

REFINITIV STREETEVENTS

EDITED TRANSCRIPT

Q4 2021 Pfizer Inc Earnings Call

EVENT DATE/TIME: FEBRUARY 08, 2022 / 3:00PM GMT

CORPORATE PARTICIPANTS

Aamir Malik Pfizer Inc. - Executive VP & Chief Business Innovation Officer
Albert Bourla Pfizer Inc. - Chairman of the Board & CEO
Angela Hwang Pfizer Inc. - Group President of Biopharmaceuticals Group
Christopher J. Stevo Pfizer Inc. - Senior VP & Chief IR Officer
Douglas M. Lankler Pfizer Inc. - Executive VP & General Counsel
Frank D'Amelio Pfizer Inc. - Executive VP & Chief Financial Officer
Mikael Dolsten Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical

CONFERENCE CALL PARTICIPANTS

Andrew Simon Baum Citigroup Inc. Exchange Research - Research Analyst
Carter Lewis Gould Barclays Bank PLC, Research Division - Senior Analyst
Chris Shibutani Goldman Sachs Group, Inc., Research Division - Research Analyst
Christopher Thomas Schott JPMorgan Chase & Co, Research Division - Senior Analyst
Evan David Seigerman BMO Capital Markets Equity Research - MD & Senior BioPharma Research Analyst
Geoffrey Christopher Meacham BofA Securities, Research Division - Research Analyst
Kerry Ann Holford Joh. Berenberg, Gossler & Co. KG, Research Division - Analyst
Louise Alesandra Chen Cantor Fitzgerald & Co., Research Division - Senior Research Analyst & MD
Mohit Bansal Wells Fargo Securities, LLC, Research Division - Senior Equity Analyst
Stephen Michael Scala Cowen and Company, LLC, Research Division - MD & Senior Research Analyst
Timothy Minton Anderson Wolfe Research, LLC - MD of Equity Research
Umer Raffat Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research
Vamil Kishore Divan Mizuho Securities USA LLC, Research Division - MD

PRESENTATION

Operator

Good day, everyone, and welcome to Pfizer's Fourth Quarter 2021 Earnings Conference Call. 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, Sylvia. Good morning, everyone. Welcome to Pfizer's Fourth Quarter Earnings Call. I'm joined today by Dr. Albert Bourla, our Chairman and CEO; Frank D'Amelio, our CFO; Mikael Dolsten, President, Worldwide Research and Development and Medical; Angela Hwang, Group President, Pfizer Biopharmaceuticals Group; Aamir Malik, our Chief Business and Innovation Officer; and Doug Lankler, our General Counsel. We expect this call to last 90 minutes.

The materials for this call and other earnings-related materials are on the Investor Relations section of Pfizer.com. Please see our forward-looking statements disclaimer on Slide 3. And additional information regarding these statements and our non-GAAP financial measures is available on our earnings release and in our SEC Forms 10-K and 10-Q under Risk Factors. Forward-looking statements on the call are subject to substantial risks and uncertainties, speak only as of the call's original date, and we undertake no obligation to update or revise any of these statements.

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

Albert Bourla Pfizer Inc. - Chairman of the Board & CEO

Thank you, Chris. Hello, everyone.

2021 was a watershed year for Pfizer, a year in which we set all-time highs in all major areas of focus for Pfizer. We reached an estimated 1.4 billion patients with our medicines and vaccines. That's more than 1 out of every 6 people on earth. Never before has Pfizer's patient impact been so wide reaching.

We improved our ranking from fourth to second among large biopharma companies in the PatientView Global Survey. According to

Morning Consult, 61% of Americans have a favorable view of Pfizer, which is up 33 points since January of 2020. Just last week, Fortune ranked us 4th on its annual World's Most Admired Companies list, the highest ranking we have ever achieved. 95% of our colleagues said in an internal survey that they are proud to work for Pfizer, which ranks among the best in corporate America. We increased our investments in research and development from \$8.9 billion in 2020 to \$10.5 billion in 2021, and we initiated 13 pivotal clinical studies, the highest number ever for Pfizer. Last but not least, we grew revenues by 92% operationally to \$81.3 billion and Adjusted diluted EPS by 92% operationally to \$4.42.

Our success in leading the fight against COVID-19 have not only made a positive difference in the world. I believe they have fundamentally changed our company and our culture forever. Colleagues across Pfizer are inspired by what we have achieved and most are more determined than ever to be part of the next potentially game-changing breakthrough. To that end, we are applying the Lightspeed principles developed for our COVID-19 work to our other therapeutic areas to make sure we continue to move at the speed of science for the benefits of all patients.

As a result, we believe we can do even better with each of these metrics in 2022, each one of them. Our full year 2022 financial guidance, for example, includes, for the first time ever, a forecasted revenue midpoint, that it is triple digit, \$100 billion, and an Adjusted diluted EPS midpoint of \$6.45.

While Comirnaty is having a significant positive impact on Pfizer's financial performance, it is the tremendous impact that COVID-19 vaccines have had on society that it is most important. In the U.S. alone, the COVID-19 vaccination program is estimated to have saved more than 1 million lives and prevented more than 10 million hospitalizations, according to a December 2021 Commonwealth Fund report.

The economic impact is equally astonishing, astounding. According to December 2021 Heartland Forward report, the rapid deployment and wide availability of COVID-19 vaccines in the U.S. created an estimated economic savings of \$438 billion in 2021 alone, which amounted to U.S. GDP being 2.3% higher than it otherwise would have been, 2.3 points.

I'm proud to say that Pfizer contributed significantly to these benefits, given that approximately 6 out of 10 doses administered in the U.S. as of February 6, 2022, were Comirnaty. This is the value of our science, what our culture has enabled and what drives our people.

Now I would like to speak to 3 factors that will help drive our growth going forward. The first is the long-term outlook for COVID-19 and why we believe we are well positioned to continue to lead the battle against this disease. Second, our thoughtful capital allocation strategy and why we believe it can help drive our growth in the second part of the decade. And third, how our commitment to ESG principles is designed to create sustainable growth for Pfizer to deliver meaningful value to patients and society.

Let me start with the COVID-19 pandemic. Our scientists continue to monitor the SARS-CoV-2 virus and believe it is unlikely that it will be fully eradicated in the foreseeable future. They believe this for several reasons. The global distribution of the virus makes it difficult to contain. The virus has shown an ability to mutate often, making it difficult to stay ahead of it. And the data appear to show that natural infections do not lead to the type of durable protection needed to prevent all transmissions and viral mutations. As a result, people can become reinfected by the same or different strains over time.

That said, we now have the tools in the form of vaccines and treatments, that we believe will help enable us to not only better manage the pandemic, but also help countries move into an endemic phase. In other words, we believe these tools will help us allow us to go back to normalcy and spend time with family and friends, travel, attend indoor dining and concerts and enjoy many other activities, while lowering the risk of overburdening hospitals and health care systems around the world.

All of us at Pfizer are extremely proud of the role we have continued to play in bringing these tools to the world. Throughout 2021, we continued our efforts to bring our COVID-19 vaccine to more populations and to further ramp up our manufacturing and distribution capabilities. As a result, the market share of our Comirnaty vaccine has continued to grow, representing 70% of all doses distributed across the U.S. and EU as of February 5.

When it comes to Paxlovid, we expect to produce 6 million treatment courses during the first quarter of '22. Overall, we expect to produce 30 million courses in the first half of 2022 and 120 million courses for the full year, of course, depending on the global need. Having recently received a conditional marketing authorization from the European Medicines Agency, Paxlovid has now received emergency or conditional authorization for use with certain populations in approximately 40 countries so far. We are in discussions with governments around the world and expect that as the number of authorizations increase, so will the number of contracts for this treatment, which could truly be a game changer.

At Pfizer, we are keenly aware of our responsibility to continue to invest in R&D to maintain our leadership in providing these tools and other meaningful solutions to the world. That's why we continue to develop and test different versions of our vaccine to potentially address variants of concern as they emerge, and why we are currently working on a new Omicron-based vaccine candidate and on a bivalent COVID-19 vaccine candidate. It is also why just 2 months after receiving Emergency Use Authorization from the U.S. Food and Drug Administration for Paxlovid, we are already working on a potential next-generation oral COVID-19 treatment. Going forward, we are confident in our ability to maintain this leadership position because of our significant investments in R&D; combined with our ability to move at the speed of science without compromising quality or safety; the strong credibility we have earned with governments, health care providers and consumers; combined with our extensive global field presence and our unparalleled capabilities for high-quality manufacturing at scale.

Now the second thing I wanted to touch on is how we think about our capital allocation and to repeat once more our strategy. We feel that the entirety of our business continues to demonstrate a robust top line growth trajectory through 2025. Consensus estimates are beginning to slowly recognize this momentum. However, consensus estimates currently saw our top line shrinking from 2025 to 2030. I want to repeat that this is inconsistent with our own plans. Our goal is to continue to be a growth company from '25 to 2030, despite the impact of LOEs expected during that period.

Our confidence in our ability to achieve that is underpinned by the momentum of our business, the durability of our COVID-19 offerings, which as I just described, the underestimated strength of our internal pipeline; and of course, by our ability to deploy capital into growth-focused business development to access external science.

A few words about that. We leverage business development opportunities to advance our business strategies and objectives. The strength of our balance sheet and cash flows allows us to pursue new business development opportunities going forward that could add at least \$25 billion of risk-adjusted revenues to our 2030 top line expectations. We expect to do this while still maintaining our growing dividend as well as flexibility for other uses of our cash.

The focus of our business development efforts will continue to be on compelling external science in the form of both later-stage assets as well as earlier medical innovations that have the potential to be breakthroughs for patients. Our focus will largely be in the therapeutic areas and platforms where we have the scientific skills and acumen to add substantial value and select the most successful targets. In addition, we feel that we have distinctive attributes, such as world-class excellence in clinical development and unsurpassed manufacturing and commercial capabilities at scale that makes us a very attractive partner across a variety of deal arrangements. We believe the opportunities to deliver on this approach exist, and I will be personally focusing on this execution.

I want to emphasize that despite our significant capital flexibility, we will never lower the scientific and financial standards we apply in our business development. As we pursue these opportunities, we will continue to be highly disciplined in our evaluation and prioritization processes.

