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PFE.N - Pfizer Inc Analyst and Investor Call to Discuss Pfizer-BioNTech COVID-19 Vaccine and Pfizer's Novel COVID-19 Oral Antiviral Treatment Candidate

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OVERVIEW:

PFE provided an update about Pfizer-BioNTech COVID-19 Vaccine and PFE's Novel COVID-19 Oral Antiviral Treatment Candidate.

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PRESENTATION

Operator

Good day, everyone, and welcome to Pfizer's Analyst and Investor Call to discuss the Pfizer-BioNTech COVID-19 vaccine and Pfizer's novel COVID-19 oral antiviral treatment candidate. Today's call is being recorded.

At this time, I would like to turn the call over to Mr. Chris Stevo, Senior Vice President and Chief Investor Relations Officer. Please go ahead, sir.

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

Thank you, Sophia. Good morning, everyone. I'd like to welcome you all to Pfizer's investor event to discuss our COVID-19 vaccines and therapeutics franchise.

DECEMBER 17, 2021 / 1:30PM, PFE.N - Pfizer Inc Analyst and Investor Call to Discuss Pfizer-BioNTech COVID-19 Vaccine and Pfizer's Novel COVID-19 Oral Antiviral Treatment Candidate

Presentation at today's investor event includes forward-looking statements about, amongst other things, our efforts to combat COVID-19, including our development of a vaccine to help prevent COVID-19 and our investigational protease inhibitors, our anticipated future operating and financial performance, business plans and prospects and expectations for our in-line products and product candidates.

By their nature, all statements about future events and expectations for our in-line and pipeline products are forward-looking. Each forward-looking statement contained in this presentation is subject to risks and uncertainties that could cause actual results to differ materially from those projected in such statements.

Additional information regarding these factors appears on this slide and under Risk Factors and forward-looking information and factors that may affect future results in our 10-K and 10-Qs. The forward-looking statements in this presentation speak only as of the original date of the presentation, and we undertake no obligation to update or revise any of these statements.

On this slide, you can see our presenters today. I won't read everyone's title, but Mikael will begin the call with an introduction, and then he will turn it over to Nanette Cocero and Kathrin Jansen from the Vaccines team to discuss our COVID vaccines. They will be followed by Angela Lukin, Liesa Anderson and Jim Rusnak from the Hospital business unit to speak about PAXLOVID.

Finally, Frank will make some comments on updated COMIRNATY 2022 guidance, and then we will have a Q&A session. During the Q&A session, besides the presenters, Luis Jodar and Bill Gruber from the Vaccines business will also join us.

With that, I will turn the call over to Mikael.

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

Thank you, Chris. Good morning, everyone. It's remarkable to see the progress we have made since the early days of the pandemic in 2020. Back then, not a lot was known but it was evident that vaccines and treatments would be the tools to take on SARS-CoV-2.

Today, around the world, there are vaccines and treatments available, yet COVID-19 continues to prove a formidable foe. Pfizer has kept our scientific engine focused on anticipating the evolution of the virus, preparing for different scenarios. I want to discuss the unmet needs informing our thinking.

In terms of scientific needs, we have seen SARS-CoV-2 mutations emerge and our focus is now on Omicron, which I will discuss shortly. Waning immunity and boosters are also an important consideration. Pfizer's analysis from the Phase 3 study and our ongoing real-world effectiveness studies have shown a decline in efficacy, particularly against symptomatic infection over time. The data are illustrating the impact of a booster and that our vaccine works best as a primary regimen of 3 doses. We will continue to follow the science and epidemiology to determine the need and impact of additional potentially annual doses in the future.

Like we shared last week, preliminary laboratory studies demonstrate that the 3 doses of the Pfizer-BioNTech COVID-19 vaccine neutralized the Omicron variant, while 2 doses show significantly reduced neutralization titers. We will continue to collect more laboratory data and evaluate real-world effectiveness to assess and confirm protection against Omicron and inform the most effective path forward. Kathrin will discuss this in greater detail.

There are also potential effective oral therapies on the horizon. We know that some available therapies do not work well against significant mutations. PAXLOVID is focused on the protease of the SARS-CoV-2 enzyme, which is not as likely to mutate. Therefore, we believe it's unlikely that we will see resistance or reduced efficacy as a result of Omicron or other variants. We continue to study this and are encouraged by early data.

Lastly, it seems like over the next year or 2, some regions will transition to an endemic model, while other regions will continue in pandemic mode. When and how exactly this happens will depend on evolution of the disease, how effectively society deploys vaccines and treatments and equitable distribution to places where vaccination rates are low. The emergence of new variants could also impact how the pandemic continues to play out.

On the societal side, the focus should be on helping overcome barriers to vaccination and treatment. The vaccine hesitancy is prevalent in many parts of the world, in some countries, more prevalent than others, leading to concerning low level of vaccination in some communities.

Pfizer and BioNTech are evaluating our COVID-19 vaccine in kids younger than 5 and down to 6 months. Potential expanding the availability of COMIRNATY to people in all age groups will be an important step in the efforts to control the pandemic. And nobody is protected unless everyone is protected.

Access to vaccines and therapies in developing nations continue to be a top priority for Pfizer. We have pledged to provide 2 billion doses of our COVID-19 vaccine to low- and middle-income countries in 2021 and 2022, at least 1 billion doses each year.

Finally, we need to plan ahead and think about how we manage the burden of COVID-19 over the next decade. Planning for future pandemics, while managing the current one, is critical. We will continue to take a leading role in this.

While we are proud of what we have accomplished, we can't be complacent. And Pfizer is working to anticipate virus with a robust surveillance effort and process to address variants of concern with an updated vaccine, if needed. We are constantly monitoring for emerging variants that have the potential to escape protection from our vaccine or resist treatment. We generally analyze whether BNT162b2 elicited sera effectively neutralize emerging viral variants using both pseudovirus and recombinant SARS-CoV-2 with mutations.

For PAXLOVID, we are conducting predictive modeling among other tools for surveillance. At the same time, we're closely monitoring the real-world [impact of] (added by the company after the call) COMIRNATY in Israel and across the world. If needed, we have the ability to modify our existing vaccine to encode for a different variant.

We have already applied this process to multiple variants of concern, including Beta, Delta and now Omicron. We are advancing updated prototype variant versions of our COVID-19 vaccine that use a new construct based on studies of the Beta and Delta variants. These studies provide valuable data that regulators can evaluate should an update to the current vaccine be needed for any future variant of concern.

For Omicron, we are wasting no time and have already begun work on a DNA template tailored to the sequence of Omicron, a critical step in the process of advancing a variant version of our vaccine if, in fact, we find one is needed. We started to develop an Omicron-specific COVID-19 vaccine. The development will continue as planned if a vaccine adaptation is needed to increase the level and duration of protection against Omicron. First batches of the Omicron-based vaccine can be produced and be ready for deliveries within 100 days, pending regulatory approval.

Beyond the vaccine, we know COVID-19 mutations can be resistant to some treatments that are focused on the spike protein expressed on the surface of the virus. PAXLOVID was developed with mutations in mind. Recent in vitro data, which Liesa will discuss, confirmed that PAXLOVID is a potent inhibitor of the Omicron 3CL protease, which, combined with existing in vitro antiviral and protease inhibition data from other variants of concern, including Delta, indicates that PAXLOVID will retain robust antiviral activity against current variants of concern as well as other coronaviruses.

Now I want to discuss Pfizer's integrated strategy with COMIRNATY and PAXLOVID. We are the only biopharmaceutical company with an integrated approach that includes prevention with a vaccine, COMIRNATY, and intervention with an oral antiviral candidate, PAXLOVID.

Let's start with COMIRNATY on the left. The Pfizer-BioNTech COVID-19 vaccine is now available for people starting at 5 years of age. We have also received the booster recommendation for people 16 and older in the U.S. and other countries. Our vaccine has a favorable tolerability and safety profile. Pfizer has taken a careful approach to determine the vaccine dose that could create the preferred balance between tolerability and a protective immune response for each age group.

While vaccination remains the best tool, we have to help protect lives and prevent disease. We know that in parts of the world, there is resistance to vaccination. And in other places, the logistics for consistent boosting do not exist. That is why it is important to have treatment options available to support those who become ill from or exposed to the virus. Our antiviral candidate, PAXLOVID, has demonstrated strong efficacy in a Phase 2/3

trial in high-risk patients with mild to moderate disease, and we have a robust ongoing development program, including studies in standard risk population who are either vaccinated or unvaccinated, and also for prophylaxis in exposed individual.

As long as COVID exists, effective treatments are critical due to many factors. People with compromised immune system who don't have a strong response to the vaccine; different rates of vaccination across geographies and population; disease evolution, including new variants; need for a therapy for breakthrough cases among patients; and of course, there is vaccine hesitancy, which continues to put so many at risk of infection.

Having public health tools and options to manage both scenarios will be key. COMIRNATY, and if authorized or approved, PAXLOVID, can be very synergistic. Along with our robust COVID-19 surveillance approach to help evaluate the evolution of the pandemic, COMIRNATY and potentially, PAXLOVID, can help Pfizer stay vigilant against the virus.

Pfizer's global supply engine will be essential as we work to meet the large demand for COMIRNATY and, if authorized or approved, PAXLOVID. From the start of the pandemic, the challenge wasn't just developing vaccines. We also had to make it and by the billions.

Pfizer invested more than \$2 billion at risk in our COVID-19 vaccine development program, with \$500 million of that spend on scaling up of our manufacturing capabilities before we knew the results of our clinical trials. But with years of manufacturing experience on our side, we have arguably developed the most efficient vaccine in manufacturing capability that the pharmaceutical industry has seen.

Led by my colleague and friend, Mike McDermott, and thanks to the ingenuity and hard work of Pfizer scientists, engineers and skilled workers and multibillion dollars of investment, Pfizer has already manufactured 3 billion doses this year, of which, at least 1 billion will go to middle- and low-income countries. We expect to manufacture 4 billion doses in 2022.

Ramping up to a potential 4 billion doses in 2022 required numerous improvements, iterations and continued investment in our manufacturing capabilities. So what did it take? Let me share just a few examples. We reduced our COVID-19 vaccine manufacturing timeline from approximately 110 days from start to vial ready to an average of 60 days, an almost 50% improvement. We increased the number of sites from 6 to 30, utilizing a global network of internal sites and CMOs. We optimized the design of machinery and storage solution. An example is the prefabricated formulation for dry ice operation. Pfizer developed packaging and storage innovations fit-for-purpose to meet the needs of our global network, including specially designed temperature-controlled thermal shippers utilizing dry ice to maintain the recommended temperature conditions. We have also worked to continuously expand capacity, including bringing new suppliers and contract manufacturers. You can find more information on how much effort it took to do this in our Appendix slides.

Pfizer and BioNTech's global COVID-19 vaccine supply chain and manufacturing network now spans 4 continents. As of December 14, more than 2.4 billion doses of COMIRNATY have shipped to more than 162 countries and territories in every region of the world. We have a 95% success rate in getting shippers containing the Pfizer-BioNTech COVID-19 vaccine to their destination within all prespecified parameters.

This same ingenuity is at work for PAXLOVID. Our plan is to manufacture 80 million treatment courses in 2022. We have been able to accelerate our expected deliveries by again making important investments and innovation across the board.

We have conducted a massive network expansion to 14 sites including 2 API and drug substance sites, 3 drug product sites, 3 packaging sites. This includes a combination of CMOs and internal sites. We have implemented process improvement, resulting in higher yields, bigger batches, reduced cycle times, which enabled to double our API output.

At the same time, PAXLOVID requires no special storage conditions and can be stored at room temperature. Pfizer's global supply will be essential as we work to meet the large demand for COMIRNATY and PAXLOVID, if authorized and approved. We have the expertise and flexibility for our manufacturing capacity to potentially meet the demand year-over-year in the next decade.

I want to spend a few minutes discussing what we call our Lightspeed approach to vaccines and treatments. What we were able to do with COMIRNATY and PAXLOVID didn't just happen by chance. As you probably all know, the last decade at Pfizer has been one of deep R&D transformation and evolution. We have been revving up our engine of innovation and making profound changes across multiple dimensions, including our deep

understanding of biology, doubling down on exciting new modalities and the efforts to empower our scientists for critical decision-making on their program.

COMIRNATY and PAXLOVID are not one-offs. They are the results of a systematic approach to R&D that is embedded in everything we do today. And we are now applying this lightspeed approach to other areas of our pipeline. Lightspeed development entails pulling multiple levers.

