 5 minutes or so. But I'll finish the gene therapy session now first.

Bob, if I may just switch gears just a little bit and ask these -- the children in these trials, they're at a growing age. And I guess how should we think about whether the -- we should get separation in the 12-month study or not?

Robert Smith - *Pfizer Inc. - SVP of Global Gene Therapy Business, Pfizer Rare Disease*

In terms of the...

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

In functional scores, the NSAID?

Robert Smith - *Pfizer Inc. - SVP of Global Gene Therapy Business, Pfizer Rare Disease*

Yes. I think for the Phase 3 study and certainly based upon what we've seen and reported to date on the Phase 1b study, it looks like we are seeing a benefit in terms of functional improvement versus age match natural history. We'll certainly be presenting more complete data set with 52-week follow-up on the Phase 1b study, Umer, and you'll see that in the first quarter of 2022, so just a few months away.

And I think based upon that data and in the design of the protocols, we're expecting that with the homogeneous age stratified across some baseline functions, that we should be able to demonstrate a meaningful clinical benefit in terms of both function and then a number of secondary end points on biomarkers. So we're pretty optimistic about the program.

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

Okay. I guess, Bob, said another way, I'm just referring to how in the Sarepta study, for patients above a certain age, they don't necessarily -- I think it was above 6 years old, they don't see much of a functional benefit. And even in some of the data you guys have shown, it seems like the trends at -- the trends in patients above the age of 9, they weren't necessarily on the improvement side. So do you guys feel reasonably comfortable on being able to show functional benefit across ages?

Robert Smith - *Pfizer Inc. - SVP of Global Gene Therapy Business, Pfizer Rare Disease*

And I think -- as I said, we're going to be presenting a more complete data set on the Phase 1b. So that will be the extent of the data that we'll have on age groups in the ambulatory studies over the age of 8. So the -- in the Phase 3 studies, we're looking at a population of 4 up to less than 8. So we won't have additional data above 8-year-olds in the pivotal study.

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

Got it. Okay. Got it. That's very important. And then perhaps before we round it off, any difference to expect on clinical versus commercial batches? And Jessica, if you want to jump into any last-minute gene therapy questions before we pivot back to COVID?

Robert Smith - *Pfizer Inc. - SVP of Global Gene Therapy Business, Pfizer Rare Disease*

Yes. I think we're -- from the work that we've done in terms of the specifications for the clinical material versus the commercially representative material is very similar. We're not expecting that, that's going to be a variable in any type of variability of patient responses. And as I said, we have a very comprehensive biologics pharma sci group as well as our Pfizer Global Supply group, who, I think, are at the cutting edge of gene therapy manufacturing.

So we feel that this is actually a strategic advantage to us, not just in clinical development as we can move seamlessly through various stages across our supply network but also in terms of the overall ability to supply on a commercial basis with capacity that's probably unmatched in the industry.

Jessica Hui - *Evercore ISI Institutional Equities, Research Division - Equity Research Associate*

And I have one question on the Phase 3 trial design. Sarepta has indicated that their EMBARK trial has a fairly narrow inclusion criteria in order to reduce variability and increase probability of success, including -- only including patients with the time to rise of less than 5 seconds and excluding patients with mutations at exon 45 because they have milder phenotypes. Is this also a strategy that Pfizer is employing? Or does Pfizer have a broader eligibility criteria?

Robert Smith - *Pfizer Inc. - SVP of Global Gene Therapy Business, Pfizer Rare Disease*

Yes, we have not included those 2 specific exclusion criteria that you mentioned, Jessica. But with that said, we do have a very robust program, probably the most robust program with both age and other baseline stratification, so that -- our intent is that we're going to have a very homogeneous pool for both to treat it in the placebo and then for the placebo patients who would subsequently cross over. So we're confident in the trial design. We're not expecting that there's going to be any issues with the quality of the data and the resulting statistics that come out of it.

Jessica Hui - *Evercore ISI Institutional Equities, Research Division - Equity Research Associate*

Got it.

