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EDITED TRANSCRIPT

PFE.N - Q3 2021 Pfizer Inc Earnings Call

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OVERVIEW:

PFE reported 3Q21 revenue growth of 130% YoverY operationally. Co. expects 2021 revenue to be $81-82b and adjusted diluted EPS to be $4.13-4.18.

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PRESENTATION

Operator

Good day, everyone, and welcome to Pfizer's Third 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. Welcome to Pfizer's Third Quarter Earnings Call. I'm joined today by Dr. Albert Bourla, our Chairman and CEO; Frank D'Amelio, our CFO; Mikael Dolsten, President of Worldwide Research and Development and Medical; Angela Hwang, Group President, Pfizer Biopharmaceuticals Group; Aamir Malik, our Chief Business and Innovation Officer; and Doug Lankler, General Counsel.

We expect this call to last 90 minutes. Materials for this call and other earnings-related materials are on the Investor Relations section of pfizer.com. Please see our forward-looking statements disclosure on Slide 3, which is shown right now. And additional information regarding these statements and our non-GAAP financial measures is available in our earnings release and in our SEC Forms 10-K and 10-Q under Risk Factors. Forward-looking statements on the call speak only as of the call's original date, and we undertake no obligation to update or revise any of the 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. I'm happy to report that Pfizer generated another solid performance in the third quarter, recording 130% operational revenue growth compared with the third quarter of 2020. When excluding direct sales and alliance revenues provided by our COVID-19 vaccine, we generated 7% operational revenue growth compared with the previous year quarter. We also are raising our 2021 total company guidance for both revenues and adjusted EPS.

While we are proud of our financial performance, we are even more proud of these financial results -- of what these financial results represent in terms of the positive impact we are having on human lives around the world. In the first 9 months of 2021, our innovative medicines and vaccines reached nearly 1 billion people. It's fair to say millions of lives have been saved because of this. Excluding our COVID-19 vaccine, we reached nearly 300 million people during that time. These are humbling numbers for all of us at Pfizer. At the same time, we delivered to our shareholders the 331st consecutive quarterly dividend.

We also continue to advance our R&D pipeline. Some key milestones include the first COVID-19 vaccine authorized for emergency use in the U.S. for children 5 to 11 years of age, the first patient dosed in our large Phase III RENOIR study for our RSV bivalent vaccine candidate and the initiation of Phase II/III studies for both IV and oral protease inhibitor candidates for COVID-19.

Let me start with commentary on some of our key growth drivers in the quarter, the biggest of which was COMIRNATY, which contributed $13 billion in global revenue during the third quarter. Today, we have produced 2.6 billion doses and shipped 2 billion doses to 152 countries or territories. So far, 75% of our COMIRNATY revenues have been generated outside the U.S., and we continue to sign agreements with governments around the world. We also remain on track to produce 3 billion doses this year, of which, at least 1 billion will go to middle- and low-income countries.

In addition, our weekly market share of COVID-19 vaccines administered continues to increase. In the U.S., our 4-week average market share increased from about 56% in April to about 74% as of October 31. And in the EU, it went from about 70% to about 80% during the same time period. These market share increases are primarily the result of our booster being the first to receive emergency use authorization and our 2-dose series being preferred by some countries around the world for use in certain younger populations.

We also continue to follow the science to help ensure we stay ahead of the virus. Let me speak to 2 examples. First, top line results from our Phase III randomized control trial demonstrated that a booster dose administered to individuals 16 years of age and older who previously received the Pfizer-BioNTech primary 2-dose series restored vaccine protection against COVID-19 to the high levels achieved after the second dose.

Second, the U.S. Food and Drug Administration has authorized our COVID-19 vaccine for emergency use for children 5 through 11 years of age, the first and only vaccine to receive such authorization. For this age group, the vaccine is to be administered in a 2-dose regimen of 10-microgram doses given 21 days apart. The 10-microgram dose level was carefully selected based on safety, tolerability and immunogenicity data.

Last week, we announced that the U.S. government exercised its final purchase option under the existing U.S. supply agreement to purchase 50 million additional doses of COMIRNATY. This brings the total number of pediatric doses purchased by the U.S. government to 115 million, which is enough to vaccinate every U.S. child. Overall, the U.S. has now purchased a total of 600 million doses across all age ranges under this supply agreement.

Now let's take a look at some of the quarter's other key growth drivers. Eliquis has continued to deliver strong performance with global revenues up 19% operationally to $1.3 billion in the third quarter. In the U.S., sales growth for Eliquis was driven mainly by a 16% growth in prescription volume.

VYNDAQEL and VYNDAMAX revenues were up 42% operationally to $501 million globally. Our disease education efforts in the U.S. continue to support increases in appropriate diagnosis, while the main driver of growth in Japan has been the successful establishment of several referral networks in select areas resulting in new patient starts.

IBRANCE continues outside of the U.S. Revenues outside of the U.S. were up 9% operationally to $500 million. This growth was driven by accelerating demand as the delays in diagnosis and treatment initiations caused by COVID-19 show signs of recovery across several international markets. Global revenues for IBRANCE were up only 1% operationally as the international growth was largely offset by a 3% decline in the U.S. The U.S. decline was driven by an increase in the proportion of patients accessing IBRANCE through our Patient Assistance Program.

We continue to be pleased with the performance of our oncology biosimilars portfolio, which is now the largest in the industry with 6 biosimilars approved in the U.S. for patients living with cancer. Global revenues from this portfolio grew 51% operationally during the quarter to $398 million. This growth was primarily driven by continued strong results from our U.S. therapeutic monoclonal antibody launches.

In international developed markets, oncology biosimilars contributed 29% operational growth, driven by new launches of ZIRABEV and continued growth of TRAZIMERA. Of course, with such a broad portfolio of life-changing and life-saving products, it would be uncommon to not have a few challenges. U.S. revenues for our Prevnar family, Prevnar 13 and Prevnar 20, for example, were down 2%, primarily due to a 36% decline in the adult indication of Prevnar 13 due to the ongoing prioritization of primary and booster vaccination campaigns for COVID-19 and the later start of the flu season compared with last year.

Other contributing factors were the continued impact of the lower remaining unvaccinated eligible adult population and the June 2019 change to the Advisory Committee on Immunization Practices, the change of ACIP recommendation for the Prevnar 13 adult indication to shared clinical decision making.

Just 2 weeks ago, ACIP voted to recommend Prevnar 20 for routine use to help protect adults against invasive disease and pneumonia caused by the 20 streptococcus pneumoniae serotypes in the vaccine. Specifically, the ACIP voted to recommend Prevnar 20 for adults aged 65 and older and adults aged 19 to 64 with certain risk conditions without the need to be followed by PPSV-23 vaccination. This recommendation recognizes for the first time the significance of helping protect more population under age 65 with co-morbid and immuno-compromising conditions who are at increased risk of disease against these 20 disease-causing serotypes. This new 1-dose regimen option, once endorsed by the CDC Director, also will help simplify long-standing adult pneumococcal recommendation. As a reminder, Prevnar 20 is the only vaccine that FDA has approved not only for invasive pneumococcal disease but also for pneumonia.