Since 2019, we have already invested almost \$25 billion in business development transactions, adding more than \$13 billion in consensus, I repeat, in consensus 2030 revenue. I would point out that the \$13 billion of consensus currently includes nothing for the Trillium assets, the Biohaven collaboration or the recently announced mRNA deals, all of which have substantial potential. I see this pace of business development accelerating going forward, and I'm confident it will be an important driver in ensuring Pfizer as a growth company in the back half of this decade.

One highly visible example of our approach to business development is the recent investments we are making in mRNA technology and

collaborations. mRNA has emerged as a versatile technology with potential application across many infectious diseases, cancer, rare genetic disorders and even autoimmune diseases. Although mRNA is not the holy grail, we believe the technology has the potential to have a game-changing impact on global health, which is why we have developed a robust mRNA strategy and are aggressively building our platform.

While the pandemic has demonstrated that it is not that easy to deliver mRNA vaccines at scale, Pfizer has emerged as a leader in this space. With decades of experience on our side, we have developed what is arguably the most efficient clinical development and vaccine manufacturing capabilities the world has ever seen. We also have rapidly scaled and built out new capabilities in record time by hiring nearly 2,400 new colleagues in these functions in a 9-month time frame. Going forward, we plan to continue to invest to capitalize on the leadership we have built in terms of both mRNA R&D and manufacturing.

In addition, of course, to these internal investments and improvements, we are also making external investments to build out our capabilities in this space. For example, Pfizer recently has entered into 4 important business development deals to help advance our mRNA strategy. We are expanding our collaboration with BioNTech to use the existing platform to co-develop an mRNA vaccine candidate for herpes zoster virus to protect against shingles.

Our agreement with Beam Therapeutics expands our mRNA efforts to another core therapeutic area for Pfizer, the rare disease, with a 4-year research collaboration for 3 targets for rare genetic diseases of the liver, muscle and central nervous system. We believe this will give us the potential to use mRNA to treat diseases, not just prevent them.

Our agreement with Acuitas gives us the ability to collaborate with and license their proprietary lipid nanoparticle technology for up to 10 targets for mRNA vaccines and therapy. We believe this will give us greater independence in this space. And we have signed a strategic collaboration and licensing agreement with Codex DNA, a leader in the development of automated solutions for on-demand synthesis of genes and mRNA, potentially allowing enzymatic assembly of DNA at the front end of the mRNA production process. This could possibly reduce the time to produce a new vaccine from 3 months down to 2 months. If successful, this would be an important differentiator when developing a vaccine for the flu, for example, as it would allow us to select a strain much closer to the start of any flu season.

These deals represent only 4 pieces of a much bigger strategic puzzle. As we continue executing on our mRNA strategy, you should expect to see more targeted activity in this area.

Of course, our business development activity in the last quarter went beyond executing on our mRNA strategy. This is an update of the slide I showed you last quarter, and I would like to highlight a few of the other recent deals. They are marked as new in this slide.

The acquisition of Trillium builds on our strong track record of leadership in oncology, enhancing our hematology portfolio as we strive to improve outcomes for people living with blood cancers around the globe. Our strategic collaboration with Biohaven leverages our leading commercial capabilities in pain and in women's health.

(technical difficulty)

I apologize. We're back. I apologize for the technical issue. I will repeat my script for this last slide, and then we go forward.

So of course, our business development activity in the last quarter went beyond executing on our mRNA strategy. This is an update of the slide I showed you last quarter, and I would like to highlight a few of the other recent deals. You can see them with the indication of new.

The acquisition of Trillium builds on our strong track record of leadership in oncology, enhancing our hematology portfolio as we strive to improve outcomes for people living with blood cancers around the globe. Our strategic collaboration with Biohaven leverages our leading commercial capabilities in pain and women's health, with Biohaven's groundbreaking oral CGRP receptor antagonist, the only one approved in the U.S. for both acute and preventative treatment of migraine, so that we can potentially bring a valuable new treatment option to patients living with this debilitating neurological disease outside the U.S.

And through our proposed acquisition of Arena, we plan to leverage Pfizer's leading research and global development capabilities to accelerate the clinical development of etrasimod for patients with immuno-inflammatory diseases.

Now I would like to share some details about Pfizer's enhanced ESG strategy. The strategy is focused on 6 areas where we see opportunities to create a meaningful and measurable impact over the next decade: product innovation, equitable access and pricing, product quality and safety; diversity, equity and inclusion; climate change and business ethics.

Each quarter going forward, I will provide examples of how we are embedding ESG into all core areas of our business. This quarter, I would highlight our efforts to improve clinical trial diversity, to improve diversity within our colleague base and help ensure equitable access to our COVID-19 vaccine and treatment.

Last year, Pfizer published an industry-first retrospective analysis of demographic data of U.S. participants in 213 of our interventional clinical trials that initiated enrollment from 2011 through 2020. The analysis demonstrated that overall trial participation of Black or African American individuals was at the U.S. census level, 14.3% versus 13.4%; participation of Hispanic or Latino individuals was below U.S. census, 15.9% versus 18.5%; and female participation was at U.S. census, 51.1% versus 50.8%.

We published this analysis to be transparent and for it to serve as the baseline as we measure progress in this area. We believe that diversity in trials is a matter of equity and good science and are taking decisive steps designed to improve diversity in our trials. Our goal is to achieve racially and ethnically diverse participation at or above U.S. census or disease prevalence levels, as appropriate, in all our trials.

The second item I want to highlight is the significant progress we are making in diversifying our colleague base, particularly at more senior-level positions. In the last 3 years, for example, we have increased the percentage of women at the vice president level and above globally from 32% to 42%. Over the same time frame, we have increased the percentage of minorities at the vice president level and above in the U.S. from 19% to 25%.

The third item I wanted to highlight is the progress we are making to help ensure our COVID-19 vaccine and oral treatment are accessible by everyone everywhere. I am thrilled to say that we remain on track to meet or exceed our global -- our goal of delivering at least 2 billion doses of our vaccine to low and middle-income countries by the end of 2022, having just met our goal of delivering the first 1 billion by the end of 2021.

I also want to highlight 2 data points about our 2 billion dose commitment. One billion of these doses are being provided to the poorest countries completely free of charge. Thanks to our agreement with the U.S. government, Pfizer is providing these doses to the U.S. government at a not-for-profit price, and the government is then providing them to the poorest countries for free. Also, the 1 billion doses we delivered in 2021 represented 37% of all doses we delivered this last year.

In terms of our oral COVID-19 treatment, we have signed a voluntary license agreement with the Medicines Patent Pool, which we hope will lead to expanded access, pending country regulatory authorization or approval, in 95 low- and middle-income countries that account for approximately 53% of the world population. Lastly, I'm pleased to announce that the Compensation Committee of our Board of Directors has been reviewing methods for linking executive compensation with ESG performance, which we expect to begin this year. For details regarding the impact of our ESG strategy had on our business in 2021, please keep an eye out for Pfizer's 2021 ESG report, which will be published online in mid-March.

In summary, 2021 was an outstanding year for Pfizer, and we look forward to continuing to apply the lessons learned from COVID-19 to deliver breakthroughs for patients across all our therapeutic areas. We remain focused on being nimble, investing in our R&D organization and exploring dynamic partnerships that will enable us to fully realize the power of our science.

None of this is possible without the contributions of our amazingly purpose-driven colleagues, who continue to rise to the challenge of addressing the world's most devastating diseases. In 2021, our colleagues exceeded expectations. Therefore, we will once again use part of the bonus pool that the Board approved for bonus-eligible colleagues and executives to provide a onetime, special COVID-19

Circumstances Bonus to our non-bonus-eligible colleagues across the board to reward them for their hard work and to help them cover personal, family and living expenses incurred because of the COVID-19 pandemic.

With that, I will turn it over to Mikael to update you on our R&D efforts. After Mikael, Frank will provide financial details on the fourth quarter and our outlook for 2022. So, Mikael?

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

Thank you, Albert. I'm delighted to share updates from this quarter as we continue to deliver first-in-class science. Today, I will share updates from our COVID-19 programs and select other assets in our pipeline. Let's start with Paxlovid.

As the COVID-19 pandemic continues to burden public health, we have advanced the science on our novel oral antiviral therapeutics. Importantly, we see consistent, potent antiviral activity in vitro against all current variants of concern, including both Delta and Omicron.

This would be expected from how the compound was designed. On the left, you can see a crystal structure showing how tightly nirmatrelvir binds to the active site of the Omicron variant. History has told us from the HIV protease field that the closer the therapeutic is designed to mimic the substrate, the harder it is for resistance to emerge. That, combined with the essential nature of the protease, the short duration of treatment and the co-dosing with ritonavir to drug exposures that are over 5 to 6x the amount of compound needed to kill the virus in an in vitro assay, suggest there is reduced risk for resistance.

External data support our findings. In this slide, the lower values, the stronger potency, illustrated by nirmatrelvir being on the lower end of the Y axis on the left, having the most potent activity. Nirmatrelvir maintains in vitro potency in the low nanomolar range, as you can see in these graphs that include other authorized or approved therapeutics.

On the left is in vitro data from a study done with the Icahn School of Medicine at Mount Sinai and Pfizer. Nirmatrelvir demonstrated potent antiviral activity, as measured by IC50, a measure of drug efficacy indicating the concentration needed to inhibit infection by half. This is consistent with findings from the Rega Institute at KU Leuven in Belgium, shown on the right.

We anticipate a New Drug Application decision by the FDA in the high-risk population in second half of '22; pivotal readouts of our household contact and standard-risk studies in the second quarter and second half of '22, respectively; and the study start in children 6 to 18 years old in the first quarter of '22. In the standard-risk study, we're expanding enrollment by 750 non-hospitalized patients with symptomatic COVID-19, and vaccinated standard-risk patients may also be eligible, provided their last SARS-CoV-2 vaccine dose was received at least 12 months prior to screening. This expansion will allow us to further evaluate the secondary end points seen in the interim analysis, which showed a 70% reduction in hospitalization and no death in the treated compared to placebo.

We also are advancing work on a potential next-generation SARS-CoV-2 antiviral with the aim of achieving similar high clinical efficacy in pan-coronavirus design properties that maintain activity with a favorable safety profile and counter potential viral resistance, but without the need for ritonavir boosting. A first in human study is expected in the second half of '22.