While not all programs will lend themselves to every dimension, there are different strategies to move faster through the process. First, parallel testing. This is something both the vaccine and the protease inhibitor exemplified. We designed and tested multiple candidates of the Pfizer-BioNTech COVID-19 vaccine, deciding on the strongest one.

Second, expert dose selection. As mentioned previously, something we approached meticulously at Pfizer, relying on decades of expertise in vaccines and medicines design and development. Our scale and expertise are also critical to implement trials faster as well as long-standing relationship with study sites.

Third, streamlined governance for rapid decision-making. We have established a simplified governance model for lightspeed programs that allows decisions to be made nearly in real-time. We have multiple disciplines and levels of management together in one meeting without lengthy pre-meetings and with a single leader empowered to endorse critical decisions.

Fourth, investment at risk. Few companies can deploy capital to scale up commercial manufacturing early in development. Pfizer spent \$3 billion at risk for the development of the Pfizer-BioNTech vaccine and PAXLOVID. This is, and will continue to be, a strategic capability at Pfizer which we will leverage to win early when we see promise.

Fifth, faster regulatory collaboration. This is a key element of the paradigm that we hope will help us accelerate the pace of innovation. The U.S. FDA has established a new model of working with much faster interactions with sponsors. Our hope is that this will help us establish a new normal for working together. However, there is need to ensure the same sense of urgency in other diseases outside of the pandemic.

Pfizer is supplying the lightspeed approach beyond COVID-19 vaccine and oral protease. We are applying different elements of this paradigm to our next-generation mRNA influenza program, our RSV vaccine candidate, elranatamab, a B cell maturation antigen, BCMA/CD3 bispecific antibody in patients with relapsed refractory multiple myeloma. Now that we've seen what's possible, the lightspeed mentality exists deep within each of our research and development teams.

We see each of our research areas as individual biotech company with autonomy and nimble structure to research multiple programs at once powered by the resources of a large global company. And every successful lightspeed project provides resources to develop the next one, potentially creating a virtuous cycle for patients and shareholders.

So we are more confident than ever in Pfizer's future for what we believe is an industry-leading innovative pipeline, increasingly driven by our disruptive drug development paradigm.

With that, I will turn it over to Kathrin.

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

Thank you, Mikael. It is a pleasure to speak with everyone. My name is Kathrin Jansen. I'm Senior Vice President and Head of Vaccine Research and Development at Pfizer.

Today, I will update you on the enormous progress we have made and what we learned since we last shared data with you on our COVID-19 mRNA vaccine developed in partnership with BioNTech.

I first read about SARS-CoV-2 from my New York City apartment in December 2019. I've worked in vaccine research and development for 30 years and have never experienced anything like this pandemic that is unfortunately still claiming too many lives. We have made tremendous progress, and I want you to know that the people behind the data shared today, our internal R&D colleagues as well as external partners, are all committed to help transform the COVID-19 pandemic into a manageable endemic.

I had the privilege of speaking with you at our investor event in September 2020. Since then, the Pfizer-BioNTech COVID-19 vaccine has demonstrated high efficacy against COVID-19 in randomized controlled clinical studies in individuals 5 years and older. In the U.S., we received an EUA for 16 and older in December 2020 and EUA for 12 to 15 in May 2021 and an EUA for 5 to 11 in October 2021 and are now authorized to protect populations ages 5 years and older. And we are the first to have received full licensure in the U.S. of our vaccine for 16 years and older population in August 2021. I'm proud to say that BNT162b2 is the only COVID-19 vaccine approved or authorized in individuals 5 years of age and older.

Earlier this year, we reported COMIRNATY's 91.3% vaccine efficacy after 6 months follow-up. When carefully examined in this efficacy data, we noticed some evidence of declining efficacy over time, as you can see here on this graph. Real-world effectiveness studies in the U.S., U.K. and Israel showed increasing breakthrough cases over time, while protection against severe disease remained high. These data were the basis of announcing earlier this year that booster doses may likely be needed after 6 to 8 months to maintain high-level protection against COVID-19.

As you can see, the appearance of higher breakthrough cases also correlated with a reduction in virus neutralizing antibodies at 8 months post dose 2 compared to 1 month post dose 2 shown here for both the wild-type and Beta variants. Thus, waning neutralization titers could be considered a proxy for waning effectiveness over time.

To see whether a third dose of 30 micrograms would restore the 1 month post dose 2 neutralization titers, Phase 1 clinical trial participants who received 2 doses of BNT162b2 received a third dose of the vaccine. Using the data in the 65- to 85-year-old cohort as an example, shown here, a third dose not only restored post dose 2 titers for wild type, but actually increased the virus neutralization titers by over sevenfold for wild type and over twentyfold for Beta.

In addition, the gap between wild-type and data titers that we saw at 1 month post dose 2 was now greatly diminished, indicating maturing B cell responses resulting in broader variant neutralization capability.

But how about Delta, that is now the most prevalent variant globally? Here, we show that for both 18 to 55 and 65 to 85-year-old cohorts, the third dose augments the neutralizing antibody responses for both wild type and Delta variants to levels that exceeded those after 2 doses and for which high level protection was observed. Given this data, we wanted to validate the restoration of high levels of efficacy of BNT162b2 in a randomized clinical study and determine vaccine effectiveness against Delta that today is still the dominant variant globally.

We asked clinical trial participants in our ongoing Phase 3 program, who have received 2 doses of COMIRNATY, to return for third dose, which was between 6 to 8 months following their second dose. We randomized participants to receive a third dose of BNT162b2 or placebo. When analyzing the data approximately 2.5 months post third dose, we saw that the third dose of the vaccine had a relative vaccine efficacy of 95.6% compared to 2 dose participants. These data confirmed that the third dose restores high-level efficacy and also demonstrated that the vaccine is highly effective against the Delta variant as the majority of cases observed were caused by the Delta variant.

We believe that these data are indicative that longer-term protection requires 3 vaccine doses and potential future regular boosters. Based on the strength of our data, we received emergency use authorizations for a third dose for adults 18 and older in November, and an additional authorization for a third dose in 16 and 7-year olds earlier this month.

Now let's talk about variants. SARS-CoV-2 has been changing its spike protein and other sequences since day 1, and large number of variants have emerged over the last 2 years. We are part of a surveillance system, including outside partners, to monitor closely vaccine effectiveness against these variants using recombinant virus neutralization assays. And we are gathering real-world effectiveness data.

On this graph, you can see that BNT162b2-elicited sera effectively neutralized a broad range of SARS-CoV-2 spike variants, including variants of concern after 2 doses. And you can see, this is true whether we are talking about the wild type variant, the previously prominent Alpha variant, the

Beta variant, or the more recent Delta variant. I would highlight that even in the circumstance where we noted a threefold lower neutralizing response of the Beta variant compared to wild type, high efficacy was observed in the South African cohort from our pivotal trial.

While these data are reassuring, we are now faced with Omicron, a variant that has accumulated far more mutations in the spike protein sequence than any other variant to date. We are still learning about the disease severity of Omicron, the extent to which it will spread, and to what extent BNT162b2 will provide protection as data are becoming available over the next few weeks to months.

And why does Omicron give us all the cause for concern? As you can see on this table, the Omicron variant contains a larger number of mutations than any other variant we have previously seen. Omicron has mutations in common with other variants such as Alpha, Beta and Delta. However, it contains new mutations that we have not seen previously.

The good news is that human CD8 T cell epitopes are largely preserved in Omicron, which we hope helps prevent severe COVID-19. However, as you see on the next graph, it appears that 2 doses of BNT162b2 induce much reduced neutralization titers to Omicron compared to wild type or other variants.

My friend and colleague, Dr. Ugur Sahin, presented this slide last week. BioNTech ran a pseudovirus neutralization test comparing the neutralization titers of BNT162b2 to a number of spike variants, including wild type, Beta, Delta and Omicron shown here in the purple bars. As you can see, after 2 doses of BNT162b2, the neutralizing antibody titers to Omicron are much reduced, over twenty five-fold, compared to wild type. Please note that these titers are roughly in line with one we have observed after a single dose of BNT162b2, and where we did observe approximately 50% efficacy between the first and second dose in our pivotal trial.

Very encouraging are the neutralization titers after 3 doses of BNT162b2 shown in the right path of the graph. Three doses of the vaccine restore neutralizing antibody titers to comparable levels across all variants, including Omicron, and to levels that were shown to be highly protective after 2 doses against all previous variants that emerged over the last 2 years.

These are preliminary pseudovirus assay data, and we are in the process of assessing BNT162b2 sera in our standard plaque reduction neutralization assay using recombinant viruses. And we are collecting real-world effectiveness data from the U.S., U.K. and Israel that will provide us the opportunity to judge whether a vaccine update is needed. So are we ready for potential vaccine update if needed? The answer is yes.

First of all, we have announced that we can update our vaccine to any variant if needed in approximately 100 days. Second, we have been working on a regulatory pathway that would allow us to a vaccine with minimal additional clinical data. We are still working with regulatory agencies on some details.

To create a regulatory pathway, we are conducting clinical studies for both Beta and Delta variants as test cases that are designed to establish safety and tolerability comparable to BNT162b2 for updated vaccine candidates and demonstrate that immune responses, as measured in validated virus neutralization assays, are noninferior to those induced by BNT162b2.

The design you see here uses Beta as an example, where both a de novo 2-dose updated vaccine in the naive individuals as well as an updated vaccine booster in BNT162b2-experienced people is assessed. We expect to seek EUA with these data and the CMC data package, once available, after March 2022, at which time, we expect to know if an updated vaccine is required or not.

Now let me turn to our pediatric studies to assess safety tolerability and immunological noninferiority in pediatric populations from 6 months to less than 5 years of age. Earlier this year, we began dose-ranging studies to understand the optimal dose levels for our pediatric populations to determine a dose level with an acceptable safety and tolerability profile and an appropriate immune response likely to meet noninferiority criteria.

We suspected we would have more reactogenicity in these younger age groups with a full 30-microgram dose level, which indeed is what we found. Here, I'm showing you unblinded Phase 1 data in our 6 months to less than 2 years of age and 2 to less than 5-years-of-age cohorts. For the 2 to less than 5-year cohort, we are showing you both the 3-microgram and 10-microgram dose levels. We have noticed that fever and chills are 2 of the most important systemic events for decision-making. Based on the occurrence of somewhat higher severe fever levels in the 2 to less than

5-year-old population compared to the 5 to 11 year olds and older populations at the 10-microgram dose level, we decided that the 3-microgram dose level given 21 days apart would be most appropriate for moving ahead into Phase 3 as it has acceptable fever profiles in both pediatric populations.

Now for immunogenicity. Again, I'm showing you unblinded Phase 1 data in our 6 months to less than 2-years and 2 to less than 5-year old cohorts. For the 2 less than 5-years of age cohort, we are showing you was the 3-microgram and 10-microgram dose levels. In that Phase 1 study, we saw neutralizing titers in our pediatric groups that were about the same or greater than those observed in the 16- to 25-year old comparator. Thus, we chose 3 micrograms as a dose level for both pediatric populations.

We previously shared that we expected to have preliminary data from the COVID-19 vaccine in the under age 5 population before the end of this year. And now I would like to fill you in on what we have learned and our plans for going forward.

The Phase 3 study remains ongoing and actively enrolling. Following a routine review by the external independent data monitoring committee, they have informed us that they have seen favorable safety in the 6 months to less than 5-year-old population. We believe this reflects our commitment to careful dose selection to maximize the benefit risk profile.

We have conducted a prespecified noninferiority immunogenicity analysis on a subset of the pediatric population. Compared to the 16- to 25-year-old population, noninferiority was met for the 6 months to 24-month old population but not for the 2 to less than 5-year-old population at this time.

The effectiveness data for 3 doses of the vaccine in general for people 16 years and older and the early laboratory data we have seen with Delta and other variants of concern, including Omicron, suggest that people vaccinated with 3 doses of our COVID vaccine may have a higher degree of protection. Therefore, we have decided to modify each of the pediatric studies to incorporate a third dose to the series and seek licensure for a 3-dose series rather than a 2-dose series as originally anticipated.

If successful with this strategy, and following consultation with regulatory authorities, we would have a consistent 3-dose vaccine approach for all ages. It is important to note that this adjustment is not anticipated to meaningfully change our expectations that we would file for emergency use authorization and conditional approvals in the second quarter of 2022.