In September, I assume many of you saw that the FDA issued a drug safety communication related to its completed review of the Xeljanz ORAL Surveillance trial. We are in continuing dialogue with the FDA about its assessment and the resulting final context in the Xeljanz label. With this important step taken, we hope we are a step closer to having an update regarding the new drug application for abrocitinib in atopic dermatitis and the supplemental NDA for Xeljanz in ankylosing spondylitis, both of which are currently under FDA review.

In terms of Xeljanz, in it's currently approved indication in the U.S., we believe that Xeljanz prescribing behavior will adjust in the coming months based on the FDA's update, resulting in an initial correction in the short term. But based on the trends we have observed and the broad application of Xeljanz across its approved indications, we believe Xeljanz has the potential to return to growth, again, once the final U.S. label is issued and physicians have adjusted their prescribing habits accordingly as we go into 2022 and beyond.

CIBINQO, abrocitinib, received marketing authorization for the treatment of moderate to severe atopic dermatitis in adults and adolescents aged 12 years and over from the U.K. Medicines and Healthcare Products Regulatory Agency and the Japanese Ministry of Health, Labor and Welfare in both doses. It also received a positive opinion in adults from the European Medicines Agency Committee for medicinal products for human use. We are hopeful this momentum will continue. We have applications currently filed for review with regulators around the globe, including in the U.S. and Australia. Overall, we remain confident in the importance of the JAK inhibitor class for appropriate patients with inflammatory diseases. And they are pursuing a variety of options for advancing additional JAK inhibitor assets within our portfolio.

For example, Pfizer has granted an exclusive license to brepocitinib and TYK2 both in Phase II development to a new company, formed in collaboration with a partner that has a proven track record in late-stage inflammation and immunology drug development. The new company will direct all future development decisions while Pfizer will have a 25% stake and retain certain ex-U.S. commercial rights for brepocitinib and TYK2. This transaction will enable the allocation of resources to advance development of brepocitinib and TYK2 while allowing Pfizer to focus on diversifying its pipeline.

Another way in which we are continuing to bolster our pipeline is through strategic business development agreements. This slide highlights 10 such agreements we have entered in recent years, spanning 4 different therapeutic areas. To further build on our strength in cancer research, we acquired Array BioPharma. The team in Boulder, Colorado, has become a center of excellence for targeted therapies in not only cancer, but other diseases as well, with an expected 1 to 2 new compounds entering the clinic every year. Leveraging our strength in gene therapy, we entered into a collaboration with Vivet Therapeutics for a potential gene therapy for Wilson disease, a rare genetic disorder that can cause severe hepatic damage, neurological symptoms and potentially death. Our acquisition of Therachon builds on our rare disease team's 30 years commitment to develop innovative medicines that address significant unmet medical needs of people with rare diseases.

Regarding our worldwide exclusive licensing agreement with Akcea, we believe our expertise and breadth of experience in cardiovascular and metabolic diseases makes us well suited to accelerate clinical development of AKCEA-ANGPTL3-LRx, an investigational antisense therapy being developed to treat patients with certain cardiovascular and metabolic diseases. We are excited about our collaboration with Valneva to develop and commercialize with Valneva to develop and commercialize Valneva's Lyme disease vaccine candidate, VLA15, the only active Lyme disease vaccine program in clinical development today. Of course, our collaboration with BioNTech on the COVID-19 vaccine led to the first mRNA vaccine ever approved. And this relationship was borne out of our company's initial collaboration to develop an improved flu vaccine based on mRNA tech.

Building on our strengths in prostate cancer and women's health, we have entered into an agreement with Myovant to jointly develop and commercialize Orgovyx, relugolix, advanced prostate cancer and relugolix combination tablet in women's health in the U.S. and Canada. Our global collaboration with Arvinas to develop and commercialize ARV-471, an investigational oral PROTAC estrogen receptor protein degrader, builds on our metastatic breast cancer franchise allowing us to potentially go into earlier non-metastatic patients and add to efficacy of IBRANCE in a metastatic setting.

Trillium's CD47-SIRPa-focused technology has the potential to be as foundational in cancer immunotherapy as PD-1/PD-L1s have been. We look forward to that acquisition closing later this year and in the first half of 2022. With 3 approvals, 4 EUAs and multiple submissions and readouts, these transactions are already bearing fruit and positioning us to reach even more patients.

Before I close, I want to welcome to the call Aamir Malik, who joined us in August as Executive Vice President and Chief Business Development -- and Chief Business Innovation Officer. Aamir came to us from McKinsey where during his 25-year career, he has developed growth strategies, guided mergers and acquisitions and implemented large-scale programs to improve patients' lives and transform performance for life science companies. This includes working closely with Pfizer on several strategic initiatives. I have known Aamir for more than 15 years, and I'm certain he will be an incredible addition to Pfizer as we look to the next era of innovation.

Looking ahead, we continue to focus on driving operational excellence across the organization and pursuing the kinds of first-in-class science that will define the new Pfizer. Given our third quarter performance and our current expectations for the near term, we continue to expect a revenue CAGR of at least 6% on a risk-adjusted basis through the end of 2025 and double-digit growth on the bottom line. I would remind you that these projections do not include any potential impact from COMIRNATY, recent or subsequent business development activities or potential future mRNA programs. Rather, we remain very confident in our ability to achieve these growth rates because of the strength of our current product portfolio and R&D pipeline.

Now I will turn it over to Mikael to speak more about our R&D efforts, and then Frank will provide financial details on the quarter and our outlook for the remainder of 2021, which looks solid. Mikael?

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

Thank you, Albert. I appreciate the chance to share updates on Pfizer's robust R&D pipeline. As a measure of the transformation that we've instituted in our R&D organization, we track our average clinical success rates against peers. In every phase and end-to-end, we achieved greater success rates than peer average in 2020 and have continued to sustain those higher rates in '21.

Today, I will provide updates on our vaccines, rare disease, inflammation immunology portfolios and on our oral protease inhibitor. In several cases, I will reference publicly available data on other agents so that you can understand our enthusiasm about what we are seeing in our development program. Of course, head-to-head clinical trials would be necessary to support any comparative claims.

Last Friday, the FDA granted emergency use authorization for 5 to 11 year olds, and the CDC's Advisory Committee on Immunization Practices is meeting today to discuss recommendations. On the left, we show the comparable immune response observed with 10-microgram dosing in children 5 through 11 compared to 30-microgram dosing in 16 to 25 year old. On the right, we show 90.7% vaccine efficacy observed. This too is comparable to what we have seen in older populations.

The rate and severity of fever and chills after the first and second doses were less in the younger children than either adolescents or adult. We believe that vaccinating younger children is one important step in making our way through this pandemic. Looking ahead, we expect initial pivotal data from the studies in 2 to less than 5 year olds this quarter and in 6 months to less than 2 year olds next quarter with full data readout to follow.