Now we also continue to advance vaccine development and have achieved Emergency Use Authorization for use in children as young as age 5. Effectiveness data for 3 doses of the vaccine for 12 -- people 12 years and older, and early laboratory data observed with Delta and other variants of concern, including Omicron, suggest that people vaccinated with 3 doses of Comirnaty may have a higher degree of protection against both symptomatic and severe outcomes compared to 2 primary doses.

Informed by this data, in addition to the immuno-bridging data, we are evaluating a third 3-microgram dose in our study of children 6 months through 4 years of age, with the belief that a third dose may be optimal for this age group. However, as pediatric cases and hospitalization are at an all-time high, FDA urged us to start a rolling EUA authorization submission with the 2-dose efficacy, immunogenicity and safety data we have accumulated thus far, while we continue to collect data, including on third-dose administration. We plan to submit third-dose data once they're available.

In the meantime, FDA has scheduled an Advisory Committee meeting for February 15 to consider the 2-dose pediatric data collected

today. If Emergency Use Authorization of 2 doses is granted and the CDC recommends usage, parents will have the opportunity to begin a COVID-19 vaccination series for their children between 6 months and 4 years of age, while awaiting potential authorization of a third dose.

Turning to the adult population. In the wake of surging Omicron cases, in January, we completed a lab analysis of the effect of a third dose boost of Comirnaty on live virus neutralization. Encouragingly, there was a more than 25-fold increase in Omicron live virus neutralization titers observed between day of dose 3 and 1 month post-dose 3. We observed a moderate 4-month post-dose 3 antibody decay for wild type and the Omicron variant. Between 1 month and 4 months post-dose 3, neutralizing titers were at 1.6 and twofold lower for wild type and the Omicron, respectively.

We're now starting to see effects of a third dose boost in maintaining a high level of protection against Omicron in the real world. These data from Kaiser Permanente Southern California show Omicron-related emergency department visits without hospitalization on top and hospitalization on the bottom. Three doses of Comirnaty provided better vaccine effectiveness against Omicron than 2 doses. And there was high vaccine effectiveness of 3 doses against Omicron-related hospitalization, similar to Delta-related hospitalization. We did see some waning of effectiveness against emergency department admissions due to Omicron 3 months or more after third dose, which suggest the potential need for another boost of the current vaccine or an Omicron-based vaccine.

We have started an Omicron-based vaccine candidate trial in adults 18 to 55 years of age. This study will evaluate more than 1,400 participants across 3 cohorts. Those who have already received 2 doses of the current vaccine 90 to 180 days prior to enrollment will receive 1 or 2 doses of the based Omicron-based vaccine. Those who have already received 3 doses of the current vaccine 90 to 180 days prior to enrollment will receive 1 dose of the current vaccine or the Omicron-based vaccine. And those who are vaccine-naive will receive 3 doses of the Omicron-based vaccine. This study is part of our science-based approach to develop a variant-based vaccine that we hope achieves a similar level of protection against Omicron as the current vaccine has with both wild type and earlier variant, but with potentially longer duration of protection.

Now let's turn to our next-generation CDK inhibitors for cancer. Most patients with advanced or metastatic breast cancer eventually develop resistance to both endocrine and CDK4/6 inhibitor therapy despite their transformative efficacy. Inhibition of CDK2 delivered with a CDK-selective active drug or a triple-active CDK2/4/6 agent may prevent, delay or reverse resistance and prolong survival.

These are data from a subset in the CDK2/4/6 inhibitor Phase 1 dose escalation and antitumor activity study of heavily pretreated patients with hormone receptor positive metastatic breast cancer. The most improvement in terms of tumor size reduction was seen in patients treated with monotherapy or in combination with fulvestrant. We observed 3 confirmed partial responses and 3 patients with stable disease for more than 12 months. One patient has been receiving ongoing treatment for more than 28 months. There's been an acceptable safety profile at the recommended Phase 2 dose, which is 25 milligrams twice daily. We plan to conduct a Phase 1 dose expansion and expect to complete it in the fourth quarter of this year.

Selective CDK2 inhibition with a CDK2-only inhibitor may allow dose titration and has the potential to be used in combination with approved CDK inhibitors, such as palbociclib or other next-generation CDK selective inhibitors. There were 2 confirmed partial responses in the Phase 1 study of our selective CDK2 inhibitor in patients with advanced or metastatic hormone receptor HER2-negative breast cancer, who had received/progressed on prior CDK4/6 inhibition and endocrine therapy. One patient had a maximum tumor shrinkage of 54% following CDK2 inhibitor treatment for approximately 8 months, and the second had 100% shrinkage of all target lesions following treatment for approximately 9 months.

We are showing scans of the first patient at baseline and 8 weeks. There was an acceptable safety profile as a monotherapy, and we're currently exploring combinations. We expect the Phase 1/2 study to be completed in the second quarter of '23.

Now let's turn to our 6-valent Lyme disease vaccine candidate, which we are developing in partnership with Valneva. We have received further positive data from our Phase II proof-of-concept study and expect to start Phase 3 in the third quarter of this year with a dosing regimen of 0, 2 and 6 months to prime, followed by routine boosters before the start of a Lyme season. Our Phase 2 studies continue and includes a pediatric population ages 5 to 17 years.

Since Lyme disease is seasonal, our goal is to establish a regimen that results in high antibodies at the beginning of each season. We therefore looked at a boost 1 year after the primary series. We saw a substantial boost antibody response in Phase II to all 6 serotypes present in North America and Europe following the 3-dose primary series vaccination schedule, with a 14- to 31-fold rise in season 1 and a 51- to 69-fold rise in season 2. The vaccine candidate was generally well tolerated at all dose levels tested, and we are excited about further development and the potential to help prevent this debilitating disease.

Last quarter, we told you that we saw robust dystrophin expression out to 1 year in our Duchenne Muscular Dystrophy gene therapy Phase 2b study. I will show you encouraging functional motor data in a moment. We recently shared some very sad news that a DMD patient with advanced disease in the non-ambulatory cohort of the Phase 1b trial passed away after presenting with hypovolemia and cardiogenic shock. The patient was 16 years old and the first in the non-ambulatory cohort treated with Rapamune, along with steroids, as part of the immunosuppressive regimen. Rapamune is not used in the Phase 3 ambulatory study. Like most non-ambulatory DMD patients, he had more advanced disease with underlying cardiac dysfunction. There is evidence of an active viral infection, and we're investigating how this may have contributed to the outcome. Additional assessment will be required to define next steps to restart the Phase 1b study in non-ambulatory patients who are more progressed in the disease.

I will now share data from this study. The ambulatory cohort -- sorry, I had one more sentence to say here. 19 patients were enrolled in this study, 16 of whom received the dose selected for our Phase 3 program, and 3 of whom received a previously studied lower dose. At 1 year post treatment, there was a 5.6-point improvement in ambulatory function, as measured by North Star Ambulatory Assessment, compared to an external control matched for age and baseline function. This is particularly encouraging given that patients at this age and stage of disease typically experience a considerable decline in ambulatory function, as illustrated by the external control.

On the right, we show time in study with 6 participants nearing or more than 3 years in treatment. The ambulatory cohort in Phase 1b is similar but slightly older on average to the population in the Phase 3 Cliffreo trial. Considering the favorable benefit-to-risk profile in this study and observed in the ambulatory patient population and in consultation with the Data Monitoring Committee, we believe the safety profile of our DMD gene therapy is manageable in this patient group.

Additional mitigation are being added to our study in consultation with eDMC and other medical experts. Pending regulatory feedback, we anticipate Phase III study sites to begin reopen in the next few months, with a potential to report top line results and, subject to clinical trial success, submit a BLA by the end of '23.

Turning now to Internal Medicine and ponesegromab, our candidate for cachexia due to cancer. It targets GDF-15. GDF-15 is frequently elevated in cancer patients, drives reduction of appetite and body weight loss and is associated with poor outcomes. There may also be a potential to treat cachexia associated with other chronic diseases, such as heart failure and COPD. We have encouraging Phase 1b data, which I will show next.

Ponesegromab was evaluated in 10 cancer patients who are undergoing antitumor treatment and had more than 5% body weight loss in the last 6 months or more than 2% body weight loss with a body mass index of less than 20 kilogram per meter square or diagnosed sarcopenia. Ponesegromab administration was found to suppress circulating GDF-15 levels in cancer cachexia patients, below the level observed in healthy subjects. Preliminary data from the Phase 1b trial show ponesegromab treatment resulted in significant body weight gain compared to historical placebo.

You can see the nice trend in body weight increase remained even after the dosing was stopped at week 12. The gray dotted line indicates the historical cut-off associated with improved survival. We are co-developing a companion diagnostic with Roche Diagnostics designed to enable precision medicine. And we expect to start the Phase 2 study in cancer cachexia in the fourth quarter of this year.

Injectable GLP-1 receptor agonist offer potent lowering of glucose and weight in diabetic and obese patients with proven cardiovascular benefits, but this drug class is underutilized due to its injectable administration route. Our small molecule oral GLP-1 receptor agonist danuglipron could potentially offer a convenient oral alternative to injectables and is being evaluated for the treatment of type 2 diabetes, obesity and NASH. It has been developed in our Internal Medicine research group with a vision to expand the use of this potent,

easily administrated GLP-1 drug class to a primary care setting.

Here are data from the Phase 2 study in type 2 diabetes. We recorded strong dose-dependent reduction in both HbA1c, a measure of long-term blood sugar levels, and body weight compared to the marginal effect noted with placebo. After 12 weeks of treatment with a 200-milligram twice daily dose, HbA1c decreased by almost 1.6% and body weight decreased by 5.4 kilograms. The safety and tolerability profile is consistent with the GLP-1 class, and the most frequent adverse events were GI-related. We expect to start a Phase IIb titration optimization study mid-'22 with doses up to 200 milligram twice a day and complete the Phase IIb study in nondiabetic subjects with obesity in the first quarter of next year.

Finally, here are select recent and upcoming milestones from across the pipeline. The solid blue dots represent milestones achieved, and the open blue dots represent anticipated milestones. Programs in bold are major anticipated events. Some of the programs on the right have already been designated as Lightspeed, meaning they have accelerated development time lines or are being considered for Lightspeed designation.