To end, in September 2020 when we met last, we presented 3 potential scenarios for the ongoing pandemic. The pandemic was ending, the pandemic was staying and/or an updated vaccine was required to control the pandemic. Today, we are reasonably certain that SARS-CoV-2 is here to stay. And we believe that over the next year or so, we may be able to help control the pandemic, either with our current or an updated vaccine. We now have evidence, both from our clinical studies and real-world effectiveness, that 3 doses of BNT162b2 provide better duration of protection than 2 doses. And control of Omicron may only be possible with 3 or more doses.

We are prepared for either scenario and are committed to providing data to support potential EUA submissions for the pediatric population in the first half of 2022. We continue to follow the epidemiology of the disease and variance, so we can be prepared for vaccine update if needed. And we look forward to updating you with new data as they emerge.

Overall, we have shown you data that support Pfizer's ongoing and strong commitment to help transform the COVID-19 pandemic into a more manageable endemic. We have also provided evidence for most of the assumptions supporting our business that will now be discussed by my colleague, Global President of Vaccines, Nanette Cocero. Nanette?

Nanette Cocero - Pfizer Inc. - Global President, Vaccines

Thank you, Kathrin. While we are tremendously proud of the profound impact COMIRNATY has had on so many people's lives around the world, as Kathrin said, we know our work is far from done, and our scientists believe that COVID is here to stay.

As the pandemic evolves, we expect that COMIRNATY will continue to play a critical leading role in the ongoing prevention of COVID-19, bringing value to patients, global public health, Pfizer and shareholders.

There is a lot that we are proud of today, starting with how quickly we have been able to help address COVID-19 moving at lightspeed to obtain first authorizations and approvals for our COVID-19 vaccine in partnership with BioNTech. COMIRNATY is the only COVID-19 vaccine that has FDA approval for people aged 16 and older, and it is the only COVID-19 vaccine authorized in the 12 to 15 and 5 to 11 age groups in the United States. Globally, COMIRNATY is the only messenger RNA vaccine that has received authorization in the 5 to 11 age group. Therefore, COMIRNATY is the only COVID vaccine by a major manufacturer authorized by regulatory bodies to be used in all individuals 5 years and older.

To date, we have shipped over 2.4 billion doses to over 160 countries around the world. And as Mikael shared earlier, Pfizer has already manufactured 3 billion doses this year. With this outstanding leadership, we have been able to provide tremendous value to patients, governments and our investors. We expect to close the 2021 fiscal year with an estimated \$36 billion in direct sales and alliance revenues from our COVID-19 vaccine.

We take great pride in headlines like this one from the Wall Street Journal because our Pfizer-BioNTech vaccine is the most preferred around the globe, as evidenced by our strong market share and leadership in both the United States with a 58% market share to date, and in Europe with a 74% market share to date. Our market share is strong in part due to our booster being the first to receive emergency use authorization and our 2-dose series being preferred by some countries for use in certain younger populations.

The fact that the Pfizer-BioNTech vaccine is the most used vaccine around the world gives us the ability to conduct rigorous analysis regarding the safety and population impact of our vaccine. I'll talk more about our expectations for our COVID-19 in 2022 and beyond in just a moment. But we are excited about the opportunity to potentially further our leadership next year and over the long term, given recommendations for boosters and the approval or authorizations we have in the adolescent and pediatric populations.

As I shared a moment ago, we have distributed over 2.4 billion doses across both developed markets and low- and middle-income countries. And in order to help ensure our doses reach vulnerable populations, we have pledged to provide 2 billion doses of our COVID-19 vaccine to low- and middle-income countries in 2021 and 2022 together, at least 1 billion doses for each year. And we are very proud to say that we are on pace to deliver on our 2021 pledge and expect to reach this milestone before the end of this year.

As we look to 2022, we believe that COMIRNATY has the potential to be a large, long-term sustainable business for Pfizer and whether in a pandemic or endemic market, Pfizer is well positioned to continue to be a clear market leader. For 2022, we currently expect to deliver 1.9 billion doses and have sales of approximately \$31 billion during the fiscal year. We continue to engage with governments regarding potential orders for 2022 and including doses for which certain governments have the option to order and take deliveries in 2022.

In the event that we need to produce an Omicron variant vaccine, we believe this could result in additional demand. Should an Omicron variant vaccine be needed and receive regulatory authorization, we expect to further reinforce our leadership position due to our proven ability to advance development, broad manufacturing capabilities and ability to bring vaccines to market at a lightspeed on a global scale.

While still early, we have already set a significant foundation for 2023, having contracted more than 500 million doses with governments as a result of multiyear agreements with the European Commission, Canada, Japan and other countries. We are in active discussions with governments across the globe for additional supply agreements while also anticipating the formation of private markets in certain countries.

At this point, our best expectation is that countries around the world will prioritize annual revaccination for broad populations and young children who become eligible for primary vaccination, if authorized or approved. We believe COVID will transition to an endemic state potentially by 2024. But regardless of when that transition occurs, we believe we are well positioned to continue our leadership due to our robust global development and commercialization capabilities.

While we expect increased competition, we expect messenger RNA to continue to be the leading class with Pfizer continuing to be a class leader. We are firm in this conviction for several reasons. First, we have the ability to quickly adapt and manufacture messenger RNA vaccines should a new variant is required. And second, our approach to carefully selecting dose to balance efficacy and safety is expected to continue to drive the trust that Pfizer has established with patients, health care professionals and government stakeholders across the globe. In an endemic state, operating in a primarily commercial market, we expect significant annual revenues from our COMIRNATY business over the long term.

Now in addition to leading in science, we have a strong heritage in manufacturing. And with our broad manufacturing footprint, we expect to produce 4 billion doses in 2022, even if a variant vaccine is needed. We also continue to have a strong record of timely production and delivery to markets around the world, which has been and we expect will continue to be, an advantage for us.

With our relentless focus on innovation, some examples of what we have been able to do are: reduce our production cycle time significantly by 50% from 110 days down to an average of 60 days. We also have improved product formulation with storage up to 10 weeks at refrigerator temperatures, which is longer than for other messenger RNA vaccines available today. We also enable pack size flexibility for use -- for ease of use in both retail and health care providers' offices, while making our thermal container more user friendly.

Now in closing, we believe we are well positioned to continue leading the fight against this deadly virus and our breakthrough science and end-to-end capabilities set us apart from other manufacturers. Over the near and longer term, our commercial strengths are vast and unmatched. Our vaccine medical and field colleagues hold long-standing, trusted and deep relationships with health care professionals in large systems and small offices across adult and pediatrics, key opinion leaders and across retail and distribution channels. Our organization is adept and agile in developing innovative contracts with an ability to execute agreements across our broad and growing vaccine portfolio.

Additionally, we have demonstrated the ability to effectively reach, engage, educate and motivate patients to take action and will continue to harness these proven capabilities for years to come. We believe our manufacturing leadership truly sets us apart with our agility, product innovation and demonstrated strong supply, reliability time and time again. And our ability to expand capacity will help us to rapidly respond to potential variant vaccine production if needed.

And finally, we expect to continue to be the leaders in this fight by leveraging our scientific expertise. Our medical colleagues will continue to cultivate strong partnerships such as with the Israeli Ministry of Health and Kaiser Permanente to generate real-world evidence and critical epidemiology insights to help us address public health needs and inform our product life cycles plans and our regulatory strategy.

Now allow me to close by sharing again that we are filled with tremendous pride given the profound impact we have had on global public health. And as we look to a future where we eventually transition to an anticipated endemic environment, we are confident in our ability to continue to lead the fight against COVID-19 by bringing all of Pfizer's market-leading capabilities to bear.

And thank you for your time today. And now I'll pass it over to Angela Lukin, who will share latest updates on our protease inhibitor, PAXLOVID.

Angela Lukin - Pfizer Inc. - Global President, Hospital

Hi. My name is Angela Lukin, and I am the President of our Global Hospital Therapeutic area. My R&D partners and I are pleased to have this opportunity to share our excitement and further details on PAXLOVID.

By way of brief background, I have more than 25 years in the industry with over 20 of them being at Pfizer. I led the hospital therapeutic area along with Annaliesa Anderson, our Chief Scientific Officer, and Jim Rusnak, our Chief Development Officer. Liesa and Jim will briefly introduce themselves to you during his presentation.

First, I'd like to provide you a very brief overview of the Hospital therapeutic area, which was created in 2019 to address the growing needs of hospitals and the patients that they serve by combining the leading anti-infective and sterile injectable portfolios.

With one of the broadest portfolios available to treat millions of hospital patients globally, Pfizer Hospital provides 300-plus medicines across 14 different therapeutic areas. We are also expanding our R&D in 2019, and we started with 1 novel asset. And 2 years later, we have already advanced that to 6 new novel new molecular entities.

This work truly changed lives. In 2020, our products impacted over 200 million patients globally. We also have unmatched capabilities rooted in decades of experience with thousands of colleagues working to bring patients crucial medicines and innovative delivery systems.

Today's focus is on PAXLOVID, which we are incredibly excited to discuss with you. With more than 5 million deaths and hundreds of millions more lives impacted by COVID-19 worldwide, we believe oral antiviral therapies have the potential to be a game changer in the global efforts to halt the devastation of this pandemic.

If authorized or approved, PAXLOVID will be the first oral antiviral of its kind. It includes nirmatrelvir, a protease inhibitor that was specifically designed in Pfizer laboratories to combat SARS-CoV-2. It was developed to be administered orally so that if approved or authorized, it can be prescribed at the first sign of infection or at first awareness of exposure subject to clinical success, potentially providing a treatment option that can be taken at home.

I will now turn it over to Annaliesa to introduce herself and walk you through our clinical program and early data.

Annaliesa Anderson - Pfizer Inc. - Chief Scientific Officer, Hospital

Thank you, Angela. I'm Annaliesa Anderson. And by way of brief background, I have 30 years of vaccine and antimicrobial research and development experience and have been at Pfizer for the last 14 years. Here, my focus has been on supporting our bacterial vaccines, including those for the pneumococcal franchise and TRUMENBA. More recently, I have expanded my role to infectious disease therapies.

As Chief Scientific Officer of our Hospital therapeutic area, I oversee all scientific operations across current and emerging areas of business. I've worked closely on the development of PAXLOVID, which is comprised of nirmatrelvir co-administered with a low dose of ritonavir, the R&D program for which was initiated in advance by Pfizer scientists in March 2020.

As Angela said, today, we'll be providing an update on PAXLOVID, the status of our development program, how we got there and some information on how we are working to get the antiviral to the patients who need it. Mikael explained earlier, if approved or authorized, we envision PAXLOVID could be a strong weapon in the fight against COVID-19 and could supplement vaccination for individuals at the greatest risk of severe disease outcomes. I would like to share with you details about the patient populations we are evaluating.

First, there are patients who have an increased risk of hospitalization and death due to comorbidities such as age, weight, conditions such as diabetes and hypertension as similarly defined by the Centers for Disease Control and Prevention. This is the population that we studied in the EPIC-HR Phase 2/3 clinical trial that Jim will present.

Secondly, there are patients who are characterized the standard risk for progressing to severe illness, either with no risk factors or who are at high risk, but have been fully vaccinated. Our second Phase 2/3 study, EPIC-SR, covers this population.

Finally, we are evaluating whether PAXLOVID could also be used for post-exposure prophylaxis in household contacts for someone with a confirmed COVID-19 infection. The Phase 2/3 EPIC-PEP study is designed to evaluate this, and if successful, would provide a way to prevent COVID-19 illness in individuals who live with a COVID-19 patient. Examples of this may include household contacts such as families living with elderly relatives or parents caring for a sick child.

As with COMIRNATY, we conducted our PAXLOVID development program with great urgency and with the goal of providing a critical treatment option to patients. In March of 2020, realizing that the COVID-19 pandemic could have a lasting global impact and would require many different approaches to stop it, we initiated a program to design a safe and effective oral treatment could prevent severe illness.

We built a committed multidisciplinary team with the goal of developing an antiviral compound that was orally bioavailable with potent anti-SARS-CoV-2 activity. We did everything we could to allow our scientists a single focus so that they could really explore the possibilities. The discovery team moved urgently using structure-based design, state-of-the-art computational and synthetic technologies. This, combined with our experience in designing oral drug molecules, led to the design of nirmatrelvir, the active antiviral component of PAXLOVID.

In particular, the 4 months expedited design was enabled by artificial intelligence and machine learning techniques such as virtual screening to rapidly select the most promising molecules to make and profile. We used machine learning tools to predict the molecules with the best oral drug properties built on millions of data points, thanks to our long legacy in designing oral therapeutics.