On the right, we show improved handling conditions that have been approved for vials to dose 5 through 11 year old. Of note are the smaller pack sizes and the ability to refrigerate for up to 10 weeks. We plan to submit data to regulators for potential approval of similar handling conditions for vials used to dose the 12-and-older population. We are the first manufacturer to report Phase III clinical efficacy data on a third dose boost and, to the best of our knowledge, are the only company with an ongoing pivotal efficacy boost study. In a study of participants 16 and older, shown on top, a booster demonstrated a relative vaccine efficacy of 95.6% compared to the original 2-dose schedule during a period in which Delta was the prevalent strain, affirming the protective impact of the early immunological data, which led to the EUA.

It's projected that the third dose boost vaccine efficacy is even higher compared to the unvaccinated population, potentially above 98%. This assumes that vaccine efficacy for those vaccinated with 2 doses versus unvaccinated is above 55% at this time point. We observed consistent efficacy in younger and older adults. While the majority of cases were in the older age group, as would be expected, we recorded a relative vaccine efficacy of 100% in individuals aged 16 to 30 years.

Data from Israel shown at the bottom and published by Professor Marc Lipsitch of Harvard and others in Lancet show that the third dose protected individuals against severe COVID-19-related outcomes. We plan to monitor the participants in our clinical study and at an appropriate time consider a randomized fourth dose booster study to document the impact of additional and possibly annual repeat vaccinations. This will be supplemented with real-world evidence data.

Countries have started to recognize the favorable risk-benefit profile of our vaccine. In each country shown here, our vaccine is recommended or the only one permitted in younger populations and in the case of France, not restricted for boosting. News over the weekend from another manufacturer suggest that their vaccine may not be available in the near term for younger population. We are encouraged by these science-driven decisions, which have helped make COMIRNATY one of the most used COVID-19 vaccines globally.

Next, gene therapy. In hemophilia A, we have temporarily and voluntarily paused screening and dosing in our Phase III study evaluating Factor VIII gene therapy, which we are developing with Sangamo, in order to implement the protocol amendment following the observance of Factor VIII levels greater than 150% in some trial participants. To date, no patient has experienced a thrombotic event and some patients are being treated with oral anticoagulants to reduce the risk of thrombosis. We are committed to resuming dosing as quickly as possible once a protocol amendment, which is intended to provide guidelines for clinical management of elevated Factor VIII levels is implemented.

Separately, based on recent interaction with the FDA, Pfizer no longer plans to conduct an interim analysis of Phase III data from our hem A and B gene therapy programs. We anticipate pivotal data readouts to be based on full analysis of at least 50 study participants for hem A and 40 participants for the hemophilia B program. This will push out the timing of readouts of those trials compared to our previous expectations. For hem A, we're working to evaluate the impact of both the FDA feedback as well as the protocol amendment on time lines, and we'll share an update at the appropriate time. For hemophilia B, we anticipate the readout in the first quarter of '23. We continue to collect long-term follow-up data in our Phase Ib DMD study in which 19 ambulatory boys in the U.S. have been treated and plan to represent the 1-year data set at a scientific meeting.

We recently shared information on muscle weakness, presumed myositis, in some cases with myocarditis in 3 participants in Phase III ambulatory trial with a specific subset of dystrophin truncation mutations. They were treated with higher doses of steroids and all improved within a few weeks, were discharged from the hospital and have recovered or are still recovering. The data monitoring committee have confirmed that immunological assessment performed in the trial supports the hypothesis that an immune response against the mini-dystrophin protein caused these changes.

This type of reaction is a risk potentially inherent to any gene replacement therapy, and similar severe adverse events reported in other programs support the notion that this is a class effect. We have proposed a protocol change to exclude patients with any mutation affecting exons 9 through 13, inclusive, or a deletion that affects both exon 29 and 30. A few sites have resumed new patient activities, and we anticipate that nearly all ex-U.S. trial sites will have restarted clinical activity by the end of this month. These mutations are estimated to represent less than 15%, 1-5, for patients with DMD. We recognize the devastating impact that DMD has on these boys and their families and plan to include patients with some of these excluded mutations in future studies.

In addition, we continue to work with the FDA to address outstanding IND questions related to the Phase III study, including technical aspect of our potency assay matrix. We have made considerable progress with development of the CMC assay as per FDA guidance and are now in an active phase of filing this update. While we cannot speculate as to when sites may open, we're working to reach alignment with the FDA as soon as possible.

In addition, we have 12 preclinical gene therapy programs and are anticipating approximately 1 to 2 first-in-human study starts each year. We'll now turn to high potency PDE4+ immune modulator we are exploring in atopic dermatitis and psoriasis. Topical delivered high-potency PDE4+ inhibition may offer a differentiated efficacy and safety profile compared to other mechanism of action, whether used orally or topically. PDE4 inhibition could provide both rapid and deep responses versus other agents with the potential for further improvement at higher doses. Even at a significant lower dose, we observed promising clinical efficacy compared to what we have been seeing with PDE4 topicals in other trials. We expect to initiate Phase IIb studies in both diseases in 2022 exploring higher doses.

On the left, we show in vitro potency at a low dose versus roflumilast and crisaborole. Our asset demonstrated approximately 240-fold greater inhibition of IL-4 and approximately 25-fold greater inhibition of IL-13 versus roflumilast. On the right, we observed clinically significant improvement in eczema area severity versus comparators in other studies with a 45% reduction from baseline at week 6. Our asset showed stronger or similar efficacy at week 6 as compared to reported data from another study at week 8 with the recently approved topical JAK 1/2 inhibitor, ruxolitonib. There was no stinging observed at the application side.

On the left, we saw an approximately 80% reduction in IL-23 versus activated skin plus vehicle in an in vitro skin model. This displays a relevant mechanism of action for high-potency PDE4+ in psoriasis. On the right, in patients, we saw significant clinical improvement in psoriasis area and severity versus a comparator in a separate study with a 4.5-point reduction from baseline at week 6.

Let's turn to a TL1A inhibitor, which targets a newly identified member of the TNF superfamily being explored for ulcerative colitis. In a Phase IIa study, we saw promising endoscopic improvement. Based on the benefit-risk profile seen, there is a potential for TL1A inhibition to be used earlier in the treatment paradigm. Phase IIb studies in inflammatory bowel disease are ongoing with estimated primary completion in the fourth quarter of '22. On the left, our TL1A inhibitor demonstrated greater endoscopic improvement than what tofacitinib demonstrated in a similar trial with 34% of patients responding at week 14. We match the population based on the characteristic of those enrolled in our TL1A study using propensity score matching. The week 14 data for tofacitinib is interpolated based on week 8 data of the induction study and month 12 data from the maintenance and open-label studies.