Finally, I would like to take a moment to thank Morrie Birnbaum, our outgoing Chief Scientific Officer with the Internal Medicine Research unit, for his immense contribution over the last 7 years. And welcome Bill Sessa, who joins us from Yale School of Medicine, following a decade-long career in academia, including service as Vice Chair of Pharmacology, Professor of Medicine and Director of the Vascular Biology and Therapeutics program at Yale. Bill is an eminent leader in the field, a groundbreaking scientist and a celebrated innovator, and I know he will bring his tremendous vision and insights to our investigation of cardiovascular and metabolic diseases.

Thank you for your attention. I look forward to your questions. Now let me turn it over to Frank.

Frank D'Amelio Pfizer Inc. - Executive VP & Chief Financial Officer

Thanks, Mikael. I know you've seen our release, so let me provide a few highlights regarding the financials. The COVID-19 vaccine, once again, had a positive impact on our quarterly results, and Albert and Mikael have already addressed the key points on the COVID-19 landscape.

Turning to the income statement. Revenue increased 106% operationally in the fourth quarter of '21, driven by COVID-19 vaccine sales and strong performance from a number of our other key growth drivers. Looking at the revenue, excluding the COVID-19 vaccine direct sales and alliance revenues and Paxlovid contribution, fourth quarter was slower than the first 9 months of the year, declining by 2% operationally. As we discussed during our third quarter call, there was a 4% negative impact or approximately \$500 million from fewer selling days in the U.S. and international. Excluding that impact, operational growth would have been 2%, which is still lower than the mid- to high single-digit growth we had experienced during the rest of the year.

This was factored into our forecast for the year, but let me briefly walk you through this. In our biopharma business, you will remember that the fourth quarter of '21 faced a tough comp from the fourth quarter of 2020 for Prevnar as pneumococcal vaccinations were strong ahead of COVID-19 vaccine availability. Excluding vaccines from the current and comparable period would add 5 percentage points to the growth. Adjusting for the unusual comp period differences related to vaccines and selling days, our revenue growth would have been approximately 7%, which is similar to what we've been delivering lately.

For the year, operational revenue growth was 92%. Excluding Comirnaty direct sales and alliance revenues and Paxlovid, 2021 operational revenue growth was 6%. This is consistent with our projected revenue CAGR of at least 6% from 2020 through the end of 2025. Of course, there will be some variability in quarterly and annual growth rates due to a variety of factors, but we continue to expect at least a 6% CAGR through 2025.

The adjusted cost of sales increase, shown here, reduced this quarter's gross margin by approximately 16 percentage points compared to the fourth quarter of 2020, which is almost entirely driven by the impact of the COVID-19 vaccine. Adjusted SI&A expenses in the fourth quarter increased primarily due to increased product-level spending, including Comirnaty and higher health care reform sales-based fees. The increase in adjusted R&D expense this quarter was primarily driven by increased investments in late-stage pipeline projects, including additional spending related to our oral COVID-19 treatment.

(technical difficulty)

Albert Bourla Pfizer Inc. - Chairman of the Board & CEO

Frank, I think you were disconnected.

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

Yes, we can hear you, Frank. Go ahead.

Frank D'Amelio Pfizer Inc. - Executive VP & Chief Financial Officer

Okay. I'm not sure where I left off, but I think what I'll do is start with the '22 financial guidance. So we've again provided total company guidance, which includes the business with the COVID-19 vaccine. We will continue to provide insight into our expected revenues for Comirnaty. And now for the first time, we'll also provide some color on our expected revenues for Paxlovid. However, note that we will no longer be providing EPS guidance for the business, excluding Comirnaty. Similarly, we won't provide EPS guidance for Paxlovid.

Our revenue guidance represents a record for Pfizer, and we expect total company revenue to be in the range of \$98 billion to \$102 billion, representing an operational growth rate of 24% midpoint. Please consider that this revenue range reflects approximately \$1.1 billion of anticipated negative impact from changes in foreign currencies and also the impact of the loss of Meridian sales of approximately \$300 million, both of which your models may not take into account.

Regarding our COVID-related revenues, we now expect the COVID-19 vaccine revenue for the year to be approximately \$32 billion, an increase of approximately \$1 billion compared to our prior guidance provided on December 17. For Paxlovid, we expect sales of approximately \$22 billion. This means that excluding the COVID-related revenues, we expect sales to be \$46 billion at the midpoint, representing operational growth of 5%. While this is slightly below the 6% CAGR that we continue to expect between 2020 and 2025, I would remind you that there will be volatility along the way.

Let me give you some detail on our cost and expense guidance. For Adjusted cost of sales, we are expecting a range of 32.2% to 34.2%. Given that we are now more than 12 months past the launch of Comirnaty, we expect its negative impact on our cost of sales margins to be less than it was in 2021, assuming a similar level of revenues. Further, Paxlovid is expected to have a very positive impact on cost of sales as a percentage of revenues in 2022. On Adjusted SI&A, we expect \$12.5 billion to \$13.5 billion, an increase of \$900 million at the midpoint. We expect our Adjusted R&D guidance range to be \$10.5 billion to \$11.5 billion at the midpoint, that is about \$500 million higher than last year. We expect an Adjusted effective tax rate for the year somewhat higher than 2021 at approximately 16%. These assumptions yield an Adjusted diluted EPS range of \$6.35 to \$6.55 or 47% operational growth at the midpoint compared to '21, excluding an expected \$0.06 negative impact from foreign exchange.

I'd like to point out some additional information, which may be helpful for your models. You will note that our guidance assumes a weighted average share count of approximately 5.8 billion, which represents an increase of approximately 100 million shares over 2021. This accounts for the number of shares that we normally issue for employee compensation annually. The increase of 100 million shares over '21 decreases our EPS by about \$0.10 at the midpoint. I noticed that most of your models instead assume a flat share count for '22 as compared to '21.

From the first quarter of '22 and going forward, we've made a decision to modify our Adjusted financials treatment of amortization of intangibles. Previously, we only excluded amortization related to large mergers and acquisitions and exclude all intangible asset amortization expense. This is anticipated to contribute \$0.06 to our 2022 Adjusted diluted earnings per share, helps improve comparability with our peers. 2022 guidance once again assumes no share repurchases. We will note that Pfizer did not repurchase shares in either 2020 or 2021. And we continue -- and while we continue to have outstanding unused authorization to repurchase another \$5.3 billion of stock, can be opportunistic, given the potentially value-enhancing business development opportunities, which are available to us, we do not expect to repurchase shares in 2022.

Now a word on our 32% stake in the Consumer joint venture with GSK. As you know, GSK has announced its intention to engage in a

demerger transaction for at least 80% of its 68% stake in the JV in the summer of 2022. We talked about our stake as a noncore asset, whose value we will seek to realize over time. While we have determined neither the manner or timing of how we will do so, there are a number of possible alternatives and we will attempt to monetize this asset in the manner which will create the most value for our shareholders.

We receive approximately \$600 million in pretax income from the JV annually, and this will not change as a result of the demerger transaction, and our guidance assumes that this will continue throughout 2022 with no change to our 32% stake.

Let me quickly remind you of some assumptions and context on the projected COVID-19 vaccine contribution and our collaboration agreement. The Pfizer-BioNTech COVID-19 vaccine collaboration construct is a 50-50 gross profit split. Pfizer books the vast majority of the global collaboration revenue, except for Germany and Turkey, where we receive a profit share from BioNTech, and we do not participate in the China region. We continue to expect that we can manufacture 4 billion doses in total by the end of 2022. And -- the \$1 billion increase in expected COVID vaccine revenues to approximately \$32 billion in 2022 primarily represents the impact of contracts signed since mid-December, which we cut off from our prior guidance. While we cannot predict what may be needed due to Omicron or other variants, I would also caution you that there is less potential upside to this guidance through the year compared to the situation we faced in 2021 when the vaccine was newly available and few people have received any doses of the vaccine.

As you will remember, our cost of sales for the COVID-19 vaccine revenue includes manufacturing and distribution costs, applicable royalty expenses and payments of BioNTech representing 50% gross profit split. We expect that the Adjusted income before tax margin for the COVID-19 vaccine contribution to be slightly higher than the high 20s as a percentage of revenue that we had in 2021.

Unlike the situation for Comirnaty, demand for Paxlovid should have upside from these levels depending on the outcomes of discussions with certain governments and potential purchases for stockpiling against future coronavirus pandemics. If we remove the projected COVID-19 vaccine and Paxlovid contribution from both periods, you will see that we expect the 2022 revenue range to be \$45 billion to \$47 billion, representing approximately 5% operational revenue growth at the midpoint.

Please remember, our guidance excludes the former revenue contribution of approximately \$300 million for Meridian and all '21 quarters have been recast to exclude Meridian's discontinued operations accounting for its divestiture. Going forward, we will not give earnings guidance, excluding the estimated income from our Comirnaty direct sales and alliance revenues and Paxlovid. However, to help you with your forecasting a couple of minutes ago, I gave you my view on 2022 Comirnaty pretax margins. For Paxlovid, I would think about its margins as being typical for a small molecule drug and unlike Comirnaty, it is expected not to be dilutive to pretax earnings. To help you further, several years ago before COVID-19 existed, I spoke about our business being on a path to a 40%-plus pretax margin level in 2022, the business, excluding Comirnaty and Paxlovid. Going forward, we will continue to be prudent in our capital allocation activities with the opportunities for deployment shown here on this slide.

In summary, exceptionally strong quarter and year based on continued strong performance for our growth drivers. During the year, we raised guidance and for the year, we met or exceeded our guidance in all key metrics. Our pipeline continues to advance, and we have invested record amounts to support that advance. Last week, Arena shareholders voted to approve Pfizer's acquisition of the company. We look forward to a targeted closing of the Arena acquisition as soon as the first half of 2022, subject to the satisfaction of the closing conditions, including antitrust approvals. We continue to expect to be active in regards to business development throughout 2022 as we continue to get access to the best external science and bring breakthroughs to patients in 2025 and beyond. With that, let me turn it over to Chris to start the Q&A session.

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

Thank you, Frank. Apologies, everyone, for those technical difficulties. Just want to remind you, we do have the prepared remarks posted to the website. So if there's anything you missed because of difficulties, please refer to the prepared remarks. And given the technical difficulties, we're going to try to let the Q&A session run a little longer to answer people's questions. Sylvia, first question, please?