Jonathan Miller - *Evercore ISI Institutional Equities, Research Division - VP*

And Bob, before we head back to COVID, I know Umer is chomping at the bit to get back there, but I would love your thoughts, high level, on redosing. And obviously, I'm asking this question in the context of some of the longer-term data from various gene therapy competitors on a number of different platforms that have shown pretty material fade of efficacy over time. And especially as I think of the gene -- the DMD gene therapy program, where you've got growing children with a serious risk, I think, of dilution of effect over time, I wonder what your latest thoughts are about the potential for redosing and what the strategy might be to enable that if it does seem to be a problem.

Robert Smith - *Pfizer Inc. - SVP of Global Gene Therapy Business, Pfizer Rare Disease*

Yes, it's a great question, Jonathan, and something that we've been thinking about and I know others in the field have also been thinking about is every technology platform, recombinant AAV included, has inherent benefits and inherent limitations. And one of the inherent limitations with recombinant AAV is the fact that patients may have preexisting neutralizing antibodies.

And when they are dosed with a recombinant AAV capsid, that they may develop neutralizing antibodies to prevent redosing. So we've been looking at a variety of technologies, first to attack the challenge of limiting neutralizing antibodies to expand upon the potential eligible pool of patients. And then depending upon the outcomes of those types of work, there may be ways that we could use that approach or different approaches to address redosing.

And clearly, one of the challenges with the viral-based vectors is that you have these immune responses as a challenge. There's also alternative technologies that we're evaluating that don't require the use of viral vectors. They're a little bit further out, but with our view of building a long-lasting, long-term portfolio of gene therapy products, especially given the transformation that potentially they may deliver, we're looking at all types of technologies that may enhance and expand upon our existing technology base. So exciting area of science. And certainly, these challenges are well understood, and there's a lot of approaches that could potentially surmount them to the benefit of many, many patients.

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

Got it. Excellent. Maybe in the last couple of minutes or so, Chris, there's 2 questions that I have in front of me and if there's any other, please e-mail me for investors on the line. One of them is, you mentioned some real-world instances, which are suggestive of efficacy holding in, at least on severe disease against Omicron. Can you point us to some? Or if you want to e-mail me and I can follow up off-line with the investor, if that's more...

Christopher J. Stevo - *Pfizer Inc. - Senior VP & Chief IR Officer*

Absolutely.

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

Okay, you can -- okay, we can follow up off-line. The other one is, Chris, it's my sense that Pfizer is producing something like 250 million doses across the manufacturing network right now, 250 million doses per month of the COVID vaccine. And in a scenario where there's an emergency use authorization of a variant-specific vaccine, what investors wonder is, are you committed to continuing to produce vast majority of those 250 million on the existing COVID for some contracts you have or you could switch pretty fast? Like how does that work? And to what extent -- what percentage of the manufacturing network can be switched?

Christopher J. Stevo - *Pfizer Inc. - Senior VP & Chief IR Officer*

Yes, Umer, thank you for asking that question because I think there's been a lot of confusion about this so let me be completely clear, that our contracts with the governments that we've signed are not to deliver any specific version of COVID vaccines, right? It's essentially to deliver what is needed at the time, right?

So if the Beta version or the Delta version we produced were needed, then those contracts could have seamlessly switched over to those. And there wouldn't have -- the governments and the people in those countries would not have been lacking the right vaccines. So with Omicron, if we determine that there is a need, we can switch over our production pretty quickly. And again, next year, we're talking about 4 billion doses, right, so that's roughly 1 billion doses a quarter.

And the production process for the product, including like release time and things like that, is down to about a month right now. So we could switch pretty quickly if we determine there was a need and at reasonably large scale within a relatively short period of time.

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

Got it. And I guess my -- I guess what people -- if there is enough demand for it, could you switch all of it to Omicron-specific variant for, let's say, a few months and just produce -- that's all you guys produce?