On the right, a post-hoc analysis found that 48% of patients who had biomarkers achieved endoscopic improvement versus 13% of patients who were biomarker negative. Approximately 70% of patients who are positive with this biomarker, and we believe a precision medicine approach utilizing key biomarkers may enhance patient selection and improve patient outcomes.

Next is an interferon beta inhibitor, a potential breakthrough therapy for dermatomyositis that we developed in a research collaboration with Mass Gen Brigham. This is a disease with very limited treatment options. In an ongoing Phase II clinical trial, we have observed significant reductions in clinical disease activity in skin compared to placebo. We anticipate the readout of the full Phase II study in the first quarter of '22.

On the left, in this figure, treatment compared -- demonstrated an 83.6% decrease in gene signature scores from baseline at week 12 compared to 11.8% with placebo. On the right, treatment also showed significant decrease in clinical disease activity at week 12 compared to placebo. An important step in addressing the pandemic will be the availability of effective outpatient treatments for people who acquire COVID-19. In a paper published today in Science, we shared the design and preclinical profile of our novel investigational oral protease inhibitor, including its in vitro pan-coronavirus antiviral activity, in vivo efficacy, selectivity and preclinical safety profile. A robust program to study the breadth of both treatment and prevention in high-risk, standard-risk and household contact population is well underway. Projected pivotal readouts start potentially this quarter and extend through mid-'22.

Finally, our recent milestones are a reflection of those high clinical success rates that I shared at the beginning, and we look forward to continuing the momentum in '22. Select milestones expected in the fourth quarter include: a pivotal data readout for our C. diff vaccine candidate, a proof-of-concept readout for vupanorsen for severe hypertriglyceridemia and cardiovascular risk reduction, and a proof-of-concept readout for danuglipron for diabetes. Milestones expected in the first half of '22 include: Phase III results for our RSV adult and maternal vaccine candidate, a potential pivotal Phase II readout for elranatamab in relapsed/refractory multiple myeloma, a proof-of-concept readout for our mRNA flu vaccine candidate, a Phase IIb proof-of-concept readout for the potential Lyme disease vaccine on which we are collaborating with Valneva, a proof-of-concept readout for ROBO2-Fc for focal segmental glomerulosclerosis, a proof-of-concept readout for danuglipron for obesity, and Phase III results of TALZENNA and XTANDI in first-line metastatic castration-resistant prostate cancer.

In addition, we expect continued active business development to further augment the clinical portfolio. Thank you for your attention, and I look forward to your questions. Now let me turn it over to Frank.

Frank A. D'Amelio - *Pfizer Inc. - CFO & Executive VP of Global Supply*

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 significant positive impact on our quarterly results, and Albert has already addressed the key points on the COVID-19 landscape.

Turning to the income statement. Revenue increased 130% operationally in the third quarter of 2021, driven by COVID-19 vaccine sales strong performance from a number of our other key growth drivers. And looking at the revenue growth, excluding the COVID-19 vaccine contribution from direct sales and alliance revenues, as Albert said earlier, we saw a continuation of solid performance from the businesses again this quarter, delivering 7% operational revenue growth despite a negative 5% impact from price, getting us to a robust volume growth of 12% for the business, excluding the COVID-19 vaccine contribution.

The 12% volume growth is in spite of an approximately 2% negative impact to growth from the Chantix recall and distribution pause. This supports our projected revenue CAGR of at least 6% from 2020 through the end of 2025. Of course, there will be some variability in quarterly growth rates due to a variety of factors, but we continue to expect at least a 6% CAGR through 2025.

There was no impact from the number of selling days in the quarter as compared to the year ago period like we saw in our first quarter, where we had more selling days compared to the year ago period. I'd remind you that the offset to this imbalance will be seen in the fourth quarter results, where we will have fewer selling days as compared to the year ago quarter. For the full year, these results in essentially the same number of selling days in '21 as 2020. I'll come back to this in a little bit when I discuss the updated guidance.

The adjusted cost of sales increase shown here reduced this quarter's gross margin by approximately 22 percentage points compared to the third quarter of 2020, which is almost entirely driven by the impact of the COVID-19 vaccine. Adjusted SI&A expenses increased primarily due to a level of promotional spend and sales force activity more similar to pre-pandemic levels. The increase in adjusted R&D expense this quarter was primarily driven by increased investments in COVID-19-related programs as well as other programs within our pipeline. The growth rate for reported diluted EPS was 445% while adjusted diluted EPS grew 129% for the quarter. Foreign exchange movements resulted in a 4% benefit to revenue as well as a 4% benefit or $0.02 to adjusted diluted EPS.

Let's move to our revised 2021 guidance. We've again provided total company guidance, which includes the business with the COVID-19 vaccine, and then we provided some additional sub-ledger detail on our assumptions on the projected COVID-19 vaccine contribution and the business

without the COVID-19 vaccine. Our revenue guidance has increased, and we now expect total company revenue to be in a range of $81 billion to $82 billion, increasing by $2.5 billion at the midpoint, with the COVID-19 vaccine revenue for the year now expected to be approximately $36 billion, an increase of approximately $2.5 billion compared to our prior guidance. The projected COVID-19 vaccine revenue as a percentage of total company revenue at the midpoint has increased to 44% as compared to 42% in our previous '21 guidance. I'll come back to that in a minute. We also adjusted our cost and expense guidance, mostly to reflect actual performance to date. Let me give you some more detail here.

For adjusted cost of sales, the range has decreased to between 39.1% to 39.6%. On adjusted SI&A, we have tightened the range and now expect $11.6 billion to $12.1 billion, a decrease of $150 million at the midpoint. In addition, we increased our adjusted R&D guidance range to $10.4 billion to $10.9 billion, an increase of $400 million at the endpoint (sic) [midpoint] to reflect anticipated incremental spending on COVID-19 and other mRNA-based projects. We are keeping our assumption for the effective tax rate for the year flat compared to prior guidance at approximately 16%. This yields an increased adjusted diluted EPS range of $4.13 to $4.18 or 84% growth at the midpoint compared to 2020, including an expected 4% benefit from foreign exchange.

Let me quickly remind you of some assumptions and context on the projected COVID-19 vaccine contribution and our collaboration agreement. As discussed earlier, 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 3 billion doses in total by the end of 2021. $2.5 billion increase in expected COVID revenues to $36 billion primarily represents the impact of contracts signed since mid-July, which was the cutoff for our prior guidance. This assumes deliveries of approximately 2.3 billion doses in fiscal year 2021 compared to prior guidance of deliveries of 2.1 billion doses and continues to assume that we will produce 3 billion doses during calendar year 2021. This difference of 700 million doses represents doses which will be delivered in fiscal year 2022.

To refresh your memory, our cost of sales for the COVID-19 vaccine revenue includes manufacturing and distribution cost, applicable royalty expenses and a payment to BioNTech representing the 50% gross profit split. We continue to expect that the adjusted income before tax margin for the COVID-19 vaccine contribution to be in the high 20s as a percentage of revenue. This margin level also includes the anticipated spending on additional mRNA programs and spending on the COVID-19 protease inhibitor antiviral programs.