QUESTIONS AND ANSWERS

Operator

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

Geoffrey Christopher Meacham BofA Securities, Research Division - Research Analyst

Just had to -- the first one, on Paxlovid guidance. I know you guys are factoring in only signed agreements. But could you give us a general sense as to agreements or doses perhaps that are under discussion? And is that dependent on the supply ramping? The second question, on external BD, Albert, I understand the strategy. I think the uncertainty is really the ability to scale some of the products that you brought in. So if COVID is less of a long-term contributor than you assume, what's the appetite to do higher-impact larger deals? You clearly have the capacity.

Albert Bourla Pfizer Inc. - Chairman of the Board & CEO

Thank you. Angela, do you want to take a little bit the Paxlovid?

Angela Hwang Pfizer Inc. - Group President of Biopharmaceuticals Group

Sure. So currently, we are in active discussions with over 100 countries and governments around the world. So I'd say that the discussions are going really well. In terms of where we are with the contracting, as you say, we've included some of the contracts that we already have -- that we have. But of course, this number changes every day and contracts are being secured and distribution agreements being secured literally on a day-to-day basis. So I think that this is a number to watch out for, and we do continue to expect movement.

I think that there is a tremendous amount of interest for our product. And certainly, as the clinical program continues to develop and emerge. As you know, we only have the high-risk study right now. We still have the standard risk and the prophylaxis that's coming up. And I think that the full clinical program will also be another point of impetus for contracting and ordering. So I think it's going just really well and more to come on this one.

Albert Bourla Pfizer Inc. - Chairman of the Board & CEO

Thank you. Aamir, maybe some comments on the BD.

Aamir Malik Pfizer Inc. - Executive VP & Chief Business Innovation Officer

Sure. Thanks for the question, Geoff. I think in terms of the top line, we're going to be incredibly flexible. We have said repeatedly that we are most interested in compounds that have potential to be real breakthroughs. And this can take the form of later-stage clinical development as well as earlier-stage medical innovation. We're going to bias to the TAs, Oncology, I&I, Rare, Vaccines, Internal Medicine and Hospital where we've got the scientific chops to make good choices and add real value. And we're going to be flexible on the deal types. Acquisitions are obviously very much in the cards, but strategic partnerships and alliances are well. And in fact, some of our best successes have come from some capital-light collaborations. If we see a larger opportunity that's strategic and creates value and meets the criteria that I just described, we've obviously got the balance sheet to utilize to do that. So we certainly will look at those. But we're going to talk about and focus on the priorities that I described more so than synergy-driven deals per se.

Albert Bourla Pfizer Inc. - Chairman of the Board & CEO

Thank you, Aamir. And Geoff, just to add to both points because I'm sure that both will be asked a lot. On the Paxlovid, clearly, the numbers could become way bigger than what we have right now. But this is not something that we have done in the past, and we don't plan to do right now to give based on what could be the potential as a guidance. We are giving guidance based on what it is more or less secure, either signed deals or already agreed but not signed yet deal, but agreed price and volumes, I mean.

So clearly, if you remember, when we started with the vaccine, we -- in the beginning, we had a guidance of, I think, \$15 billion in the first quarter, something like that. Eventually, it made \$36 billion. Here, we start even stronger on our first production with Paxlovid. So -- and that's why we manufacture and we move ahead with our plans and already, we are at 120 million treatments, and we have the ability to go higher if the discussions that we are having materialize at all.

In terms of also the business development, I just want to emphasize that because I'm getting a lot of this question on the size. We are agnostic to size. Where we are biased, it is deals. But in order to justify the premium, we will have to do significant cost synergies. This is

not -- these are -- could be very profitable deals for other, let's say, periods of the history of the company, not now.

Right now, the company is having a manufacturing machine, but it is performing at its best; an R&D machine, but it's performing at its best; a commercial machine that keeps being the leader in the industry in terms of the ability to execute and deliver. So the last thing I want to do, it is to do a deal that in order to justify the premium to the shareholders of the other company, we will have to shut down manufacturing sites and to consolidate research sites and consolidate field forces so that we can justify -- so we can generate the cost synergies.

This is not the time to disrupt the momentum of the company. This is the time to bring into this manufacturing machine, the research machine, the commercial machine more substrate in addition to what we produce organically ourselves. And this is why the business development is aiming in these areas. So let's go to the next one.

Operator

Your next question comes from Mohit Bansal from Wells Fargo.

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

Maybe one on Paxlovid. So there have been some news reports talking about logistical and access issues for Paxlovid. And I understand that supply is tight for now. But would love to get your thoughts on how you're working on improving the logistics when the supply is no longer an issue, especially in a world where home testing will become a norm and one needs to take this drug within 5 days of diagnostics.

Albert Bourla Pfizer Inc. - Chairman of the Board & CEO

I wouldn't say that we have logistical issues of supply. But Angela, would you like to take that, please?

Angela Hwang Pfizer Inc. - Group President of Biopharmaceuticals Group

Sure. So first of all, again, our deliveries and our allocations for the doses have gone extremely well here in the U.S. Just to give you some context, 265,000 doses have been allocated by the U.S. government since the EUA was approved. And of that 265,000, 85% of all the doses have been ordered. So -- and we see a range of ordering patterns from the states. Some states are ordering 100% of the allocation. Others are at 80%, 70%, so on and so forth. So there's really only a handful that haven't really ordered up to their allocation. But I would say, for the most part, the weekly orders are going up and increasing week by week, and there is a very strong placement of orders. So I'd say that the drawdown, right, of the doses and the utilization is going really well. And again, it's different by state what the allocations are and how that's going.

And then as Albert said, I don't know that we have logistical -- there are not logistical issues. I think initially, what was difficult was that it was not clear where the doses were being located because every state had a different system for where to actually distribute Paxlovid from. But there are a number of tools now that have gone up online, both at the state level as well as on Pfizer's website.

We've taken the state government tool and also loaded it on our website so that both HCPs and patients can see where Paxlovid is being -- where it's available and where the orders as well as prescriptions can be placed. So I think in that regard, that's all been ironed out. I think looking forward into the future, I mean, clearly, having a seamless sort of end-to-end from diagnosis, positive results to them being able to prescribe quickly and having the patient be able to acquire the drug quickly, is our goal. And I think on all of those fronts, we're working with a number of partners, both from a testing and a diagnostics perspective, but also from a telemedicine perspective and from a pharmacy perspective to ensure that we have as fast and as efficient, I can say, a patient journey, right, from diagnosis right onto treatment. So all of that is in place, and you'll hear more -- you'll continue to hear more about that as the launch and as the utilization increases.

Albert Bourla Pfizer Inc. - Chairman of the Board & CEO

So again, to punctuate and give a little bit of context to what Angela said. The 85% that -- it has already been ordered from the quantities that we are making available to the U.S. government, it's a very, very high number. For example, the same number in the first month for vaccines, if you remember well, if you remember from that time, was dramatically lower than that because it takes time for the

states to get their act together. And it is really variable state by state.

So there are states right now that once the quantities are made to them available, they are ordering immediately. And there are states that take their time until they get their act together for the distribution. In general, way, way, way more efficient than what used to be in the first month of the vaccine. Also, what is extremely important it is that every week, there is constant replenishment, which although we do not have right now data for scripts because it's too early, what we do have, it is that the quantities that the states are accumulating, they're disappearing and then immediately, they are placing orders.

So I would say we have, let's say, we are pretty happy with the way that the first month, the collaboration with the U.S. government went in terms of allocating doses. And there is dramatically also improvement in the tools as Angela described. But the bigger improvement will come from the fact that the second month, we'll make available way more quantities. In the third month, way more quantities because the issues right now for people trying to find it, it is that it is in a few places in the state because you can't expand the network of places that it is available when you have smaller quantities. So that will be very, very different in this month. And basically, all over the place, I think, in the third month where significant quantities will be delivered. Okay. I think let's go to the next question.

Operator

Next question is from Evan Seigerman from BMO Capital Markets.

Evan David Seigerman BMO Capital Markets Equity Research - MD & Senior BioPharma Research Analyst

I was wondering if you could provide an update on the SEC review process for the Arena deal. If I'm not mistaken, there was a recent procedural move where you and Arena were through the -- where you refiled the HSR Act filing essentially to allow the FTC an additional 30 days for review. And then I'd also love for you to walk me through your assumptions on how you forecast \$13 billion in revenue from BD transactions. That would imply that your specific targets and combination of targets in mind. Any color here that you could provide would be very helpful.

Albert Bourla Pfizer Inc. - Chairman of the Board & CEO

Yes. Thank you very much. On the last one, just to make sure, but this is not our assumption. Our assumption is way higher of the \$13 billion. What I just gave you, it is what is the consensus of the deals that we have signed so far. But on the FTC review, I would like to ask Doug to provide us maybe a review on that, Doug Lankler, our General Counsel.

Douglas M. Lankler Pfizer Inc. - Executive VP & General Counsel

Yes. As you pointed out, we did request to refile, which is not unusual. Under -- it's -- the deal is, of course, subject to customary closing conditions and typical antitrust clearance and shareholder approval, which, as you know, we've received. We don't expect a significant break in time from our proposed sense that the deal will close in the first half of this year. We still expect it to close in the first half of this year.

Albert Bourla Pfizer Inc. - Chairman of the Board & CEO

Thank you. And Aamir, although I did explain that this is consensus numbers, not our numbers. Do you want to make any other comment on the \$13 billion of 2030 revenues? That consensus for cash for the deals that we have signed?

Aamir Malik Pfizer Inc. - Executive VP & Chief Business Innovation Officer

Yes. The only thing I would add is we feel very good about the progression of all of the substrate and the deals since 2019 that Albert outlined. We've seen a significant number of approvals and EUAs in that group, submissions as well as quite a few Phase 3 starts. So we think that, that substrate is progressing well. And the \$13 billion is the consensus number. Our expectations of what's there are materially higher. And there are a number of transactions. We spoke to Trillium, Biohaven and even some of the recent things that we've done in mRNA that are not yet factored in the consensus forecast on those transactions.

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

Perhaps 2 on vaccines today, if I may. First, on the flu vaccine, I know you've had a trial ongoing on your modRNA since September. And I noticed you just initiated a new trial of a self-amplifying mRNA for flu. And I wonder if the decision to progress a second mRNA program in flu was triggered by any emerging data from your first-gen flu Phase 1 that's been ongoing? And then secondly, on Omicron-specific booster, perhaps in light of some of the emerging data on immunogenicity differences or lack thereof versus regular COVID vaccine, I guess my question is, what's your confidence on ability to show superiority of an Omicron-specific booster versus regular? And what would be the regulatory criteria?