Nirmatrelvir was first synthesized in July 2020 and had potent SARS-CoV-2 antiviral activity and high oral bioavailability. With these data, we commenced scale-up activities and toxicology studies in parallel to enable the initiation of the Phase 1 study just 12 months after we started the program.

To continue with this unprecedented urgency, our pivotal studies, which started in July of this year, only 12 months after the molecule was synthesized. Thanks to the early at-risk investments in the manufacturing process, we were able to scale up from the 7 mgs of nirmatrelvir that was first synthesized and are now projected to manufacture 80 million treatment courses next year.

The EPIC-HR study provided the first compelling data that an oral antiviral compound is highly effective at reducing the severe outcomes of COVID-19. Yesterday, the Committee for Medicinal Products for Human Use of the European Medicines Agency issued advice under Article 5(3) on the use of PAXLOVID to treat high-risk adults with COVID-19 who do not require supplemental oxygen, providing support for the EU member states, who may decide to allow the supply and use of PAXLOVID, for example, in emergency new settings prior to EU conditional marketing authorization. We are working closely with other regulatory agencies to ensure that this potentially life-saving medicine can reach patients as quickly as possible.

Though vaccines have been highly successful at preventing COVID-19, treatments for those who contract disease are still limited. We believe that high-level potential first-in-class oral COVID-19 therapy, PAXLOVID, could play a critical role in treating patients in stemming the pandemic, if approved or authorized.

Early in the pandemic, we decided to purposely prioritize the SARS-CoV-2 main protease, which is also known as Mpro, due to its critical role in viral replication and the precedent for the mechanism of action to treat other viruses such as HIV and hepatitis C.

On infecting the cell, the virus co-opts the host cell to make new viruses that exacerbate the infection and may be transmitted to other people. As illustrated in the panel on the left, first, the virus sheds its code so that the internal RNA molecule can encode the polypeptides. These will form the basis of the replication machinery once the Mpro cleaves them into independent proteins. Thus, if Mpro is successfully inhibited, it can prevent further viral replication, thereby helping to treat COVID-19 patients.

Our protease inhibitor, nirmatrelvir, is co-administered with a low dose of ritonavir, and I'll discuss this further momentarily. First, I'd like to review some of the information on nirmatrelvir's preclinical profile.

First, we do not expect nirmatrelvir to lose activity against the currently circulating SARS-CoV-2 variants of concern. This is because the current variants of concern are defined by changes in their spike protein and not the protease. The protease is conserved across different coronaviruses and, due to its essential nature, has very little tolerance for change. On the left is efficacy of nirmatrelvir in, in vitro antiviral assays recorded as the amount of drug that is required to kill 50% of the virus in the assay.

Nirmatrelvir is highly potent, delivering EC50 values in the low nanomolar range. With all of these results being considered similar in line with the sensitivity of the assay. We reported this week that nirmatrelvir does inhibit the protease from the Omicron variant in a biochemical assay.

Structural modeling, as shown on the right, predicted that we would not see a loss of activity. The pink represents the active site and sitting inside the active site is nirmatrelvir. Differences between the Washington strain protease that was used to design the molecule and Omicron are highlighted. We're working with different organizations to test nirmatrelvir against Omicron in an antiviral assay and expect data soon.

The molecule also highlights how we design nirmatrelvir to have a very efficient binding interactions between the protease inhibitor, active site and the target Mpro enzyme, making it more difficult for the virus to develop resistance without losing any function of the protease, which is essential for replication.

The nonclinical safety package for nirmatrelvir fully supports the clinical indications. Specifically, there are no known human homologs for Mpro and as expected, nirmatrelvir is highly selective versus human proteins. We observed favorable safety margins in nonclinical safety studies and have a clean genetic toxicology profile.

As I mentioned earlier, PAXLOVID is comprised of nirmatrelvir and ritonavir. The co-administration with the low dose of ritonavir is because nirmatrelvir is metabolized by the CYP3A enzyme and ritonavir is a potent inhibitor of this enzyme. Ritonavir helped slow the metabolism or breakdown of nirmatrelvir in order for it to remain active in the body for longer periods of time at higher concentrations to help combat the virus.

There is a well-established precedence for autonomous use in combination with other antivirals to slow drug metabolism in this way. By co-administering, we can ensure that we have high plasma concentrations of nirmatrelvir that are 5 to 6x higher than the EC90 that we derived for the SARS-CoV-2 virus in a lung cell line.

This illustrates the clinical dose of 300 mg nirmatrelvir and 100 mgs of ritonavir with the plasma concentrations on the y-axis and the time on the x-axis. And the black line shows the plasma concentrations of nirmatrelvir over the 12-hour dosing period.

The dotted blue line represents the amount of drug that is required to kill the 90% of the virus in the assay. This is the EC90. As you can see, the nirmatrelvir consultations are several fold higher than this. The EC90 for SARS-CoV-1 and are MERS also illustrated, providing an example of the potential pancoronavirus activity for this treatment.

Ritonavir has a well-characterized safety profile used alone and in combination with other antivirals to slow drug metabolism. Its effect on drug metabolism may result in drug interactions, which are also known as DDIs, and some drugs may be contradicted. However, in light of the fact that PAXLOVID has a short duration of treatment of 5 days combined with the low dose of ritonavir of 100 milligrams, we believe that health care providers and pharmacists should find that most of the DDIs to be generally manageable.

Its effect on drug metabolism may result in drug interactions that are also known as DDIs and some drugs may be contraindicated. However, in light of the fact that PAXLOVID has a short duration of treatment of 5 days, combined with a low dose of ritonavir of 100 milligrams, we believe that health care practitioners and pharmacists should find most DDIs to be generally manageable.

I will now turn it over to Jim Rusnak, who will share more information about our clinical development program for PAXLOVID.

Jim Rusnak - Pfizer Inc. - Chief Development Officer, Internal Medicine & Hospital

Thank you, Liesa. I'm Jim Rusnak, the Chief Development Officer for Internal Medicine and Hospital, and I've been at Pfizer for over 12 years. My background includes training in internal medicine at Mayo Clinic, and I have over 20 years of both early and late development experience, including responsibilities for Eliquis, Chantix and PAXLOVID.

As Liesa mentioned, the EPIC or, evaluation of protease inhibition for COVID-19, clinical development program consists of 3 Phase 2/3 studies with trial populations, including adults at both high risk and standard risk of progressing to severe illness as well as adults with confirmed household exposures to the virus. This comprehensive program was designed with a global footprint, including sites in North and South America, Europe, Africa and Asia with nearly 7,000 planned participants from diverse backgrounds.

In July of 2021, Pfizer initiated the first of these trials known as EPIC-HR, a randomized double-blind study of non-hospitalized adults with COVID-19 who are at high risk of progressing to severe illness. At the recommendation of an independent data and monitoring committee and in consultation with FDA, and Pfizer ceased further enrollment into the study in early November of 2021 due to the overwhelming efficacy demonstrated in these interim results. These data were shared with the FDA as part of our submission for emergency use authorization following this news.

In August 2021, Pfizer began the Phase 2/3 EPIC-SR study to evaluate efficacy and safety in adults with a confirmed diagnosis of SARS-CoV-2 infection who are at standard or low risk of developing severe disease. EPIC-SR includes both vaccinated and unvaccinated adults. Earlier this week, we announced interim results from this ongoing trial.

In September, Pfizer initiated the Phase 2/3 EPIC-PEP study to evaluate efficacy and safety in adults exposed to SARS-CoV-2 by a household member. One unique factor of this study to note is that participants are randomized 1:1:1 to receive PAXLOVID or placebo orally every 12 hours for 5 or 10 days. This trial is ongoing, and we expect interim data in the second quarter of 2022.

At the time of the decision to stop recruiting patients, enrollments in the EPIC-HR study was approximately 70% of the 3,000 planned patients from the clinical trial sites, with 45% of the patients located in the United States. It's important to note that while EPIC-HR did not include participants who have been previously vaccinated, approximately half of the patients were seropositive, meaning that they had previously been exposed to SARS-CoV-2.

Taking a closer look at the study design for EPIC-HR. Enrolled patients had a laboratory confirmed diagnosis of SARS-CoV-2 infection within a 5-day window and were required to have at least 1 characteristic or underlying medical condition associated with an increased risk of developing severe illness from COVID-19.

As Liesa mentioned, we based our definition of high risk predominantly following the CDC guidelines, including conditions such as diabetes, hypertension, cardiovascular lung disease and a BMI greater than 25, among others.

Patients were randomized 1:1 to receive PAXLOVID or placebo orally every 12 hours for 5 days with follow-up at planned intervals through day 28 for the primary endpoint analysis, with longer-term ongoing follow-up through week 24.

Although the primary endpoint focused on the proportion of patients with COVID-19-related hospitalization or death when treated within 3 days of symptom onset, a key secondary endpoint extended that analysis to treatment within 5 days. We also looked at viral load and safety data, among other factors in our secondary end points.

The scheduled interim analysis showed an 89% reduction in risk of COVID-19-related hospitalization or death from any cause compared to placebo in adults treated within 3 days of symptom onset, which was the primary endpoint. 0.8% of patients who received PAXLOVID were hospitalized through day 28 following randomization. Three of 389 hospitalized with no deaths compared to 7% of patients who received placebo were hospitalized or died. That is 27 of 385 hospitalized with 7 subsequent deaths. Put another way, PAXLOVID prevented 9 of 10 hospitalization and all deaths in high-risk adults. The statistical significance of these results was high, p less than 0.0001.

The full analysis confirmed these interim results, showing a consistent and robust 89% reduction in risk in adults treated within 3 days of symptom onset. 0.7% of the patients who received PAXLOVID were hospitalized through day 28 following randomization. Five of 697 hospitalized with no deaths compared to 6.4% of patients who received placebo and were hospitalized or died, 44 of 682 hospitalized with 9 subsequent deaths. The statistical significance of these results was high, p less than 0.0001.

On the key secondary endpoint of COVID-19 hospitalization or death within 5 days of symptom onset, the interim analysis showed a similar reduction. 1% of patients who received PAXLOVID were hospitalized through day 28 following randomization. Six of 607 hospitalized with no deaths compared to 6.7% of patients who received placebo, 41 of 612 hospitalized with 10 subsequent deaths, with high statistical significance, p less than 0.0001.

In the overall study population, through day 28, no deaths were reported in adults who received PAXLOVID compared to 10 or 1.6% deaths in patients who received placebo. In the full analysis, the observed risk reduction increased to 88%, up from the 85% seen in the interim analysis in patients treated within 5 days of symptom onset. 0.8% of patients who received PAXLOVID were hospitalized through day 28 following randomization. Eight of 1,039 hospitalized with no deaths compared to 6.3% of patients who received a placebo, 66 of 1,046 hospitalized with 12 subsequent deaths, with a high statistical significance of p less than 0.0001.

In the overall study population, through day 28, no deaths were reported in adults who received PAXLOVID as compared to 12 or 1.2% deaths in patients who received placebo.

In another secondary endpoint, SARS-CoV-2 viral load at baseline and day 5 were evaluated. After accounting for baseline viral load, geographic region and serology status, PAXLOVID reduced viral load by approximately tenfold or 0.93 log₁₀ copies per mill relative to placebo. The results indicate robust activity against SARS-CoV-2 and represents the strongest viral load reduction reported to date for an oral COVID-19 agent.

Treatment-emergent adverse events were comparable between PAXLOVID and placebo, 23% versus 24%, most of which were mild in intensity. Fewer serious adverse events, 1.6% versus 6.6%, and discontinuation of drug due to adverse events, 2.1% versus 4.2%, were observed in patients dosed with PAXLOVID compared to placebo, respectively. The adverse events observed both in patients dosed with PAXLOVID and placebo were generally similar to those that we would expect to see in patients with COVID-19.

A second and distinct study, EPIC-SR, or evaluation of protease inhibition for COVID-19 in standard risk patients, enrolled more than 1,140 non-hospitalized symptomatic patients with COVID-19. Earlier this week, we reported out interim results from this trial.

The EPIC-SR study enrolled patients who had a laboratory confirmed diagnosis of SARS-CoV-2 infection within a 5-day window and were either unvaccinated adults who were at standard risk, meaning low risk of hospitalization or death, or vaccinated adults who had 1 or more risk factors for progressing to severe illness.

Patients were randomized 1:1 to receive PAXLOVID or placebo orally every 12 hours for 5 days with follow-up at planned intervals. Primary endpoint assessment was at 28 with longer-term ongoing follow-up through week 24. Because this study is ongoing, we will not be sharing secondary endpoint data beyond what was included in the press release issued on December 14.