If we remove the projected COVID-19 vaccine contribution from both periods, you will see that we slightly decreased the 2021 revenue range to $45 billion to $46 billion, so representing approximately 6% operational revenue growth at the midpoint. The decrease in guidance at the midpoint largely reflects the impact from the Chantix recall and pause in shipments.

In terms of adjusted diluted EPS without the contribution from the COVID-19 vaccine, we have increased the range to be between $2.60 to $2.65 for the year, which represents approximately 12% operational growth at the midpoint. These growth rates are all consistent in how we've been publicly positioning the business post the Upjohn separation. You may notice that the implied Q4 guidance suggests non-COVID-19 operational revenue to decline by 1%, especially as compared to the revenue growth that we've seen year-to-date of 8%. Let me walk through the drivers of this.

The largest driver of the decline is a difference in number of selling days compared to the comparable quarter in 2020. You will remember my discussion of extra selling days in Q1 when we had 3 more selling days in the U.S. and 4 more selling days in the international markets. And I talked then about how Q4 would largely offset that impact, leaving 2021 as a whole with approximately the same number of selling days as 2020. So in Q4, we will now have 4 fewer selling days each in domestic and international, 8 less in total as compared to Q4 2020. This is expected to decrease sales by approximately $600 million or have a negative impact to the growth rate of 6% for the company, excluding COVID vaccine sales. We expect the Chantix sales to be 0 in Q4 due to the recall and pause in shipments, representing another 2% headwind to growth.

And while it is not our normal practice to discuss 2022 outlook during the Q3 conference call, I wanted to make a brief comment related to potential COMIRNATY sales next year as we've noticed some estimates of those sales to be very high. While we have the capacity to produce 4 billion doses in 2022, at this point, we expect to recognize revenues for 1.7 billion doses in 2022, representing COVID vaccine direct sales and alliance revenues approximately $29 billion. We continue to engage with governments regarding potential future orders for 2022, including doses for which certain

governments have the option to order and take deliveries in 2022. And 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, a strong quarter and first 9 months of the year based on continued strong performance for our growth drivers. We have increased our revenue and EPS guidance for the remainder of the year, mainly driven by increased expectations for COMIRNATY sales. Our pipeline continues to advance, and we have invested to support that advance. We look forward to an expected closing of the Trillium acquisition as soon as this quarter or in the first half of 2022, subject to the satisfaction of the closing conditions.

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*

Thanks, Frank. Sylvia, we're ready for our first question, please.

QUESTIONS AND ANSWERS

Operator

Your first question comes from Umer Raffat from Evercore.

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

I have 3 today, if I may. Perhaps, first, Albert, do you expect vaccine efficacy on hospitalizations to fade over time? I know this has been a big point of discussion and has direct implications for longer-term booster usage. Do you expect the hospitalization efficacy below, let's say, an 80% number?

Number two, on the protease inhibitor, I was curious if you guys are expecting different activity in the high-risk versus the low-risk trial. I acknowledge the endpoints are different. But is there any reason to expect viral load reduction to look different between the 2?

And then finally, on the DMD gene therapy trial, I was curious if you have evaluated anti-dystrophin antibodies, perhaps beyond the patients with exon 9 to 13 or 29 and 30. I'm just trying to understand if there's a bit of an immune response against the dystrophin being made in other patients as well and whether that could be relevant for the primary endpoint or not.

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

Thank you very much. But I think I will give all 3 questions to Mikael because they are clearly in his domain. Mikael, what do you think about the vaccine efficacy, the protease activity and the DMD?

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

Thank you very much. Our own studies, the real-world evidence studies coming from Israel all show that you do get waning over time, driven by the immune system, as expected, gradually reducing antibodies in the blood and activated immune cells as well as appearance of more aggressive strain in this case, the Delta strain. We think that the data show that you first lose protection against symptomatic disease as you have noted in our trials, and then you lose some protection but more stage loss over severe disease and hospitalization. We were really pleased to share with you today that when you look at the real-world evidence data, we are able in a very meaningful and substantial way improve with a third dose boost against all facets of disease, whether symptomatic, whether severe, hospitalization and even death. So yes, there is just a shift in time. And that's

why we already now are preparing for revaccination, when the third boost immunity may start to fade possibly after a year, which we think would be the type of data to generate to support more of an annual vaccination, similar as flu.

For the oral protease inhibitor, we think there is an opportunity with our approach where we are able to have high levels of the oral drug to get robust efficacy against high risk and low risk. And that's obviously what we would like to see as the trial reads out and we have to wait for data. I just wanted to emphasize that our standard-risk group includes vaccinated breakthrough infection and non-vaccinated with standard risk. This is the only trial currently running to the best of my knowledge that contains a study population that are vaccinated and will get possibly breakthrough infections. So it's really a unique indication which is expected to have more and more prominence once the majority of people are vaccinated.

And finally, the household study, exposure study. In that one, we expect based on previous experiences from Tamiflu and other antiviral drug that you're likely to get a good probability for even higher -- hopefully, a very high antiviral effect.

On DMD gene therapy, we're looking at ways to support this patient group that lack a part of the DMD protein, so they are not tolerant to their own protein, and hence, they generate an immune response to that part when they get the new gene. I don't think that will happen in any individual that are born with all components of the dystrophin but may be mutated to be not highly functional. So our focus right now is to executing the majority of patients, 85%, and then developing supportive protocols, which we think are very feasible also for those that have less tolerance and are more prone direct when they're given their full normal dystrophin transgene.

Operator

Your next question comes from Vamil Divan from Mizuho Securities.

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

So maybe just a couple if I could. So one, I appreciate, Frank, the comments you made around 2022 in terms of the COVID vaccine sales. Can you maybe share just updated thoughts on how you guys are seeing the revenue stream from these vaccines are playing out over time? A lot of focus obviously on '23, '24, '25. And sorry, connected with that, but maybe a broader question. About a year ago, you guys listed at R&D Day and kind of went through the whole pipeline and talked about the $18 billion to $20 billion of revenue that you expect to lose because of that expiration starting in 2026. At that point, you mentioned that the pipeline felt -- was at least sufficient to replace that revenue stream. I'm curious, given the -- everything that's happened in the past year, kind of what's your updated expectations on your ability to overcome those patent losses in the future.

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

Yes. Thank you. Frank, do you want to take out this? And then also, Angela, you can chime in on the revenue stream.

Frank A. D'Amelio - *Pfizer Inc. - CFO & Executive VP of Global Supply*

Thanks, Albert. So Vamil, the way I would think about '22 is kind of a rhythm that's similar to '21. And what I mean is we'll continue to update the numbers for '22 based on the contracts that we've signed and then obviously, the deliveries that will be shipped in '22 that go with those contracts. So think about this year, as we've updated our guidance each quarter, we've been able to increase our revenue guidance to the COVID vaccine because of incremental contracts signed from 1 quarter to the next. We're using that same approach for 2022.