Albert Bourla Pfizer Inc. - Chairman of the Board & CEO

I think Mikael can take that question. On the flu vaccine, just to make sure that I clarify, the plan was always to initiate an samRNA for flu and to run the 2 programs in parallel. It's not that we saw data that forced us to do an SA. It was always the plan. We are advancing new forms of mRNA technology in SA. It is one of the most promising next generation of RNA technologies. But Mikael, any comments on that and on the Omicron-specific, our confidence for superiority?

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

Thank you. Yes, we are accumulating, first of all, from our mod mRNA data trial data on various regimens and on multivalent constructs. We remain of the view that we aspire to develop a flu vaccine. Currently, the most aggressive timelines are focused on the mod mRNA. Our plans is to develop something that have differentiation versus the current heptavalent standard of care. I know other companies have spoken about being similar, while at this moment, we still see opportunities to possibly differentiate with an mRNA based on mod mRNA.

As Albert alluded to, we are actually filing the IND for the self-amplified. I think the protocol may have gone up already on ClinicalTrials.gov, but dosing is going to be within the next couple of months or so. And it's entirely based on us aiming to develop that platform, which has particular relevance for combination vaccine given that possibly, we expect to have much lower mRNA burden and can, over time, build vaccine combination of several different pathogens. We'll keep you updated on progress with the mod mRNA in flu. And we certainly see data that suggests that this is a feasible path, and we are working to refine our approach to aim for a differentiated vaccine.

Albert Bourla Pfizer Inc. - Chairman of the Board & CEO

What about Omicron? How confident we are about the superiority?

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

Yes. The regulatory path is that we expect to have -- if successful, an Omicron boost would show higher neutralizing antibodies for Omicron versus a similar boost by the wild type vaccine and acceptable titers to the other previously available strains to provide -- preserve broad protection, but possibly with higher Omicron.

I really think we should let the science play out here. We are talking about a number of weeks before we get data. And as I alluded to, it has 3 different arms on top of 3 doses, Omicron versus a wild type. That was on top of 3 previous doses on top of 2 previous vaccine doses, 1 or 2 Omicron. That will be a very interesting data set and then Omicron or naive. So I think it's a really interesting trial and we'll extract a lot of data and we'll report whether we can get that superiority.

But in any case, I would just want to punctuate that our current vaccine is active of the 3 doses and raise relevant neutralizing antibodies. And the T cell responses that we see are likely the one that contribute in real-world evidence to provide effective protection of the current vaccine against hospitalization and death. Omicron vaccine is an interesting opportunity that we learn more about. But our science is progressing against several dimensions on how to further improve over time mRNA vaccines, although they're all pretty good ones. So you should expect Pfizer continue to be a leader in this field through multiple approaches together with BioNTech.

Operator

Your next question comes from Louise Chen from Cantor.

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

So my first question for you is, what are the key pushes and pulls to your underlying business, excluding COVID? And what gives you confidence that you can still meet that top line sales guidance that you gave through 2025 despite some of the volatility that we're seeing right now? And then I just wanted to ask you on your TL1A antibody and where you are with development of that product and the reporting of data. Have you changed any of the timelines for when you report data?

Albert Bourla Pfizer Inc. - Chairman of the Board & CEO

On the 6%, what gives us confidence, it is that we are -- we keep meeting the goal, as I said, that we set the goal in '19 for a 6% all the way CAGR. And then we had -- year-to-date, we are at 6% right now. The year, particularly, it is at 5% for the underlying business. But there is a little bit of volatility. But always, we knew that this will be a year that we are losing some of the revenues of Chantix and compared to previous year, which affects quite significant this deal, which then as we are launching new products that are coming up. Maybe I will ask Angela to give a little bit more details on the inputs and how this is progressing and also, Mikael, on the antibody question. Angela?

Angela Hwang Pfizer Inc. - Group President of Biopharmaceuticals Group

Thank you, Louise. I think the 6% confidence is really driven by 2 things. First of all, the launches, right, that will take place between now and 2025, which will continue to drive growth for us. But also importantly, in our in-line portfolio, Louise, every single one of our products still have opportunities to grow. They can grow from a number of different ways, right? There's still under-diagnosed patients. So from new diagnosis, we can continue to drive a tremendous amount of growth in Eliquis and in Vyndaqel. In many of our products, we still have class growth.

I mean think about the CDK4/6s, think about XTANDI, think about BRAF/MEKTOVI. These are all therapies that are still, I think, underutilized from a class perspective. So there's growth there. And then finally, for all of them, there's the opportunity to grow in terms of market share, just given just the strong clinical profile and strong life cycle support that we have for all of our products. So I think we see tremendous amount of growth still. We just have not tapped out of growth in our core in-line brands. And then you add on top of that the launch brands, this is where we're going to get our growth from.

Albert Bourla Pfizer Inc. - Chairman of the Board & CEO

Mikael?

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

Thank you, Angela. On the TL1A, as you remember at the previous earnings call, we showed some really strong data in the range of 34% endoscopic improvement and with a biomarker of 48% in the patients, way above expected standard of care. That trial has enrolled very fast. It's fully enrolled. Full trial readout will be Q4. We are obviously considering, based on the encouraging data in the previous trial, opportunity for interim analysis that pending data could allow us to accelerate development of the program towards potential pivotal studies. So all in, it's moving very well and very fast.

Operator

Next question comes from Steve Scala from Cowen.

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

Just to be absolutely clear, I understand that Pfizer wants to be conservative on Paxlovid. But it seems that Pfizer has merely scratched the surface on its 2022 potential and that scratching of the surface is what's in 2022 Paxlovid guidance. So please just tell me if you disagree with that statement.

Secondly, and just to be clear, once again, do you not see growth for Pfizer overall in '25 to '30 without business development? And then lastly, on danuglipron, Slide 39 shows some very good data. I'm curious what was the discontinuation rate in the study? Can the dose be increased further? And does Pfizer expect additional weight loss beyond 12 weeks?

Albert Bourla Pfizer Inc. - Chairman of the Board & CEO

Yes. So let me take the 2 first questions, and then Mikael can take the research one. Look, it's not that we are giving a conservative guidance. What we do, we have principles that we follow because otherwise, we can be lost. And the principle that we are following, it is that we are only giving guidance for contracts that have been signed or they are very close to be signed because we have agreed critical terms, predominantly, right? So this is what you have heard about Paxlovid.

Clearly, this is only a very small fraction of the 120 million treatments that we are right now preparing to manufacture. And it is a small fraction of things that we are discussing right now around with different governments. But we are not taking, for example, an approach that we take all the discussions that we are having with the different governments, we risk adjust them to see how many things can go part through and then we give a guidance. This is not what we do. We only give -- and this is the same with the vaccines, things that have been signed or are already agreed by the time in a specific deadline. And I think that Frank said it was last week, I think, this deadline. So clearly, there is a lot of potential, but it is not that we are putting a little bit of our own conservatism in the numbers. We are following a principle so that we can always be clear with what we say and why we say it. So that's the thing then. What about the study dose and the 12 weeks delay, Mikael?

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

On the danuglipron, I'm pleased that you were happy and impressed with our data. And indeed, I would say the glucose lowering through HbA1c and the body weight that you know are probably among the best in such a short treatment period. Tolerability and discontinuation rates improved versus previous study because we extended the dose titration from week to 2 weeks. And overall safety adverse event, I think, are very much in line with what you see comparable titration approaches with injectable. Given that we see that we can improve tolerability and the discontinuations with this medium titration rate, we have -- the next studies coming up will be a further slow dose titration maybe up to a month or so. And we think that may even bring readouts of efficacy further above this, so we are very pleased with the profile. And I think the next study will nail down for us dose regimen and will help us to move with a strong profile into a potential pivotal study.

Operator

Your next question comes from Tim Anderson from Wolfe Research.

Timothy Minton Anderson Wolfe Research, LLC - MD of Equity Research

A few questions. The RSV vaccine data previously said early '22. Now you're saying first half '22. Does that imply there's been some slippage because early to me, I always felt that mid-January, February, something like that.

mRNA flu, second question. What's a realistic time frame for a potential regulatory filing of a product like that, assuming you find success in your trials? And then last question, the IBRANCE sales, soft. You say it's due to patient assistance programs. We haven't seen that impact on other CDK4/6s. And I haven't generally heard about those programs impacting other brands, either at Pfizer or other companies. So I'm wondering what else may be putting pressure on IBRANCE where you're having to cut price to maintain access.

Albert Bourla Pfizer Inc. - Chairman of the Board & CEO

Yes. What was your question on flu, Tim?

Timothy Minton Anderson Wolfe Research, LLC - MD of Equity Research

A realistic time frame for filing for approval of a mRNA flu vaccine.

Albert Bourla Pfizer Inc. - Chairman of the Board & CEO

Yes. So why don't we go, Mikael? What about RSV? You can speak about both. We have both now, adult and maternal, and then the mRNA. And then Angela, you speak about IBRANCE.

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

Yes. On the RSV, we have enrolled very well maternal and adult and are basically, I would say, fully enrolled. So it's entirely to ensure we have the number of events that we were looking for. And we expect both trials to read out, whether it's somewhere between Q1, Q2 or at

the later part of Q2. We'll just see and as events accumulate, but it's going very well. So I feel very optimistic with RSV starting to conclude, and we're looking forward to that data.

mRNA flu, we are right now accumulating immunogenicity from several different type of dose regimens. And if we are able to conclude with the optimal dose regimen using the mod mRNA, a potential Phase 2, Phase 3 study could certainly be initiated this year. But of course, it's a little bit early to speculate before you have identified the right Phase 2/3 dose regimen. If we would embark on such a study this year, we expect it can conclude very fast given our experience to run very large trials in this sector and this population of adults. And so we're talking about possible conclusion then within next year. But it's -- I would say, one step at a time, we'll keep you informed. We are encouraged so far, and we'll go from there.

Albert Bourla Pfizer Inc. - Chairman of the Board & CEO

Thank you, Mikael. And then what about Angela on the IBRANCE?