Unlike the EPIC-HR trial, the primary endpoint for EPIC-SR was defined as sustained alleviation of all targeted symptoms for 4 consecutive days as compared to placebo. Key secondary endpoints included reduction in hospitalization or death, viral load and safety, among others.

The primary endpoint was derived in consultation with the National Institute of Health and the National Institute of Allergy and Infectious Disease, and aligned in a similar manner to a primary endpoint in the ACTIV-2B clinical trial protocol, which was derived from analyses in the ACTIV-2 study. These analyses suggested that the choice of this endpoint captured sustained symptom resolution with a low probability of subsequent relapse.

To meet the endpoint, patients needed to report improvement in all 11 symptoms in the table on the right over 4 consecutive days. In other words, they needed to show 44 consistent measures of symptom alleviation. Sustained alleviation of all targeted COVID-19 signs and symptoms is defined as the event occurring on the first of 4 consecutive days when all symptoms scored as moderate or severe at study entry are scored as mild or absent. And all symptoms scored as mild or absent at the study entry are scored as absent.

Interim analysis of EPIC-SR showed that this novel primary endpoint was not met. Interim analysis of EPIC-HR, which included 80% of the trial's planned enrollment showed results from this key secondary endpoint of a 0.7% reduction of hospitalization and death for those who received PAXLOVID, following randomization. Three of 428 hospitalized with no deaths compared to 2.4% of patients who received placebo and were hospitalized or died, or 10 of the 426 were hospitalized with no deaths. This showed a strong trend with a p-value of p 0.051.

In other words, we saw a 70% risk reduction in hospitalization and no death when patients were treated with PAXLOVID within 5 days. Based upon the totality of the data available, an independent data monitoring committee has recommended the trial continue and additional data will be released upon analysis of the full study data. These secondary endpoint interim results from EPIC-SR are consistent with, and further support, the compelling efficacy we demonstrated in our EPIC-HR study.

In addition to these results, this slide shows that there was an approximate tenfold reduction in viral load at day 5. These results are consistent with the results from our Phase 2/3 EPIC-HR study. With respect to safety, treatment-emergent adverse events were comparable between PAXLOVID, 22%, and placebo, 21%, most of which were mild in intensity. Rates of serious adverse events, 1.4% versus 1.9%, and discontinuation of study drug due to adverse events, 2.1% versus 1.2%, were also comparable between PAXLOVID and placebo.

In conclusion, we saw consistent and robust viral load reductions in both EPIC-HR and EPIC-SR, which represents the strongest viral load reduction reported to date for an oral COVID-19 antiviral agent. Final results from our EPIC-HR study were nearly identical to our 45% interim analysis showing nearly a 90% relative risk reduction in hospitalization with no deaths.

While EPIC-SR failed to meet its novel primary endpoint in our interim analysis, we are very encouraged by the positive trend we saw in the interim analysis of the key secondary endpoint of hospitalization and death, which was consistent with the results that we saw in EPIC-HR.

I now hand it over to Angela to discuss the launch strategy for PAXLOVID.

Angela Lukin - Pfizer Inc. - Global President, Hospital

Thank you, Jim. Now I'll walk you through our 3 critical success factors for launch for PAXLOVID if authorized or approved.

To ensure a successful launch, our plan is underpinned by 3 strategic pillars. The first is driving urgency to diagnosis and appropriate treatment. We all know time is of the essence in getting patients on treatment. Although we would expect our potential EUA to define that window to be less than or equal to 5 days, we will be deploying initiatives with the goal to condense that timing. I will share with you on the next slide some examples of ways in which we will look to accomplish this.

The second pillar is focused on building confidence in our protease inhibitor benefit risk profile. To achieve this, we plan to deploy initiatives supporting an omnichannel approach, which will include things like medical-to-medical education, medical response letters, congress activity, HCP website, banner ads. And we intend to leverage our collective advantage via our customer-facing colleagues to provide prescribers with the information they need to make prescribing decisions on PAXLOVID is appropriate for their patients.

Our final pillar is supporting broad and equitable access and coverage. A great example is our recent announcement with medicines patent pool which could help to provide access to 95 countries, including all low-income, lo- middle-income countries and a group of upper middle-income countries that recently moved up this category in the last 5 years, subject to local approval or authorization.

Driving urgency to diagnosis and treatment will be critical to successfully getting PAXLOVID in the hands of appropriate patients who need it upon authorization as quickly as possible. As Jim mentioned earlier, we now have the full data set for EPIC-HR showing that PAXLOVID reduced hospitalization or death by 89% when treated within 3 days and 88% compared to placebo were treated within 5 days of symptom onset. If you look at the top row, you can see that the current time to treatment initiation, as it stands today, can take up to 8 days.

Our patient journey market research shows that symptomatic patients may wait up to 3 days before getting tested. From there to take another 1 to 3 days for the patient to be tested and then another 1 to 2 today to be diagnosed as COVID positive. It could take roughly up to another 7 days for the patient to make an appointment to get to an infusion center for treatment, for example, with a monoclonal antibody. And part of the challenge has been, there's been no currently available treatments that could be taken at home.

With the potential introduction of oral antivirals like PAXLOVID, having a treatment that can be taken at home will be an important aspect of potentially shortening the timelines. However, we're not going to rely just on that. As I mentioned, our goal is to reduce this timeline by more than half to as little as 3 days.

Below, you can see a visual of what that could take. First, it's about raising awareness of COVID symptoms and the urgency to diagnosis and treatment. We will do this through a variety of initiatives, including things like public service announcements delivered through broad channels, banner ads and websites, all with the goal of increasing awareness of COVID symptoms and the urgency to get tested and treated. We are also discussing with governments what activities they will be looking to do in support of raising awareness as well.

The second key area is really all about condensing testing, diagnosis and delivery into 1 day. We know this is an ambitious goal, but we believe that this is possible because we're already hearing from key stakeholders that they are exploring ways to do this. Here, it's all about rapid test, rapid treat.

As a side note, in our high-risk clinical study, 65% of patients were treated within 3 days. Some of the ways in which sites were able to recruit clinical trial participants included advertising, banner ads, billboards, education and intervention at pharmacies. Although these were key initiatives for clinical trial recruitment, we believe these same initiatives could help in achieving our goals post authorization.

In addition to the items I just mentioned, we'll also be looking to intervene at key points along the patient journey. For example, it is an important role that pharmacists will play. We will look to have shelf coffers by testing kits at pharmacy messaging, talking about rapid test and rapid treat. We will be ready to provide education and training on the product of pharmacists as they may not only be dispensed in treatment, but potentially prescribers at least in the United States. And knowing there is currently high traffic at pharmacy websites, we will be looking to place banner ads about rapid test, rapid treat, which can then take patients to our EUA website.

Telehealth providers are another important area of focus. We have been talking to key telehealth providers in the United States with the goal of ensuring their health care professionals are knowledgeable and prepared to make appropriate treatment decisions about PAXLOVID.

And one last example is that we're looking to work with companies that have the potential to support end-to-end customer experience, testing, diagnosis, treatment and fulfillment. In summary, it's about intervening at key points in the patient journey and also finding solutions that can provide a more seamless patient experience.

Last but not least, we will share great ideas that we are seeing and hearing from countries around the world in order to help close that time gap, and we know that this is top of mind for the countries that we've been talking to. For today, I really just wanted to highlight some examples of ways in which we're looking to close that time gap from symptom onset to treatment initiation.

Our second pillar is focused on building confidence in the benefit risk profile of PAXLOVID, which we plan to achieve by educating and reinforcing the following: our clean genetic toxicology as well as tolerated clinical profile; the ability to manage potential drug-drug interactions in light of the fact that PAXLOVID has a short duration of treatment, which is 5 days. Combined with low-dose ritonavir of 100 milligrams, we believe that HCPs and pharmacists should find most DDIs to be generally manageable. PAXLOVID's overwhelming efficacy in high-risk COVID-19 patients, as demonstrated by our EPIC HR study, it's activity against current variants of concern.

You heard from Liesa earlier about our confidence in PAXLOVID against variants of concern, including Omicron. The robust and comprehensive nature of our clinical development program, which spans 3 patient populations. As you heard earlier, this comprehensive program was designed with a global footprint, including sites in North America, South America, Europe, Africa and Asia with nearly 7,000 planned participants from diverse backgrounds. Additionally, we look forward to generating data in our planned pediatric trial population beginning next year. And finally, real-world evidence, which we plan to begin generating following emergency use authorization is received.

We are committed to working towards equitable access to PAXLOVID for all people, aiming to deliver safe and effective antiviral therapeutics as soon as possible at an affordable price. If authorized or approved during the pandemic, Pfizer will offer our investigational oral antiviral therapy through a tiered pricing approach based on income level of each country to promote equity of access across the globe. High and upper middle-income countries will pay more than low-income countries.

Pfizer has also begun and will continue to invest up to \$1 billion to support the manufacturing and distribution of PAXLOVID, including exploring potential contract manufacturing options. We have entered into agreements with multiple countries and have initiated bilateral outreach to over 100 countries around the world, which are currently at various stages of negotiation. We have the capability and capacity to manufacture up to 80 million treatment courses by the end of 2022, depending on the global needs, which will be driven by advanced purchase agreements. Important to note that 30 million of these treatment courses are now expected to be available in the first half of 2022.

As I mentioned earlier, Pfizer has signed a voluntary license agreement with Medicines Patent Pool to help expand access, pending regulatory authorization or approval, in 95 low- and middle-income countries that account for approximately 53% of the world's population. Pfizer will not receive royalties on sales in low-income countries and will further waive royalties on sales in all countries covered by the agreement while COVID-19 remains classified as a public health emergency of international concern by the World Health Organization.

We've been in this pandemic for almost 2 years now, and we believe this will continue through next year. If you take the recent inception rate looking at May through October 2021 and apply them to 2022, then the potential total addressable global patient population at risk of getting COVID-19 next year could exceed 200 million. It is important to note that this does not take into account treatment rates, local access infrastructure, share. These numbers are fluid and subject to change based on vaccination rates, circulating variants and the evolution of the pandemic.

In 2022, we expect the demand for COVID-19 treatments to stem from government contracts that we have procured and will be in the process of procuring through 2022. And in 2023, we believe that there will begin to see a shift and that the potential patient pool that needs treatment will change. We may see some countries move towards more traditional types of commercial models. However, government contracts and potential multiyear agreements will be in scope for securing access to patients around the world.

In 2024 and beyond, we expect that COVID-19 will likely be an endemic and the volume will be determined by infection rates. Stockpiling may be more of an opportunity as we move towards this endemic phase. Given the potential pan-coronavirus activity of PAXLOVID as well as the efficacy and safety profile, we believe it could be the valuable tool for governments, not just in treating infected patients, but also in terms of future pandemic preparedness.

Thank you for sharing your time with us today, and we look forward to taking your questions in a few minutes. Now I'd like to turn it over to Frank to wrap up the presentation.

Frank A. D'Amelio - Pfizer Inc. - Chief Financial Officer, Executive Vice President, Global Supply

Thank you, Angela. We've told a very exciting story today, and now it's my job to wrap up.

I wanted to update you on our current expectations for 2022 sales of COMIRNATY. We will provide overall 2022 guidance, as is our usual practice, on our fourth quarter 2021 earnings call in February. At that point, I will be providing guidance with PAXLOVID for the first time.

Let me remind you again that these expectations are current based on signed contracts and delivery expectations and that these could change over the course of next year. For COMIRNATY, our COVID-19 vaccine, you can see that our expected production capacity remains at 4 billion doses for calendar 2022. We currently expect to deliver 1.9 billion doses and have revenues of approximately \$31 billion during the fiscal year based on contracts signed as of mid-November 2021.

With that, let me turn it over to Chris to start the Q&A session. I apologize that I won't be able to stay for that session, but my colleagues will be able to answer any questions on my behalf.

QUESTIONS AND ANSWERS

Operator

Your first question comes from the line of Geoffrey Porges from Leerink.

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

A really, really informative session. A couple, if I may. First, Kathrin, really extraordinary effort over the last year. But I'm trying to read into your comments -- to use a bad hockey analogy, where you think the puck is going to be in 3 months. So perhaps you could share with us a little bit more color. Are you committed already to the process of developing an Omicron variant vaccine? Or are you prepared to develop one? And what would be the evidence that would prompt you to start that process?