So right now, 1.7 billion, I'll call that kind of banked, if you will, in terms of the doses and the $29 billion that goes with that. Obviously, we've got to ship those doses, but we have contracts in hand that supports the 1.7 billion doses and the $29 billion in revenue. So that will be the rhythm of the numbers, the way to think about it going forward in '22. Beyond '22, obviously, we're working our way through those numbers. We continue

to believe that the vaccine has durability and that there will continue to be significant revenues beyond '22. But in terms of specifics there, we are continuing to work on that. Albert, I can turn that over to Angela, if you'd like.

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

Yes, please, Angela.

Angela Hwang - *Pfizer Inc. - Group President of Biopharmaceuticals Group*

Sure. Thank you. Maybe just one more add to that is that as you look into '22 and also the out years, as Frank said, we will update you as the contracts get confirmed. But many of our contracts already have been confirmed, and those are multiyear contracts. So we already know that looking into '22 in the out years, that there are some that are going to continue to be government-driven. And then maybe the one other thing that will change over the next -- in the foreseeable future is just the development of a private market.

And most likely, we'll see that developing in the U.S. sooner than the others because that's -- ex U.S. is where the multiyear contracts have already been secured. But I think that, that will be something -- a new dynamic that we are absolutely ready to manage, and we're really transitioning our portfolio. And if you look at the presentation of the vaccine that we have into smaller pack sizes, different sort of stability, different storage enhancements that we're making, all with a view of preparing to transition into vaccinations in a community setting and preparing for a durable business. So I would just add that to what Frank just mentioned.

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

Thank you, Angela. And what I will add in this question, in addition to what Angela said, I would add that also commercially, that's a position of strength for us. So I think moving into a private market, that's where we know how to make a difference as well. The other thing that I would say is, as you've noticed from the numbers, we are moving ahead to produce 4 billion doses. And we have already secured the contracts for 1.7 billion doses. And there are some more that we have secured in terms of options. And clearly, we have a big number of countries that we are negotiating with us.

But again, I will raise my concern that I had raised in August of last year when most of the negotiation for doses in the next year are coming from high-income countries and some middle-income countries. I think we are producing enough, but for the low- and middle-income countries to receive not-for-profit, at the low-income countries with very severely discounted price for the middle-income countries, they need to place orders. That's including COVAX and the WHO and all of them. So the 4 billion doses that we are going to produce, they are still highly negotiated by high- and upper-middle class countries. And I don't want to reach that level, but again, the low and middle-income countries will be behind in deliveries because they didn't place their orders enough. So that's one.

As regard the broader question on the 6%, I think nothing has changed. If anything, I think the probabilities are improving in terms of how our pipeline can cover the gap to make sure that we have a 6%. So when it comes to the 6% of all the year to after '25, I think we feel very, very confident that we will achieve it. And then I remind everyone that this is excluding all these new mRNA that we're working, excluding COVID, so all of that is COVID vaccines. All of that, I think, we are in a very, very good, let's say, state. And we are very encouraged with the modern pipeline, the pipeline that comes to fill the gap between 25 and 30. And this is also where we believe that right now, we can bring it significantly up what The Street projects as a severe decline. I think already with our pipeline, our projections are saying that we will take it to slight growth -- flat to slight growth. And we are very much looking forward to higher programs, and we are looking forward to business development to -- because the goal is to sustain a 6% growth on the second part of the decade as well, if possible. Thank you.

Operator

Your next question comes from Tim Anderson from Wolfe Research.

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

On the oral protease inhibitor, it's closely watched by investors now that Merck has positive results with molnupiravir. But it seems like in your prepared remarks, you spent more time talking about various Phase II programs in your pipeline versus this one where we'll have readouts sooner. So I'm wondering if this suggests a lower level of confidence by Pfizer in these upcoming readouts.

And then can you just talk about your views of molnupiravir and also the recent data they released? And also, how do you think drugs like this, whether it's your own PI or molnupiravir will be used in a real-world setting, will that primarily be used in the study population, which is really just the unvaccinated patients? Or will it be used more broadly?

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

Yes. Thank you very much. We are very bullish on the oral inhibitor. This is why earlier this year and during summer, I approved another $1 billion investment at risk to start manufacturing at risk and, of course, to start -- to run 3 studies in parallel, one for the high-risk population, one for the standard population and one for the household, let's say, contacts population. We -- the studies are ongoing. So there is not much to say right now other than we feel optimistic, but we need to see the results of the studies. And if positive, we will be ready.

The way that those will be used, I think it is -- there is a significant part in the high-risk population. But because the cost of these medicines is way cheaper than the antibodies, I think in the standard-risk populations also, we'll have a significant update. And of course, there is a high-volume opportunity in the contact population -- in household contact population that could really change the paradigm.

There will be unvaccinated population who, unfortunately, will have the majority of the infections. And I think these medicines will be predominantly coming to them. But there will be also breakthrough infections either with people of high risk or with other people. But vaccinated people also will be in need of something like that. Actually, Mikael made the comment about that when he spoke, that the study that we are running for standard-risk population to our knowledge is the only one that it is run. So just to make sure that there is no misunderstanding here, we are investing very heavily, and we count -- we are cautiously optimistic that the studies will reveal the data. But we will speak when the data are here.

Now as regards, Merck, I will ask Mikael to make some comments. But I would like to say that I don't think it is appropriate for us to comment on other oral inhibitor. I think the fact that Merck's product was announced, the 50% efficacy, are great news for patients and are great news for the medical community. But hopefully, if the product is approved, they will have an option in their hand. Mikael, do you have anything to add to that without going through, Mikael, through Merck's product that they should be the ones to speak about it.

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

Absolutely. I think you outlined it very well. We are optimistic, enthusiastic. But as always, we're waiting for the data that we hope to come before year-end for the high risk. The standard risk, as you heard, we're the only one running such a study for an oral drug. It's really a unique opportunity. And it will be a growing need for those that do not get repeat vaccinations. And I think for the household study, a protease inhibitor with its well-known safety is really intriguing. As you know, protease inhibitor of this kind do not possess risk for the type of side effects, mutagenicity that's seen of sometimes with polymerase inhibitor and require a longer follow-up before you know about their potential impact. So that's why we think the protease inhibitor is really a perfect fit for the pandemic moving over gradually, hopefully, to an endemic. And we're just waiting eagerly to see it read out. Thank you.

Operator

Your next question comes from Ronny Gal from Bernstein.

Aaron Gal - *Sanford C. Bernstein & Co., LLC., Research Division - Senior Research Analyst*

I have 3, if I may. First, regarding your adalimumab biosimilar, you kind of noticed the SWITCH trial has been successful. You've not commented specifically on filing for interchangeability. Can you clarify that point?