Christopher J. Stevo - *Pfizer Inc. - Senior VP & Chief IR Officer*

Absolutely. So if -- like with the Delta variant, right, where the Delta variant in -- before Omicron became essentially the predominant variant everywhere, if we had needed to produce a Delta-specific variant, yes, we could have done that. So that's not an issue.

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

Got it. And Chris, the counter-scenario that people have also asked, and this is a pre-Omicron question was, if governments are massively overbuying versus their end user demand, and I'm talking U.S., Europe and Australia, et cetera, in particular, in 2022 and 2023, is there a way they could say, "Well, hold off on these doses, give it to me in 2025, 2026," how would that whole dynamic work?

Christopher J. Stevo - *Pfizer Inc. - Senior VP & Chief IR Officer*

Yes. So the contracts that we've signed are firm contracts, right, where there is uncertainty, there is options available to the governments in some of those. So again, the U.S. government in some of their contracts had some options, which they then subsequently exercised. But our contract with the U.S. government, we expect to run until April of next year roughly, when we think they will have taken delivery of all the doses under that contract.

So there -- all these contracts do have, as I said, provisions about the options and some leeway with regards to the -- when they have to take deliveries. But everything that is firm, again, is firm, so it has to be taken at some point. As Frank would say, it's not a question of if we would be paid for the doses, it's more a question of when. So we haven't been specific whether that could mean that they could delay delivery for years.

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

Sounds good. Fantastic. Okay. This is great. Jon, Jessica, anything we missed? I want to be very respectful of the time here as well.

Jonathan Miller - *Evercore ISI Institutional Equities, Research Division - VP*

I feel like we would be remiss not asking any questions about the oral, so maybe one on that. I think we've obviously been tracking the results there very carefully, and we can't wait to see the post-exposure prophylaxis and the standard risk study, I think those will be very relevant for the kind of the broadening of the patient population there. Do you expect at this point to have an AdCom for the current approval?

Christopher J. Stevo - *Pfizer Inc. - Senior VP & Chief IR Officer*

No, that's not our expectation, and we've not been notified by the FDA that there would be an Advisory Committee. And just to be clear, right, when you look at the antibodies that were granted Emergency Use Authorization or some of the other antivirals, there were not necessarily advisory committees that were required there. So no.

Jonathan Miller - *Evercore ISI Institutional Equities, Research Division - VP*

Except for one of them. Maybe the one other question that we've been getting a ton of, obviously, unlike some of the other antivirals in development or certainly like the antibody, because you're familiar with ritonavir for PK reasons, there are worries about drug-drug interactions. Obviously, we understand it's a short course and for many drugs, dosing -- where there might be drug-drug interaction, dosing can be interrupted. But on a practical standpoint, have you gotten any feedback from [docs], how big a liability is the potential for drug-drug interactions with ritonavir? And what proportion of the population from a practical standpoint do you think might be affected by this?

Christopher J. Stevo - *Pfizer Inc. - Senior VP & Chief IR Officer*

Yes, just one slight correction before I answer that. It's not actually coformulated with ritonavir, it's co-administered with ritonavir but just a very technical point. But beyond that, in terms of drug-drug interactions or patients that wouldn't be eligible to take it, we think is a practical matter, that's a very, very small percentage of patients that couldn't adjust the dosage of their current medications to take into account this. And again, some medicines like Eliquis, for example, already have instructions in their label when used with CYP inhibitors of this type of how to adjust the dosing.

And in other cases, if it's an infectious disease specialist, that it might be like an HIV or hep C medicine that could interact with this, they know how to adjust that. Or in other cases, patients that take a drug holiday for 5 days depending on what the drug is. So again, the overarching theme is that we think that the portion of patients would not be eligible to take this at all would be vanishingly small.

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

Outstanding. Chris, Bob, thank you so much. Best of luck with the gene therapy business and with everything else. I'll be in touch. Chris, I'll follow up with you over e-mail on that thing.

Christopher J. Stevo - *Pfizer Inc. - Senior VP & Chief IR Officer*

Great. Thank you so much, Umer. Thank you, Jon, Jessica. Thank you. Bye-bye. Good night.