And then secondly, why not develop a poly-variant vaccine rather than being reactive? Is there a way to get ahead of the virus' evolution by developing a multi-component vaccine? And then just quickly on PAXLOVID, could you comment on what shelf life you will have for the finished material as you produce it?

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

Thank you, Geoff. Kathrin, can you please take the first question about the viral puck? And then about the poly-variant vaccine?

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

Sure. Thank you for the question. So as we noted today in our remarks, we are leading with science to be able to make good decisions as it pertains to Omicron or any other variants. So we -- within just a short period of time, we have demonstrated that, as it comes to Omicron, we need 3 doses of our current vaccine. And we are monitoring very closely the persistence of the antibody response against Omicron. We are looking at real-world effectiveness data as they come from the field. And we're also looking at our clinical studies, where a large proportion of individuals already received their third dose.

So in addition, as we have also noted, we are actively producing an Omicron -- an updated vaccine to address Omicron. We have reaffirmed that we can, from the start of vaccine -- of a sequence available within about 100 days, we can have an updated vaccine available. And we're actually planning to do some small clinical study starting later in the January time frame. So what we need to see, to answer the question, are we committed. We are committed to do whatever the data tell us we need to do.

And over the next few weeks and maybe a couple of months, we will carefully analyze all the data that come from the field, together with the data that we have generated, we have -- or will be generating, and then make a decision what is the best path forward for our vaccine, to update or not to update.

As your question about a poly-variant vaccine, that is also something that we have started to look into. Currently, though, it's very difficult and Omicron is a great example for that, to predict what's around the corner tomorrow. So while we are looking into potential ways of how to do this, right now, we are very focused on dealing with Omicron for the obvious reasons and using the pathways that we have described today.

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

Thank you, Kathrin. That was excellent.

Just to punctuate that with the capacity next year of 4 billion doses, we will be well prepared whether there is a need for additional boost of the current vaccine or as Kathrin alluded to, Omicron or possibly poly-variant. But please note that repeat boosting with the current vaccine has shown repeatedly that it generates antibody [breaks] like the third dose now that seem to neutralize all viral variant that have been emerging before including Omicron.

Angela, any comment on how we look upon the oral pill PAXLOVID and its stability in room temperature and shelf life?

Angela Lukin - Pfizer Inc. - Global President, Hospital

Yes. Thank you, Mikael.

Look, in terms of shelf life, dating will be dependent on stability data, which is generated over time. We will follow, of course, guidance from regulatory authorities. However, similar to vaccines, we do anticipate the initial shipments will have shorter dating. However, we expect that this will continue to improve over time.

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

Thank you. And just to underline, this is a room temperature to be stored pill and will be easy to distribute across the globe, whether in high-income and low-income countries. And that's, of course, one of the great conveniences with oral pills in addition to the ease in administration, the ease in distribution, and ease in storage. Thank you.

Operator

Your next question comes from Chris Schott from JPMorgan.

Christopher Thomas Schott - JPMorgan Chase & Co, Research Division - Senior Analyst

Can you just help a little bit with some color on the magnitude of incremental doses for the vaccine that could result if you decide to move forward with a variant vaccine? It seems like this is kind of swap out prior products. I'm just trying to understand kind of what the incremental sales. Would that just be people getting maybe a fourth shot or an acceleration of booster vaccines?

And then the second question I had was on PAXLOVID and just how to think about, I guess, for a lack of a better term, a normalized run rate for this business as we enter the endemic phase? Obviously, it will be a tremendous uptake in sales in the near term. But once we look out longer term, I guess what is the analogy for something like this? Is it Tamiflu? Or do you think this is a very different situation that could result in much higher volumes than we saw with a product like that?

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

Thank you. So Nanette, could you first discuss with us that given the rise of new variants such as Omicron, there may be a need for possibly next year, earlier rather than later, a new dose of either the current or the future before we possibly may transit to annual dosing? How does this compare to your projected use of COMIRNATY across the major regions?

Nanette Cocero - Pfizer Inc. - Global President, Vaccines

Yes. Thank you, Mikael. And yes, in 2022, we are contracted with governments and any incremental in demand will depend up on the number of doses already procured for 2022, which differ across countries. Some countries have options that they can exercise to meet any potential increase in demand while others will require a new contract or an amendment to the current contract.

For 2023, we have a hybrid of government contracts and potential for a private market. So any incremental demand will depend on if the demand exceeds the contract and if more frequent boosting was a short-term recommendation or a long-term recommendation by vaccine technical committees like the ACIP in the United States.

We currently assume annual vaccination for 2023. So in the event that boosters are recommended more than once a year, for example, we would expect to see an upside to our estimated annual revenue within the endemic phase, which we are assuming that will be more towards 2024 and beyond.

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

Thank you. Angela, will you discuss your current thinking on longer-term need, demand and use of PAXLOVID beyond the pandemic transiting to endemic? Of course, this sustained need for vaccine and treatment is probably further fueled by the recent spread of Omicron, the waning of immunity and the surge of inflections, unfortunately, across many continents, Europe, U.S. Angela, please?

Angela Lukin - Pfizer Inc. - Global President, Hospital

Yes. Thank you, Mikael. Let me just quickly start with the short term as we think about really, it's such a fluid situation as we see the pandemic evolve.

As I mentioned during my opening remarks, we really took a look at the last 6 months' worth of infection rates, applied them to 2022, just to get a general ballpark in terms of that total addressable market opportunity. And when we look at that from a patient pool point of view, exclusive of NPC markets, that's about \$150 million total addressable population, again, with the caveat that doesn't take into account infrastructure and treatment rates and things along those lines.

As we begin to shift towards more of an endemic phase, obviously, this will be driven by, as the pandemic continues to evolve, vaccination rates, circulating variants. But we also think that there may be an opportunity here in terms of stockpiling.

Although our current focus, as I said, is about ensuring that we've got sufficient supply right now to be treating symptomatic patients. However, like sometimes what we see with the flu, stockpiling may be more of an opportunity as we start to move towards that endemic phase, which we're now anticipating to be in that 2024 time period.

Given the potential pan-coronavirus activity of PAXLOVID as well as the efficacy and safety profile, we do believe it could be a valuable tool for governments not just in treating infected COVID patients but also in terms of future pandemic preparedness. So hard is going to speculate kind of the durable volume. So just to kind of give you a flavor as to some of the things that might be driving that durable volume.

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

Thank you very much. And of course, the appearance of viral variants that evade immunity, that require either new boosting campaigns or existing vaccines or possibly new variant vaccine create a pretty significant opportunity for a drug like PAXLOVID to, during that period, serve to save lives and reduce hospitalization that's putting tremendous pressure on the higher health care systems.

And unfortunately, it's likely for many years to come to be well combined comprehensive approach of using COVID vaccine and PAXLOVID oral treatment to manage such surges as well as to protect patients -- people that are vulnerable. Thank you.

Operator

Your next question comes from Louise Chen from Cantor.

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

So first question I have for you is, how do you think about sales for PAXLOVID coming from high risk, standard risk and prophylactic patients? What are the patient pools there? Secondly, in light of the data from standard risk and high risk, what do you expect to see on the prophylaxis trial that's coming up? And the last question is, do you see any cannibalization of vaccines from oral antivirals and vice versa? And where is the overlap for treatment in COVID-19 here?

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

Thank you very much. Angela, can you please address the sales perspective or maybe accessible demand in these 3 areas? And after that, Jim, could you kindly respond to how you view prospect in prophylactic setting based on other antiviral precedents?

Angela Lukin - Pfizer Inc. - Global President, Hospital

Yes. Thank you, Mikael. So as I mentioned before, it is still a relatively fluid area, as we all know, with the evolution of the pandemic. We believe all 3 patient populations that we're currently studying, high risk, standard risk and post-exposure prophylactic, will serve an important unmet need. However, given the fact we don't actually have a label yet or an EUA authorization, we think that those are going to be the things that are going to help us drive and refine in terms of what that potential opportunity is.

But as we start looking at that broader total addressable population, we are looking at all 3. But obviously, it will be critical for us to get our EUA and our label in order to fully refine what that patient population could look like in terms of size and opportunity. And again, that's also going to be driven by vaccination rates, variants of in concern in terms of which populations become of greater importance and greater size as the pandemic evolves.

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

Jim?

Jim Rusnak - Pfizer Inc. - Chief Development Officer, Internal Medicine & Hospital

Yes. So with respect to the post-exposure prophylaxis, I think that the consistent and very strong reductions that we've seen in viral load in both the EPIC-HR as well as SR, we think that would likely lead to a very favorable outcome.

I'd like to push -- point out a couple of aspects with respect to the study. So the endpoint of the trial, we'll be looking at those that have confirmed negative by PCR and they will transition over to reach an end point of both symptomatic as well as laboratory documented evidence of COVID-19 infection. So it's a very clearly delineated primary end point. And we are studying both 5 and 10 days treatment duration for this.

And this is because some other agents in the class of antiviral agents, such as Tamiflu, have shown really robust efficacy in prophylaxis trials. So with respect to Tamiflu, a prophylaxis study showed much greater efficacy in the prophylaxis indication than it showed in the treatment indication. And I think that, that could potentially be an analog for what we may see here.

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

Thank you very much. I think there was also a question, do we see cannibalization from oral PI to vaccines? And we always see vaccination as the first line of defense that should be delivered to as many as possible. We see the PAXLOVID being a terrific complementary therapeutic, both at the individual level and at the population level.

For the individual level, there may be new variants coming out. And before, you may be engaged in a new booster campaign. This is a terrific tool, particularly for high risk, and hopefully to come for standard risk patients to use to protect yourself from bad outcomes.

Unfortunately, there is a large community of unvaccinated in many different countries. And while we continue to educate, it's probably a fair assumption that for those, a treatment like PAXLOVID could be lifesaving and keep them out of hospitals.

So these are really complementary tools and modeling suggest that also earlier use of PAXLOVID-type pills will be able to contribute in addition to vaccine to contain the transmissible viral population. Thank you very much.

Operator

Your next question comes from Colin Bristow from UBS.

Colin Nigel Bristow - UBS Investment Bank, Research Division - Analyst

A couple for me. First, regarding PAXLOVID manufacturing, I understand that one of the gating factors to increasing capacity is the time for API production. And just -- could you talk about this and what work you're doing regarding optimizing this time to give yourselves a greater flexibility in the future?

And then second question is, I understand you have an IV protease inhibitor in development. Could you just give us a little more color on that and when we should expect to see data from the program?

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

Liesa, do you want to start taking on these questions?

Annaliesa Anderson - Pfizer Inc. - Chief Scientific Officer, Hospital

Thanks, Mikael. Yes, I'll start with the protease inhibitor and then maybe Angela can cover the manufacturing piece. So yes, we do have an IV protein inhibitor that currently is in a Phase 2/3 clinical study. The study is being run by the NIH as part of their ACTIV program. And we do think that it's an important study, and it's important to evaluate whether or not this IV compound, which is different to the oral medicine PAXLOVID. So we do need to see whether or not it's efficacious because it could provide something to help patients in hospital.

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

Angela?

Angela Lukin - Pfizer Inc. - Global President, Hospital

Thank you. And then, Liesa, I'll -- yes, thank you. And then I'll address the one about manufacturing. As I mentioned before, right now, we're anticipating capacity up to 80 million treatment courses in 2022 with potential for 30 million in the first half of the year. And we've just recently updated that from where we were before.

So I think we are starting to see some significant improvements in terms of yield and manufacturing in order to bring sooner and earlier doses to the first half of the year, which is great. We are currently bringing on additional capacity and ramping up further. As we know, there is a relatively long lead time around manufacturing, including getting up to API, to your point.

And as I mentioned before, we've already started to see some good improvements in terms of yield. And as we did with our vaccine, we will expect to use our strong manufacturing capabilities and, of course, our extensive supplier network to improve these outcomes -- these outputs.

So this is where we are today in terms of our ability to be able to start to drive greater efficiency. But of course, given our experience with vaccines and given our breadth and depth of our manufacturing, we'll continue to look for ways to drive even greater efficiency and improve output trying to move doses as early as possible.

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

Thank you very much. And clearly, with our leading expertise in synthesis and finding new routes for small molecules, our aspiration is to cut substantially the time to make PAXLOVID maybe even in the past times where we see desperation, and we'll keep you informed about progress.

Also, the oral PI has a very fast onset of action. And although the IV is developed for the hospitalized population, the oral gives, within hours, a very high exposure. So even in patients that are coming with severe symptoms, in the out-of-hospital population, it provides a very quick exposure that can block the protease.