Second, it was kind of going across the wire, there are some comments from D.C. about negotiating drug prices for 30 drugs by 2028 as part of the negotiated agreement. Is this something that drug industry can live with or not? Is this something you're objecting to? Or is this something that within a great bargain, that will settle drug prices for the -- drug price legislation for the next 3 years? Is this something the drug industry is comfortable with?

And last, regarding your oral GLP-1, danuglipron, are you expecting results in diabetes in the fourth quarter of this year? Some of your peers suggested that the intraday variation in blood concentration of GLP-1 is bound to lead to higher side effect profile for the efficacy delivered. Can you discuss what is your view here?

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

Thank you very much, Ronny. I will answer the drug pricing. And Angela, I will pass you the biosimilar question and also the oral GLP-1 to Mikael. So let me start with negotiating the drug price. First of all, I think that we have an issue asset in multiple times with drug pricing. But the issue is not the cost to the health care system. The issue, it is the cost out of pocket for the patients that taking their medicine. The cost of drug pricing to the overall health care system, it is 12%. So by definition, it cannot be the big problem. And this cost is going down. In the U.S., in the first quarter, was minus 5%. In the second quarter, it was minus 5%. In the third quarter, it's minus 5% in our audited numbers of Pfizer but, in fact, of pricing.

Problem is that none of our patients that are taking our medicines are experienced minus 5% in what they pay. Actually, they are experiencing increases. And this is because there is a problem with the insurance system that forces tremendous out of pocket when it comes to medicines, which is not the case when it comes to other, let's say, medical interventions, diagnostics, physician fees, hospitals, you name it.

Now what needs to be done? It is to have a reform in the way that -- in a way that will affect out of pocket for the patients. And I truly believe that there is a deal to be made right now in Washington. I truly believe that. And I think that the Congress should not miss the opportunity to find a deal right now that will reduce the out-of-pocket cost of patients, which is the main, main issue right now.

Now when it comes to negotiating drug pricing, negotiation is good and are happening right now. Medicare negotiates very effectively with us. What people, some parts of the political spectrum wants to see is not negotiation. It's price fixing. What they are suggesting as negotiation, it is that they -- we will be telling a price, but if we disagree with this price, then they will tax us 90%, 95% on everything that we sell in the private market. So this is not negotiation. This is clearly a price fixing. But I think we -- it's going to be a very big mistake to see that happening to our objective. But what I want to emphasize here is not if we are disagreeing in negotiating with our pricing, I think it is that it's a great opportunity to have a deal right now in the Congress. And that will significantly reduce the out-of-pocket cost of the patients when they're taking their medicines. Now with that, I'm passing to Angela to speak about adalimumab.

Angela Hwang - *Pfizer Inc. - Group President of Biopharmaceuticals Group*

Yes. So for the biosimilar for [adenzumumab], we will have interchangeability studies, and we're filing that in December 2021. Mikael?

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

Yes. The oral GLP-1, I think it's a class with a lot of promise. I think danuglipron is currently the most advanced true oral small molecule. It has not at all the same type of food effect interaction as been seen with oral delivered peptides. As you stated, we'll have soon this year a readout with a slower titration for diabetes to optimize efficacy, convenience and tolerability. This is well known for all introduced GLP-1 peptide. We'll later next year have an obesity readout. And the drug players of an oral has an opportunity to be possibly the most powerful within the oral segment and a

much more convenient form for the injectable, particularly for the new emerging segment of obese patients that need metabolic control. This is a very attractive type of treatment to come. And we look forward to generate more data and understand this type of new emerging true oral how to optimally position it.

Operator

Your next question comes from Steve Scala from Cowen.

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

A couple of questions. First, on the oral COVID antiviral. The initial data seems to have been delayed from the third quarter or the fourth quarter of this year to the fourth quarter of this year and the first quarter of next year. So what is the reason for the delay? For instance, are the events tracking below expectations? And secondly, a follow-up on danuglipron. So the readout in obesity in the first half of next year is quite intriguing. How quickly thereafter, assuming it's positive, could a Phase III study in obesity alone generate results?

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

Very good question. By the way, I don't think that we ever expected the oral in Q3. I'm not sure if something like that was ever said. I think we were always expecting it in the Q4. And still, this is a very big chance that this will be the expectation. We give a range of Q4 to Q1 of next year. But still, this is the expectation that there's very highly chance that we will have it by the end of the year. Again, things are moving nicely in all 3 studies of the oral. But sometimes, you need to stop and wait for the data to speak for themselves. So that's our attitude. We are preparing for it. We are manufacturing. And we will be ready if, hopefully, the data are positive. Now about our obesity drug, Mikael, can you take this question?

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

Yes. Just wanted to echo what you said, Albert. We have 300 sites enrolling well across all the oral PI, and we have used this target base for the quite -- last periods. So we are on track and all looks well. We'll just wait for the readouts. Danuglipron in obesity, we optimize, obviously, for the titration, as I discussed, because that's important in order to deliver this quite encouraging data that has recently been seen with the GLP-1 class injectable. Some reports have shown much -- above 10% body weight with metabolic gains. So that's really the purpose, to get the right titration, stage titration. And this is a small molecule that we have developed manufacturing processes. So pending data and dialogue with regulators, I think this is a study that would progress quite fast to Phase III as the CMC is not complicated. And the drug class is very well known for regulators. It's just that this is an oral with an upside.

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 is on the oral antiviral for COVID. Just curious how much you think you can -- manufacturing? How much you can manufacture? What do you think about the durability of these sales? And then is there any first-mover advantage to getting on the market with this? And then my second question is just on CD47, quite a few in development. So how do you plan to differentiate your Trillium assets?

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

On the oral, as I said, we keep manufacturing. It depends on how much we will have already product available this year. And then, of course, as we are moving into next year, our manufacturing capacity is ramping up. The durability, I think, of this franchise is more or less an analog to the durability of the COVID vaccines as a franchise. Because as long as you have COVID around, you will have a need to vaccinate and protect. And then you will have a need to treat and save lives. And I think the durability, I expect to be -- given that COVID has been really across the globe and it is in so many parts of the globe. And I think we are speaking about the years, I think, of durability. But of course, that remains to be seen. That's only my assessment. Mikael, can you speak about the CD47?

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

Yes. No, that's a great question. We think there are several aspects of unique differentiation, and that's obviously why we were keen to work on the Trillium product. Number one, this is a ligand trap with an Fc fusion to provide longer half-life. So it has a lower binding to CD47 than a typical antibody. And it has shown both in preclinical studies and now in clinical studies that you do not get the problematic on-target anemia that you see with antibodies. So that's an important unique thing. It matters a lot, particularly for blood cancer patients, which already have a fragile bone marrow function, but also for potential solid cancers that are treated with various chemotherapy backbone.

Number two is this product is, to the best of my knowledge, the only one that have showed single-agent activity in blood cancers. And we have the most advanced data set coming out in lymphoid malignancies both related to B-cell malignancies, lymphomas and myelomas. And we see opportunities to combine it with several existing Pfizer assets to give us unique life cycle management. So several unique aspects. We look forward to see a potential deal closure and to work with the staff in Trillium to accelerate these exciting assets.