Angela Hwang Pfizer Inc. - Group President of Biopharmaceuticals Group

Sure. I can confirm that the patient assistance program is indeed the primary reason for the decline in volume that you've seen on IBRANCE. Just to give you some perspective, in Q4 of 2021, our PAP prescriptions were up 32% compared to where it was in Q4 of 2020. And all of this is 53% more than what it was pre-COVID. And so this is really what has caused us a tremendous amount of paid prescriptions. And I can -- and that's really the primary reason. We also saw and throughout the year, and this has been something that we've been watching quarter-over-quarter, just some slowdown in new patient starts. And -- but we've seen this sort of phenomenon across multiple products in our portfolio. So there's a small contribution from that, but the largest contribution by far is truly this phenomenon we're seeing here in terms of PAP.

Albert Bourla Pfizer Inc. - Chairman of the Board & CEO

Thank you, Angela. Before we move to the next question, I realized that I didn't answer one of the questions that Steve made, Steve Scala, about if we believe that we need business development to grow in the period, '25 to '30. And clearly, this is not the belief right now. We think that we have a clear LOE number that we estimate around \$17 billion. And we have a pipeline that delivers more than the LOEs. So only organically, we would like to have right now in our calculations, we are a positive growth trajectory. The \$25 billion I just mentioned needs to be on top of everything, the balance between LOEs and internal pipeline does, everything new that will be invented in the meantime and, of course, the COVID trajectory through 2030. But we don't need right now business development at all to grow. What we need business development is to maintain high level of 6% growth top line all the way to 2030, for example.

Operator

Your next question comes from Andrew Baum from Citi.

Andrew Simon Baum Citigroup Inc. Exchange Research - Research Analyst

A couple of questions. First, what are your expectations that you'll need 2 shots of Omicron as opposed to one? The reason I ask is recently published animal models suggest that one Omicron mRNA vaccine actually generates lower levels of neutralizing antibody against Omicron than the ancestral spike variant, presumably due to antigenic sin. It obviously has implications for both revenues in terms of 2 shots but also compliance. And then second, perhaps you could comment on the outlook for CD47 and talk to the differences between your molecule and Gilead's, which obviously has run into some safety issues with the trial suspension.

Albert Bourla Pfizer Inc. - Chairman of the Board & CEO

Yes. I will take the first one very quickly, so that I can give time to Mikael to speak about the second one. Look, we have to wait to see the results. But I don't think it is all mRNA vaccines are the same. So I don't think we should extrapolate preclinical data for one effort to what will be the clinical, let's say, results of the other efforts. We are testing both, one sort, we are testing 2 sorts. We are testing pretty soon hybrid vaccines. But everything that we have seen so far give us confident that we will have a very strong reaction and immunogenicity of an Omicron -- against Omicron. But of course, that's based on -- preclinical. We need to wait to see the first clinical data so that this assumption can be validated. With that, Mikael, what about the Gilead? And by the way, also, Andrew, you said what about your expectations. Our expectations are not based on one sort or 2 sorts or 5 sorts, our expectation is, as I said, it is contract signed as per last week with Comirnaty. So what we'll sign further on will be in addition to whatever we have given so far. Mikael, on the Gilead.

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

Yes, the interest in our product from Trillium was triggered by its unique design. It is what we call a receptor fusion blocker protein in contrast to magrolimab that you referred to that's on hold. The Gilead antibody, it binds with a lower affinity to the target, and that was by purpose to allow it particularly to accumulate on high-expressing cancer cells and less accumulate on red blood cells to cause -- not to cause anemia or hemolytic anemia.

And indeed, in our studies that have generated proof of concept, we have seen single-agent activity in blood cancers with basically negligible effect on red blood cells. So this is playing well out. We do not know why magrolimab is on clinical hold. But of course, this differentiation that we have in our molecule may be one example of why our molecule has been doing so well thus far. While we initially focus on lymphoid malignancies of the B cell type, we think we also may become increasingly interested in to go to the myeloid space where magrolimab has been, AML and MDS, particularly if our profile now may be superior, and we're waiting readout from such studies also. So for us, the Trillium deal is delivering on all what we expected and may actually have upside due to its more unique profile.

Operator

Your next question comes from Chris Schott from JPMorgan.

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

Maybe just to start with on -- just some clarifications around guidance. I know you're not giving a lot of details around core versus COVID-related earnings this year, but there's a lot of questions on that front. But if I just take the low end of your sales range at \$45 billion, apply a 40% margin, tax adjust that, I think I may get a number somewhere around \$2.60 per share at the low end. Is there any issues with that math I'm doing? Or am I in the right ballpark there, if I just want to think about the low end of core guidance for this year?

My second question was on Paxlovid, and you're referencing here typical small molecule, I guess, gross margins for this one. Just help us frame that a bit more. I guess is something in the mid-80s a reasonable level to think about for gross margins for this product? Or is it substantially higher or lower? I'm just trying to better understand profitability as we maybe think about some of these contracts coming forward this year and maybe that Paxlovid number moving.

And then just a final one, just to wrap up. I'm still trying to get my hands around the BD side of the business and kind of the approach. I guess should we be thinking about a significantly different approach to business development for Pfizer today versus what the company was doing 2 or 3 years ago prior to the COVID upside? Or is this more just a continuation of, I guess, the focus on what you were looking at if we're thinking back to like 2019 as an example?

Albert Bourla Pfizer Inc. - Chairman of the Board & CEO

Yes. I'll take very quickly the third one, and then Frank can take the first 2 questions. I wouldn't -- I would say it is a continuation, but with a way more accelerated pace. I don't think we are changing what we're saying since 2019. We are going into the science, as Aamir said. We are going into areas that we think we'll make fewer mistakes in selecting the right targets. We will be more successful, so we will be able to meet at least the success rates of the industry. Our aim is to exceed them.

As we are selecting assets, we prefer to go to areas that we can add value. And there are significant areas that we can add value by becoming the preferred partner of several biotechs. And also, we have seen, as Aamir said, that some of the best deals we have done, were not the most capital-intensive deals, right? So there are -- so all of that, we are learning. We are not going to relax the discipline that we are having in selecting, but we are going to intensify a lot our activity in that area. Because, of course, we think that now is the time science is at the stage that we can find enough targets to be able to add value and create value. So that's on the BD side.

Now Frank, a lot of financial questions for margins, guidance, et cetera.

Frank D'Amelio Pfizer Inc. - Executive VP & Chief Financial Officer

Sure. So Chris, on the walk through you did on the, I'll call it, the business, excluding Comirnaty and Paxlovid. I would use the midpoint on the revenue. You used, I think, a 40% income before tax margin. And then you got to tax effect that. I didn't hear you say tax effected.

So if you do the math, you do the walk through and then you tax effect it, obviously, dividing that by shares outstanding, that will give you, I think, a number that's in the ballpark.

On Paxlovid gross margin, let me answer the question this way. One, because we don't give margin information by individual product, right? It's something that for many reasons, we don't do. But the way to think about it is, one, that the income before tax margin on that, the margin profile is similar to our other solid oral dose products. And remember, when you look at the gross margin, there's going to be SI&A investment in Paxlovid this year because we're launching that product. There's additional R&D investment product that year because we're continuing obviously to evolve that product.

All of that obviously is captured in the income before tax margin on that business, which is similar to our other solid oral dose products. It's all factored in our guidance.

The one place where you can really see the impact, and hopefully, this is helpful, if you look at our cost of sales as a percentage of revenue last year for the full year, 37.7%. If you look at our guidance this year, 32.2% to 34.2%, the midpoint is 33.2%, that's down at the midpoint, 4.5%, most of which is being driven by the Paxlovid revenue this year. So maybe that's a way to help you in terms of just how to work the numbers.

Albert Bourla Pfizer Inc. - Chairman of the Board & CEO

Thank you, Frank.

Operator

Your next question comes from Chris Shibutani from Goldman Sachs.

Chris Shibutani Goldman Sachs Group, Inc., Research Division - Research Analyst

Two questions. One, again, just to make sure I understand clearly the thinking about what underpins the intermediate growth expectation through '25. I believe when that was originally issued back in 2019, that did not assume contribution from business development to achieve that CAGR of 6% to '25. Is that still the case? That would be the first question.

And then the second question relates to Paxlovid. We have the standard-risk study that you've modified expanding. Can you talk about what kind of result we would need to see in order to influence the kind of decisions and discussions that Angela is having with governments? In particular, the primary end point, which just missed statistical significance on the alleviation of symptoms, do you need to hit that? Or are the discussions being guided around the ability to meet the secondary end point, which was the decreased risk of hospitalizations in severe disease from that standard-risk study?

Albert Bourla Pfizer Inc. - Chairman of the Board & CEO

Yes. And maybe I can take both in the interest of time. I can confirm that our guidance for 6% was excluding BD. So that was from '19 all the way to '25, 6% CAGR from the things that we had at that time.

As regards the standard-risk primary end point, I think most of the governments, if not all, they are focusing right now all their purchases and their discussions that we are having on the ability to reduce hospitalizations. And by the way, most of the -- I mean, FDA, for example, has already approved vaccinated and unvaccinated, which is included -- that means that includes also people that were in the standard-risk population because the high-risk population were all unvaccinated. So if we go -- the standard risk, I think, will contribute. But I think everybody is moving with the assumption that we give it to all people to prevent hospitalization. That's the main -- and that's the main thing that everybody is looking.

Now the in-house contract, it is very different. And I can say it's very much the landscape. There are no discussions around that right now. But if it comes positive, clearly, that could be used also in preventing infections in high-risk populations when someone in the household or in the senior house or in other, let's say, business -- in other settings that people are living together, one is getting infected. But this is something that will come on top of any discussions that we are having right now, if it is positive.

Operator

The next question comes from Vamil Divan from Mizuho Securities.

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

I guess I'll stick with the same theme around Paxlovid and business development. So first on Paxlovid, just to make sure we're all starting on the same page, I guess. Can you comment exactly how many doses are included in the guidance that you're giving right now? You mentioned in the release the 20 million to the U.S., I think 2.75 million to the U.K. So obviously, there's been some other contracts that have been signed. So I don't know if you can give us a number or a range just so we have a sense of kind of what's included right now.

And then on business development, I just thought one thing that's sort of interesting when you're talking about Slide 13. Albert, you mentioned the strength of your balance and cash flow has allowed you to pursue new BD opportunities going forward that could add at least \$25 billion of risk-adjusted revenues for 2030. And I'm just curious, that \$25 billion is sort of a specific number. I'm wondering sort of -- obviously, this is in your prepared remarks. So I'm sure it was well thought out. So I'm just curious what sort of drove that. Obviously, the number could be much smaller or probably a lot bigger depending on what you do over the next few years. So maybe you can just provide some clarity on why you worded that the way you did.