And finally, when we discussed oral PI, it's good to remember that the vaccine is never 100% effective. So this is another very important aspect of looking at this as a comprehensive approach in which Pfizer can interact with physicians, patients and health care stakeholders.

Operator

Your next question comes from Mohit Bansal from Wells Fargo.

Mohit Bansal - *Wells Fargo Securities, LLC, Research Division - Senior Equity Analyst*

Great. And maybe a couple of questions from my side. Number one is that some experts in the field say that the modern vaccines maybe need to be dosed with 3 doses rather than 2 doses to provide stronger protection. So is it possible that the initial strategy to use 2 vaccines, 2 doses was inadequate and possibly the third dose would at least help with the waning efficacy after a certain amount of time?

My second question is really to the prophylaxis trial. Do you -- assuming that there is a success in prophylaxis trial, do you see a possibility of CDC recommending the use of this kind of drug as a prophylactic treatment to reduce the spread of the virus?

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

Thank you very much. Kathrin, do you want to respond to the 3 versus 2 doses? And then, you -- on the prophylaxis, particularly maybe for patients that are highly susceptible to infections. Please, Kathrin?

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

Yes. So we were really under siege with the pandemic in 2020. And so our goal was to provide an effective vaccine that would that would protect people as fast as possible. And this was the reason that we developed initially the 2-dose vaccine. And we didn't know whether 2 dose would be sufficient or whether we needed boosters, et cetera.

So over 2021, we learned that 3 doses are really providing more sustained protection against COVID-19. And this is the reason why we now have EUA approval, at least in the United States, but also elsewhere for individuals 16 and older recognizing that a 3 dose gives a more longer-term protection. And this is also the reason, as I noted earlier, why we very actively and very quickly and speedily work on making -- testing 3 dose regimens in the population under 16.

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

Thank you very much. Jim, how do you see the prophylaxis indication and how patients may, if approved, use this product?

Jim Rusnak - *Pfizer Inc. - Chief Development Officer, Internal Medicine & Hospital*

Yes. So the prophylaxis study is enrolling patients who are household contacts of the index case. And I think we really can't speculate on what the potential regulatory or other policies such as CDC guidelines would be following that, although they would be very -- although they would be potentially able to consider that.

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

Thank you very much. And clearly, as Kathrin alluded to, the 3 doses is evolving to be more of a primary series. But real-world evidence data start to show that even with 3 doses, there will be waning and certainly a need to consider for the coronavirus SARS-CoV-2 boosting with a regular basis. While this has started in many counties in the older population, it's clearly a benefit to go down in age as we develop that recommendation.

And we noted today was another paper in printed medical journal this time describing the preferred profile of COMIRNATY in patients below 40 having a much more preferred safety profile than spike vax. So this just adds to the strong role for COMIRNATY in boosters in general, and particularly in the large segment, 40 years and below, that in any country is still awaiting for boosters.

Operator

Your next question comes from Vamil Divan with Mizuho Securities.

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

Great. Thanks so much for hosting the event and I guess just thanks also for all the work you're doing around COVID. So one, maybe on the vaccine side and one on PAXLOVID. For the vaccine side, I guess, just my question is around as you think about moving more to this endemic phase over time, how you view sort of the tolerability profile for your vaccine? And if there's a sort of -- evolving sort of benefit risk as you think about, the pandemic situation to endemic, do you think the tolerability of your vaccine is okay as sort of an ongoing annual booster for many years to come? Or if not, are there stuff you're taking to try and mitigate some of the side effects that are seen.

And the second one is on the standard risk trial for PAXLOVID. And I'm just wondering about the regulatory path here. Obviously, you showed the interim data and you obviously missed on the primary endpoint. I'm curious if you think that you can hit the primary on the final just given what you showed on the interim, but interestingly, the secondary endpoint hospitalization and death may be a more important one here as opposed to symptom alleviation. So I'm wondering if you think that just hitting on the secondary would be sufficient for an EUA approval or -- So maybe just your thoughts on the regulatory outlook on standard, this would be helpful.

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

Thank you, Vamil. Bill, can you share with us your view on the tolerability profile for an endemic phase? And then Jim, please share thoughts after that on a potential regulatory path for the standard risk.

William C. Gruber - Pfizer Inc. - SVP, Vaccine Clinical Research & Development

Yes. So thank you, Mikael. I'm happy to speak to the tolerability issues. Obviously, we take the safety and tolerability of our vaccines very seriously. And as Kathrin said, been very meticulous about looking at doses that minimize tolerability concerns and maximize the potential to provide a good immune response and protection.

I think we can take some encouragement the data that we've seen in those adults that have received a third dose of vaccine that the tolerability profile is equivalent or in some instances, potentially less, I'm sorry, the reactions that we're seeing are ostensibly somewhat less or comparable to those seen after the second dose.

I think as Kathrin shared with you, as we've moved into the younger age groups, you can see that when we've gone down in dose to 10 micrograms or 3 micrograms, we have an even better tolerated vaccine. We have an ongoing study now also to look at lower doses of the booster that just started yesterday, looking at 10 micrograms. So we have a number of avenues to further explore the potential for maximizing the immune response,

particularly in the circumstance of Omicron where it appears the third dose is going to be necessary while meeting any sort of tolerability concerns as we move more into an endemic phase.

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

Jim?

Jim Rusnak - Pfizer Inc. - Chief Development Officer, Internal Medicine & Hospital

Yes. So with respect to the standard risk study. While we did miss the primary endpoint on this novel endpoint, we do believe that the hospitalization and death data are critically important for practitioners and may theoretically be important for regulators as well, although we don't think that we can really speculate at this time on this particular endpoint.

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

Kathrin, do you want to share your thoughts why we choose the mRNA platform, also thinking about endemic phase with regular boosters?

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

Yes. Thank you, Mikael. That is actually one of the reasons why we chose and we're so excited about the mRNA platform because it allows us to do multiple boosters. We do not have to deal with anti-vector immunity, for example, that vector platforms -- other vector platforms have. So -- and based on what Bill just described, I mean, we have seen the data that at least now for 3 doses and we'll soon have data also for fourth dose that the safety and tolerability profile remains excellent. And as we noted, we -- even in some instances, look even better than after 2 doses. So altogether, the RNA, we have high hopes for the RNA platform that we can continue to give boosters over time as needed.

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

Thank you very much. And for an endemic phase, of course, focus on tolerability and safety will be even more prominent. Clearly, the mRNA vaccine stands out it's noticeable very recently, the CDC Advisory Committee referred to the mRNA vaccine as the preferred versus one adenovirus vaccine that's available in U.S. due to adenovirus associated unfortunately with thrombosis thrombocytotic syndromes that can be very severe. Within the mRNA vaccine, it seems from multiple publications, multiple recommendations in many countries that Pfizer- BionTech stands out to have the best tolerability, least reactogenic and in younger patients below 40 has the best profile when it comes to rare side effect. So that's very rewarding for these further steps in an endemic transition.

And as Jim alluded to, we are entertaining with regulator sorts and welcomed our advice given the favorable effect of the standard risk study on hospitalization, and that's a very hard important endpoint. And as that study is coming to a further conclusion, we will think through all those advice and validate what are the options as the (inaudible) to provide further guidance how these patients possibly could benefit from PAXLOVID than what data would be needed and get regulatory support. So clearly, that's something we are keen to explore.

Operator

Your next question comes from Umer Raffat from Evercore ISI.

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

A couple here, if I may. First, the in vitro study you guys put out on the titer reduction against Omicron, obviously, very important to the broader public health and to the market. So that study as the titer was 154 against Omicron on the third dose. Here's what I'm trying to understand better. That same study also says the titer against wild-type virus was 2.5-fold higher after taking a third dose, even though your prior data suggests after taking a booster or the third shot, the titer against wild-type virus should be 5- to 8-fold higher. So I guess I'm just trying to understand how we reconcile the titers we saw in that in vitro study versus your own data published in the New England Journal in the past, number one.

Second, just curious what your expectations are on vaccine efficacy against Omicron over time, assuming it's protective that titer is protective near term, maybe you could draw off of your observations on the beta variant efficacy over time and whether there is or isn't T cell escape. And then finally, [Albert], if I may, how many of the 4 billion doses in 2022 will be supplied to developing countries at under \$5 price point?

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

Okay. Umer, thank you for your great interest here. Kathrin, can you please first discuss the pseudovirus neutralization data that we have shared and versus previous studies with live virus. And after that, if you also share some thoughts on efficacy over time for Delta or Omicron. And maybe, Luis, you can comment from what we start to see already in some real-world evidence. And finally, Nanette on the planned distribution for 4 billion doses. So Kathrin, please first.

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

Yes. So the data that we shared recently about Omicron were generated in what we call a pseudovirus virus assay. So that's a different assay than our workhorse that we have used and have extensively published on to look at the relative neutralization capacity of our BNT162b2 Sera. So you will see differences. But trend, the trend overall is the same, but the numerical numbers will be quite different depending on what assay you look at.

The other question, I believe, you asked was about potential T cell escape. What we have demonstrated already when we compare the sequences of Omicron to some of the other variants and wild type. Actually, T cell, particularly CD8 T cell epitopes are very well maintained in Omicron, depending on which study you pay attention to. One study says that only 1 epitope was -- minor human epitope was affected in Omicron while all others were maintained. And there's other data to show that about 80% or over 80% of important human T cell epitopes are preserved in Omicron.

And then as we -- your question about the vaccine efficacy to Omicron. What we have demonstrated today is that we restore neutralizing antibody titers to levels at which we saw protection against other variants. And so what we are doing, we are actively monitoring both from our own clinical studies, but also using real-world effectiveness data, we monitor the efficacy of individuals that received 2 as well as 3 doses. And maybe Luis Jodar can add a little bit more color to this.

Luis Jodar - *Pfizer Inc. - SVP & Chief Medical Officer, Vaccines*

Yes. Thank you, Kathrin, and thank you, Umer. I think it's important to differentiate vaccine efficacy against infection and symptomatic disease. And vaccine efficacy against severe disease. So if you remember, against the Delta, the vaccine has shown in all real world studies, very high efficacy, at least in the short term, against Delta against both infection symptomatic disease and severe disease. And then it waned and after the third dose, vaccine effectiveness was reestablished. And so far, we have not seen any indication that wanes over time.

However, with Omicron what we've seen and the preliminary data that I think has been published from the U.K. and South Africa, starts to show that corresponding to the laboratory data that Kathrin was shown, but in effectiveness against symptomatic infection -- infection and symptomatic disease after 2 doses is much lower, around 40%, whereas it still protects against severe disease and then a third dose, again, corresponding to the

lab results, there is a protection against infection and symptomatic disease of around 70%. So again, we will need to continue to monitor in real time whether there is a more pronounced waning of immunity and when a fourth dose is needed. Thank you. Back to you, Mikael.

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

And Nanette, your plans and projection for the 4 billion doses.

Nanette Cocero - Pfizer Inc. - Global President, Vaccines

Yes. Thank you. Thank you, Mikael. Let me first begin addressing the question on the LMIC doses for 2022. And let me just say that we are firmly committed to work towards equitable and affordable access of COVID-19 vaccine for people around the world and are -- and we are, like we mentioned earlier, on target to deliver on our pledge of 1 billion doses by the end of 2021. We are actively working with government as well as global health partners to work towards fair and equitable access to COVID-19 vaccine, while also providing our expertise and resources for novel approaches that can help strengthen health care systems where greater support may be needed.

In addition, also like we mentioned earlier, to the 1 billion doses that we will be delivering by the end of 2021. And we will deliver an additional 1 billion doses to LMIC also in 2022. And in fact, let me just reiterate that we currently are the largest supplier to COVAX today. So I hope that, that addresses the LMIC question.

Regarding our 4 billion doses for 2022, while we have 1.9 billion doses contracted today, we continue to engage with government regarding potential orders for 2022, including doses for which certain governments have the option to order and take deliveries in 2022. And this could be driven, like I said before, by need for additional booster doses or higher pediatric demand. And again, it does provide flexibility to scale to a new variant if indeed a new variant will be needed.

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

Thank you so much. And as you heard from Kathrin and Luis, maintaining high level of immunity by boosting is our best strategy to defend against existing and new variant while the antibodies seem to some extent, correlate with protection for symptomatic disease, as Luis alluded to the severe disease protection may remain somewhat longer in durability, although over time, we have seen waning there. And that is another important driver of boost as we believe T cell immunity supplements antibodies to protect from severe disease and hospitalization. There have been many reports that asked the question is Omicron causing less hospitalization -- While we do not know the full biology of the virus, I think another assumption taking shape is that the preexisting immunities, as Kathrin alluded to, particularly T cell immunity may be the reason why we so far haven't seen as dramatic hospitalization for Omicron and maintaining through boost that is immunity may be very critical.

Operator

Your next question comes from Andrew Baum from Citi.

Andrew Simon Baum - Citigroup Inc., Research Division - Global Head of Healthcare Research and MD

Firstly, given the potential for drug-drug interactions, could you talk to what procedures you'll be recommending for patients who are on oral antithrombotics and anticoagulants where there is a risk of severe impact for drug interactions that could cause unwanted bleeding in a fairly high percentage of patients because of the ritonavir component.

And then secondly, could you just remind us how many secondary endpoints there were in the standard risk trial? I'm just obviously thinking about the multiplicity adjustments that any regulators are going to look at when determining approval? Or are you hoping that it's going to be potentially recommended for the standard risk on a sort totality of data argument.

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

Jim, do you want to start responding to both questions concerning how to inform and direct clinicians that use PAXLOVID and possibly know what's interaction and you're thinking about the multiple secondary endpoints.

Jim Rusnak - Pfizer Inc. - Chief Development Officer, Internal Medicine & Hospital

Yes. So first, with respect to the drug-drug interactions, I think that we need to sort of consider with the strong efficacy of PAXLOVID. We do believe the associated drug-drug interactions can be clinically managed, especially for the 5-day short-term duration period. Through the EUA fact sheet for PAXLOVID, we will be providing a comprehensive list of DDRs. And when you use for that fact sheet, the DDRs I think can be effectively managed by the health care practitioner.

With respect to the standard risk study, we didn't initially power this trial for the hospitalization and death endpoint, although it was much more clinically relevant because of the presumes very low event rates. And then after we saw the results of the EPIC-SR study, the clinical protocol, which was actually modified so that the endpoint of hospitalization and death was no longer amongst all of the secondary endpoints, but it was elevated to a key secondary endpoint. And we do believe that there could be a path forward and that we are in discussion with regulators on this particular study.

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

Thank you very much. I just wanted to punctuate that in the high-risk and standard-risk both trials showed a consistent about 1 log reduction viral load, which is among the best demonstrated for an antiviral in COVID and certainly among the oral. And please note the ritonavir dose, 100-milligram is more of an intermediate dose. And hence, we believe that the guidance provided in the fact sheet will allow pretty convenient and very manageable care of patients, including whether they use Norvasc.

Operator

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

Geoffrey Christopher Meacham - BofA Securities, Research Division - Research Analyst

Just have a few on PAXLOVID. The first one is whether you have evaluated the impact on transmission rates. I'm just thinking given the mechanism, if you thought that after some period of time, call it, a few days, whether you see an effect on viral transmission? And the second question is related to resistance. And just curious what work you've done preclinically on viral resistance, I know you guys are effective against several variants, but are you able to force resistance in the lab? And if so, what does that look like?

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

Thank you, Geoff. Lisa, do you want to take on these 2 questions, please. I'm happy to comment.

Annaliesa Anderson - Pfizer Inc. - Chief Scientific Officer, Hospital

Thank you, Mikael. Yes. So the first question about the transmission rate. We have not studied this clinically in the current Phase 2/3 studies that we have. There has been a publication by a group in Belgium in the nonclinical study in hamsters, where they were able to show very nicely that if they treat it hamsters who haven't been infected and then house them with infected hamsters that they didn't see transmission. So we don't have any clinical evidence yet, but there is strong nonclinical evidence.

So your second question was around resistance and what have we done to potentially force resistance. So first, I'd like to say that we're very confident that PAXLOVID will maintain activity as a single use agent. And this is for several reasons. So first, the essential nature of the protein in the fact that it prevents if you inhibit it, it prevents viral replication. And so therefore, if you -- it's very -- it's not susceptible to rapid change. We have done some preliminary work in the laboratory. And what we're finding is it is quite hard to develop resistance and strains a surrogate model, mass hepatitis virus do seem to be somewhat crippled in growth, which is promising. We do acknowledge that we do see that with many antivirals resistance does occur. But again, we don't put several things in place to prevent that. So first of all, we have very high concentrations of PAXLOVID in the plasma, further reducing the potential for resistance. And in fact, we purposefully added the ritonavir so that we could maintain high plasma concentrations that were above -- manyfold above the EC 90 of the compound.

In addition to that, as I explained in the slide, the way that we have designed the molecule makes it much harder for the protease to actually change and to be able to resist the molecule from a resistance perspective. And so overall, we are quite confident that it should -- see resistance emerging rapidly. But in acknowledgment for the potential for that to happen, we have put surveillance in place. And as you pointed out, we are looking at generating post-resistance range so that we could understand how resistance may occur and how we can then adapt if we see it.

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

Thank you, Lisa. And as we heard, it was an intentional strategy to use ritanovir boost to get up to 6x EC90, which likely contributes to this dramatic efficacy of close to 90%, whether treating up to 3 or 5 of the symptoms. And we believe that for the next quite many years forward, resistance for short-term treatment will not be a major problem but we really have a long-term perspective of being a leader for treatment and vaccination against coronaviruses for the decade to come -- And finally, as you spoke about the conserved protease, let us just remind you that PAXLOVID or the active ingredients is active across not just all studied variant of SARS-CoV-2 about near 12 years as the active in region of PAXLOVID effective against many different coronaviruses, further underlining how difficult it is to change that protease without crippling the virus. We are very confident that this treatment will maintain high efficacy for quite some time, many years to come.

Operator

Your next question comes from Steve Scala from Cowen.

Stephen Michael Scala - Cowen and Company, LLC, Research Division - MD & Senior Research Analyst

I have a few questions. Will the Phase 3 pediatric vaccine data coming in the first half of next year include effectiveness data or only immunogenicity? And if only immunogenicity is that enough for EUA -- And what portion of the 2022 vaccine guidance is for pediatric use. So that's the first question.

Second question is, why do you think PAXLOVID data was either roughly the same or improved from interim to final look and the molnupiravir data got substantially worse. Was it the disease backdrop variance differences in the molecules or was it something else?

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

Thank you, Bill, do you want to share the planned approach for the pediatric studies for the first part of next year. And then, Jim, you could follow on discussing the strong consistency interim final analysis for the IRIS trial.

William C. Gruber - Pfizer Inc. - SVP, Vaccine Clinical Research & Development

Yes. Thank you, Mikael. So for the first question, in terms of the path to EUA approval, we've, again, continued to have positive discussions with the regulatory authorities, particularly the FDA about immunobridging and noninferiority comparing immune response after a third dose to the immune responses we saw with wild-type after 2 doses. But as you may be aware, all of our studies continue to provide active surveillance looking for potential efficacy and effectiveness. And of course, our ability to demonstrate that is in part dependent on what the attack rate is. I think with

Omicron looming and its transmissibility, we stand in a good position to have efficacy information to inform decision-making just like we did for the 12- to 15-year-old where we saw the 016 split and as well as the 5 to 11-year-olds where we saw a 90.7% efficacy.

So we will have both bits of information, but we're not absolutely dependent based on our current regulatory discussion on having the efficacy information that would find it informative and we'll try to obtain it.

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

Jim, can you take the PAXLOVID and then Nanette will also comment on how much your pediatric is in your '22 projections. Jim, first on the consistency.

Jim Rusnak - Pfizer Inc. - Chief Development Officer, Internal Medicine & Hospital

Yes. So with respect to the consistency of EPIC-HR, I think that first, the trial was actually recruited very quickly from July through October of this year. We had a very consistent geographical footprint between the first half of the interim analysis in the second half of the interim analysis. But I think perhaps why it's so consistent may reflect, again, the choice of dosing that we went in with a dose that would give us that 5- to 6-fold EC90. And while it required ritonavir to get us to those levels, which is clinically manageable, it is what drives a lot of the efficacy in my opinion.

So in order to get an 89% efficacy, not only do you need to have the data be consistent across the pre- and post-interim analysis, but it also needs to be consistent across a broad number of sub-groups.

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

Yes. Thank you, Nanette?

Nanette Cocero - Pfizer Inc. - Global President, Vaccines

Thank you, Mikael. Yes, to address the question on the impact of younger than 5-year-old to the 2022 guidance that we have shared. We do not expect the information that we shared today to impact regarding the younger than 5-year-old group to impact 2022 revenue guidance because our timeline for expected filing and authorization remains unchanged. -- we expect to gain authorization in 2022 and, therefore, do not expect any negative impact in 2022 or 2023 and beyond. So everything continues on time.

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

That's great. And of course, there is now increasing interest to discuss the third dose. And you heard that's part of our plans to document across many doses, which would conclude a more comprehensive explanation for pediatrics as some in '22 on those already recommended ages and younger for potentially, as Nanette spoke to '23.

Operator

Your final question comes from Matthew Harrison from Morgan Stanley.

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

Great. Three for me, if I may. So two first on PAXLOVID. Can you comment, previously you commented that you don't believe an advisory committee would be necessary to confirm that, that's still your view? And then second, notwithstanding your prior comments related to resistance are you

considering or are you looking into development of other classes of antivirals to potentially pair with that drug in case resistance does become a problem?

And then third, on the vaccine, have you tested sera at other time points in the pseudovirus assay? So maybe patients that have been boosted 3 months or 5 months or 6 months out from their boost to see what the potential durability of the boost is versus Omicron.

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

Thank you very much. So Jim, can you comment on the, our belief that there may be no need for an ad committee. And Lisa, whether you are exploring other antivirals among your many approaches to secure long-term leadership. And finally Kathrin on the vaccine question other time points on the vaccine question for the assay.

Jim Rusnak - Pfizer Inc. - Chief Development Officer, Internal Medicine & Hospital

So with respect to the AdCom, at this time, we've not received any requests to participate in [Advisory] committee hearing. It's notable that other therapeutic antibodies have also not required advisory committee meetings.

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

Liesa.

Annaliesa Anderson - Pfizer Inc. - Chief Scientific Officer, Hospital

Yes, yes. All right. So I plan what we were doing regarding looking for resistance and seeing if we could force resistance. And also that we don't think that we'll see resistance in the short term based on how we've designed the molecule and also the fact that it's a very short treatment. However, resistance can occur. And so what we're doing is in the work that we're doing in the laboratories and the surveillance, we're taking learnings from that to help us to design our second-generation program. Likewise, combination approaches have been successful for other antiviral treatments, and so we're also looking into that as well. But for the near term, we're not expecting to see rapid resistance emerge, but we are prepared for the long-term view.

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

And Kathrin, on the time points for durability of neutralizing antibodies?

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

Yes. Thank you, Mikael. As we have shown today, we do look over the persistence of our antibody responses. And so far, we have data after 2 and 3 doses, and we continue to monitor the vaccine neutralization against Omicron in several assays, including our glucose assay.

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

And thank you for all those that listened in to our update on our COVID-19 vaccine and therapeutics. I think you got the sense that we have a very strong team with deep expertise. We are committed to be a leader in surveillance of how COVID variants are evolving and their impact on the health care system -- And that's linked to us performing real-world evidence in partnership with leading countries that have such instant reporting systems, whether U.K., Israel, Nordic region and U.S. CDC. We are constantly releasing as leaders in the field, new data about the COVID vaccine

different dosing, the third dose. And we are, of course, active with work both in planned randomized clinical trials in real-world evidence to understand when a fourth dose should be given with a vaccine and what type of vaccine.

And similarly, of course, concerning PAXLOVID, trying to generate the best experience for treatment initially with a high-risk trial that, as you know, already got positive opinion in CHMP and possibly maybe nation by nation in Europe available pretty soon -- We look forward to potentially having that medicine available soon post EUA in U.S.

And we'll continue to be a leader in monitoring for any potential resistance but feel pretty confident that this is more a mid- to long-term objective, but we aim to be a leader also for that longer-term perspective. Thank you for your interest in Pfizer in our COVID vaccine and therapeutics. I'll ask Steve -- Chris Stevo if there are any concluding remarks from you.

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

Thanks, Mikael. I appreciate that. Thank you, everyone, for your time and interest in Pfizer. And thank you to all my colleagues who took place -- took part in today's call. We appreciate your time -- And we wish everyone a very happy holidays and best wishes for 2022. Thank you.

Operator

Ladies and gentlemen, this does conclude today's conference. Thank you for your participation. You may now disconnect.

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