Albert Bourla Pfizer Inc. - Chairman of the Board & CEO

Why we selected \$25 billion -- to speak about \$25 billion, you mean?

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

Yes, saying at least \$25 billion in adjusted revenues.

Albert Bourla Pfizer Inc. - Chairman of the Board & CEO

Yes. I got it. Frank, would you like to take the Paxlovid and the doses?

Frank D'Amelio Pfizer Inc. - Executive VP & Chief Financial Officer

Of course. So Vamil, on the Paxlovid guidance, you heard Angela mentioned before, we're very active right now, 100-plus negotiations with different governments. We don't want to put any information out there that could, I'll call it, lead to misleading assumptions, and those assumptions being detrimental to those contract negotiations.

But now you mentioned a couple of contracts that have been announced and publicly and where the dose information was included. You mentioned the U.S., 20 million; the U.K., 2.75 million. If you look at everything we've announced publicly, give or take, it's about 30 million treatments. And so that 30 million treatments is clearly included in the guidance that we provided in the \$22 billion revenue.

Albert Bourla Pfizer Inc. - Chairman of the Board & CEO

Thank you. And Aamir, why you selected \$25 billion?

Aamir Malik Pfizer Inc. - Executive VP & Chief Business Innovation Officer

Sure. So Vamil, a couple of thoughts. One, we obviously -- between the strength of our balance sheet and the cash flows, we have the ability to deploy significant capital. And going beyond our growing dividend, we think that those cash flows deployed into business development are going to give us an attractive return. So that's one piece of it.

The second is we think that this is, frankly, a great time for scientific advancement in our industry. As you look across academia, venture biotech, big, small, there's no shortage of external substrate that we think can complement what we're doing internally. And we're going to be thoughtful and disciplined about the science that we want to pursue. And the combination of those 2 things, combined with the capabilities that we have, we think that there is significant growth that we can add to our business through business development going forward.

Albert Bourla Pfizer Inc. - Chairman of the Board & CEO

Yes. And also, it is very important also to understand, Vamil, that we believe that once you put a target, you better execute way better when you have a target in front of you. And actually, we believe that the target needs to be public because we're a public company, and we don't have a problem to do it.

So also, we went in to analyze the substrate and the opportunity. And as always, we are providing at least \$25 billion because, as always, we like to have targets that we are putting out there, and we are beating them. But we believe that with the current -- our analytics that we have done, this is a very reasonable target to achieve without, let's say, utilizing all of our fire power right now. So that will allow us to do dividend and other uses of capital and still do that. And we are confident to put it out there so that people can start measuring against it. Thank you very much.

Operator

Your next question comes from Kerry Holford from Berenberg.

Kerry Ann Holford Joh. Berenberg, Gossler & Co. KG, Research Division - Analyst

So firstly, just on the oral GLP-1. I wonder if you can confirm the number of pills per day that you'll be using in your Phase 2b study up to that maximum dose of 200 mg per -- twice a day. What's the pill burden for the highest dose?

And also on obesity, you've not discussed that today. But do you have the Phase 2a data in-house? I noted that you said you've moved another oral GLP-1 molecule into the clinic. And I'm just interested to know how that asset may differ from the initial danuglipron?

And then lastly, just on the guidance. So if I'm thinking about your \$4 billion sort of range on your sales guidance, given you've given us the point estimates or thereabouts for the vaccine and the antiviral, should I assume the majority of the flex remaining relates to the base business? And if so, can you help me understand the key moving parts within that element of the business? Which drugs may be a driver of that flex?

Albert Bourla Pfizer Inc. - Chairman of the Board & CEO

Thank you, Kerry. Let me take very quickly in the interest of time, the last one. No, the flex is spread around everything. So you should assume, for example, in the \$31 billion of -- in the \$32 billion that we gave -- for \$33 billion, right, on the vaccines, \$500 million down, that's \$1 billion on the Paxlovid, \$500 million -- not \$500 million. That's another \$1 billion. And then on the business, as always, we gave \$1 billion, up and down. So whatever you think is the midpoint, \$1 billion up, which is consistent with what we were doing all these years for that level of business.

And Mikael, on the oral, do you want...

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

Danuglipron is a BID drug and pill burden will be relatively low. You also asked for the additional GLP-1 drug we have in clinical development. That's a once a day drug. As we have now, I think, really defined what will be soon optimal titration for an oral GLP-1, and we were, of course, pioneering that, there isn't really data on it. We may actually consider to take the once daily in the same study of danuglipron, given that we have now this unique opportunity to look through what seems to be 2 great drugs. But currently, I believe danuglipron has all what it takes to go forward to a potential pivotal study based on this study that we shared with you. But it's, of course, a unique situation to have more than one molecule, and it gives us the very best option for going into Phase 3 quite rapidly after concluding that Phase 2b, pending, of course, expected outcome.

Albert Bourla Pfizer Inc. - Chairman of the Board & CEO

Thank you, Mikael. And the last question, please.

Operator

Your final question comes from the line of Carter Gould from Barclays.

Carter Lewis Gould Barclays Bank PLC, Research Division - Senior Analyst

I'll keep it to one since we're at the end. And at the risk of not getting an answer, on OUS pricing for Paxlovid, I understand the underlying aspect is driving sort of your pricing strategy between GDP and the volume-based discounts. But in practice, how consistent has the pricing been across geographies? Any color at a high level would be helpful. And as we think about potentially the standard-risk data, the prophylaxis data kind of playing out over the course of the year, should we anticipate that pricing will be relatively consistent per course in the second half relative to the first half? Any color there would be helpful.

Albert Bourla Pfizer Inc. - Chairman of the Board & CEO

Our pricing for Paxlovid is a tier pricing. So there is a tier for high-income countries, and that is more or less in line with what you have seen published for Merck's, for example, product, and we have seen published ourselves. Only exception was in the U.S., that they got a very special price because of higher orders, but the rest are more or less consistent.

And then there is, of course, there is a second tier for middle-income countries. And for the lower-income countries, we are going to provide it at cost. But also for the low-income countries, in addition to our own providing at cost, of course, we have also initiated a process that a very big number of generic companies will start manufacturing for the low-income countries, which will be 53% of the global population.

Now if the price will remain consistent, clearly, this is nothing to comment here. We will not, let's say, commenting on how prices may or may not evolve in the future.

Thank you very much. Now some closing comments very quickly. We have generated strong results, of course, for both pace and impact and financial performance, and we look forward to continue that in 2022. I want to speak a little bit about a few changes in people that we are doing.

Speaking about that, we continue to attract visionary, purpose-driven leaders, with a track record of delivering breakthrough results for patients. Case in point, last week, we announced that Dr. William Pao will join Pfizer as Executive Vice President and Chief Development Officer, effective March 21 of this year. Dr. Pao brings more than 25 years of experience as an oncologist and scientist. He joins us from Roche, where he most recently served as the Head of Pharma Research and Early Development. He oversaw the discovery and early development of a portfolio of new molecular entities to treat diseases related to cancer, neuroscience, ophthalmology, rare diseases and can go on and on and on. Of course, cancer is a very big part of his portfolio.

Clearly, I want to mention that Dr. Pao succeeds Rod MacKenzie, a legendary leader in Pfizer, who recently announced his intent to retire after 35 years with Pfizer. I want to thank Rod for his incredible contribution to Pfizer, including the outstanding leadership in helping bring Comirnaty and Paxlovid to the world so quickly.

Of course, also, I need to touch base on something that everybody has in mind. I want to take a moment to recognize my trusted colleague and friend, Frank D'Amelio, who also has announced his intention to retire from Pfizer after an incredibly impactful decade and a half with the company as CFO. Frank is one of the smartest, more respected and most effective leaders I have ever had the good fortune to work with, and the positive impact he has had on Pfizer and on all our stakeholders is immeasurable.

Frank isn't going anywhere yet, just to clarify, as he has agreed to stay on board and as we search for his successor and also to serve in a consulting role through the transition. That said, I wanted to take the opportunity to thank him publicly for all he has meant to Pfizer and to me personally. And Frank, on behalf of our 80,000 colleagues around the world, I wish you good health, every happiness as you begin a new chapter when this time comes, because it's not yet. Wherever life's journey takes you, I'm sure it will be directionally correct.

And that will bring an end to our call. Thank you for joining us.

Have a great rest of your day.

Operator

Ladies and gentlemen, this does conclude Pfizer's Fourth Quarter 2021 Earnings Conference Call. You may now all disconnect.

DISCLAIMER

Refinitiv reserves the right to make changes to documents, content, or other information on this web site without obligation to notify any person of such changes.

In the conference calls upon which Event Briefs are based, companies may make projections or other forward-looking statements regarding a variety of items. Such forward-looking statements are based upon current expectations and involve risks and uncertainties. Actual results may differ materially from those stated in any forward-looking statement based on a number of important factors and risks, which are more specifically identified in the companies' most recent SEC filings. Although the companies may indicate and believe that the assumptions underlying the forward-looking statements are reasonable, any of the assumptions could prove inaccurate or incorrect and, therefore, there can be no assurance that the results contemplated in the forward-looking statements will be realized.

THE INFORMATION CONTAINED IN EVENT BRIEFS REFLECTS REFINITIV'S SUBJECTIVE CONDENSED PARAPHRASE OF THE APPLICABLE COMPANY'S CONFERENCE CALL AND THERE MAY BE MATERIAL ERRORS, OMISSIONS, OR INACCURACIES IN THE REPORTING OF THE SUBSTANCE OF THE CONFERENCE CALLS. IN NO WAY DOES REFINITIV OR THE APPLICABLE COMPANY ASSUME ANY RESPONSIBILITY FOR ANY INVESTMENT OR OTHER DECISIONS MADE BASED UPON THE INFORMATION PROVIDED ON THIS WEB SITE OR IN ANY EVENT BRIEF. USERS ARE ADVISED TO REVIEW THE APPLICABLE COMPANY'S CONFERENCE CALL ITSELF AND THE APPLICABLE COMPANY'S SEC FILINGS BEFORE MAKING ANY INVESTMENT OR OTHER DECISIONS.

©2022 Refinitiv. All Rights Reserved.