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

Thank you, Mikael. And Angela, I didn't ask if you have to add anything on the oral in terms of the durability of the revenues, other than what I said.

Angela Hwang - *Pfizer Inc. - Group President of Biopharmaceuticals Group*

Well, the market that we're looking at, we estimate to be about 150 million -- up to 150 million people. When we look at the -- just vaccination rates, infection rates, and then on the various risk groups that we talked about today, the high risk, the low risk as well as those who just may be in contact with those that are infected, this is the size of population that we're looking at. So I think that this opportunity will -- is a very attractive one. And I think that, again, the disease patterns will determine where we go with this. But certainly, it looks to be a durable opportunity as well. And also not to forget, this is probably something that governments would likely -- would be interested in stockpiling, right, like we saw in the flu. So I think that, that's an additional commercial opportunity to consider here.

Operator

Your next question comes from Matthew Harrison from Morgan Stanley.

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

I have 3, if you don't mind. So first one is, can you talk about the 2022 revenue for the COVID vaccine? And just give us some sense of what of that is primary series and what of that is boosters and just how you think about that developing over time?

Then second, on your flu data for your mRNA vaccine. Can you, I guess, comment, one, on if you've had any regulatory discussions and if you think you could get approved for just titer data alone or you need to run an actual efficacy study? And then secondly, what should we expect to see with that initial readout?

And then third, can you just detail what the protocol changes for hem A and what you think the underlying factors are that are driving those high levels of factor?

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

Thank you. The 2022 revenues are mostly from countries in the -- for COVID, that Frank spoke, this $29 billion that we have already signed, committed contracts of 1.7 billion doses. Those doses, when it comes to high-income countries, they are mainly boosters. When it comes to middle-income countries and to low-income countries, there is a mix of second doses, of primary doses, particularly second, because it will be given a lot this year for first and also some of them are boosters. This is why I said that the low- and middle-income countries, particularly the low-income countries where we do not -- we give it at cost, right, they need to place orders so that they can secure allocations of our quantities for their boosters. They need to think that. Now I will ask Mikael to speak a little bit about our regulatory discussions on the efficacy or not for flu and then why we are doing in HA the protocol changes. Mikael?

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

Yes. We are very intrigued by the use of mRNA for flu as it can generate both an antibody response against hemagglutinin and the T cell response that can be protective, particularly for more severe flu cases. The current flu vaccine, the protein-based, are not very potent on T cell responses and generate more intermediate level of antibodies. Whether you can register a product on those type of immune parameters is something we are, of course, considering. And as we generate data, we'll have dialogues with regulators. But it's, of course, advantageous not just to get approval, but to have a strong data set on an outcome such as vaccine efficacy. So the program will include both outcomes.

As always, you do non-inferiority of antibodies, and you may have additional immune parameters that do not exist very much with the traditional flu. But the entire program will, of course, look at vaccine efficacy to also take into account this broader immune response. But we'll obviously always keep our regulatory dialogues open for opportunities to serve patients as quick as possible.

On the protocol change to hem A, we saw that we had some patients that got very high levels of hem A yield therapy, 150%. We didn't see -- actually, we have not recorded any issues in the hemophilia patients with this. We want to just have abundance of caution to have a protocol that would allow active management. And of course, if there are any patients with some risk factors, they could easily use oral anticoagulants such as Eliquis. I want to just put this into context as we finalize the regulatory submission on this protocol update that having high Factor VIII level has also some potential longer-term advantage on sustainability of gene therapy. The Factor VIII data that you have seen also from others in the field have shown some more attenuation over time for the Factor VIII molecules. We have reported so far very good efficacy with no need for transfusion and no bleedings. But to be in the upper range where we are, on average, 60% to 70%, may be something that allows much longer gene therapy benefit than if you were on the lower end of the spectrum, particularly for Factor VIII patients. Thank you.

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

Thank you, Mikael. And also let me add in my previous answer when I said that for the high-income countries, it's predominantly boosters. Of course, there are also -- as vaccine rates are getting higher, they are primary doses. But also, I forgot to mention the pediatric. And the pediatric will be predominantly in the next year's revenues. Keep in mind that in Europe, Japan, all the international markets, all revenues of COVID that will be realized next month are going to the next financial year. And over there will be a lot of pediatric. Of course, in the U.S., we will have also some pediatric booked this year.

Operator

Your next question comes from Chris Schott from JPMorgan.

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

Just 2 for me. I guess first, coming back to the vaccine targets for '22. As we think about the doses beyond the 1.7 billion that you've now contracted for, is there still incremental sales opportunity in developed markets for next year? Or have most governments contracted already? I'm just trying to get a sense if we should be thinking about most of those doses, I think, as you mentioned in the call a few times, going to emerging markets and lower-priced geographies where the vaccines sold closer at cost. Or could there actually be some still higher kind of price per dose business to be had?

My second question on the vaccine is also just on the margin. Is that high 20% margin that we saw this year a reasonable assumption for next year given the R&D work going on, et cetera? And then just a final question was on the COVID PI. Just talk about that standard-risk trial when you're looking at both vaccinated and unvaccinated populations. Is that study powered to look at those populations separately if we were to see different outcomes in that readout as we think about later this year or next year?

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

Thank you. I'll start with Angela to answer about the COVID vaccines, remaining doses next year. And Frank, if you can give an answer on the margin. And then Mikael, the standard-risk study. Angela?

Angela Hwang - *Pfizer Inc. - Group President of Biopharmaceuticals Group*

Yes. Thanks for the question, Chris. No, we are not all done with the developed markets. Certainly, the contracts are in place and many of them are in place. But also, don't forget that many of these contracts have options attached to them. And those have not been -- those have not been realized. So I think that there is still opportunity in 2022 for the developed world to acquire additional doses.

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

Frank?

Frank A. D'Amelio - *Pfizer Inc. - CFO & Executive VP of Global Supply*

And then, Chris, on the IBT as a percentage of revenue for the COVID vaccines, remember that IBT as a percentage of revenue includes manufacturing and distribution, applicable royalty expense and then the gross profit split with BNT. So that gets you to, I'll call it, gross margin. And then we also include in that IBT percentage all of the R&D associated with COVID-related programs for both prevention and treatment and other mRNA-related programs. When you put all of that together, we've guided this year to IBT as a percentage of revenues in the high 20s. For next year, you should assume the same thing. And then obviously, we'll provide updated guidance on all of the P&L line items on our next earnings call when we close out Q4, provide guidance for 2022.

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

Mikael?

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

Yes. Thank you for your interest in the standard-risk oral PI trial. As I said, no other oral drug -- actually, the monoclonal antibodies are not used there either. So it's really a unique population, which we also recognize as we enroll the trial. It's enrolling now very well in that trial. And yes, we have secondary endpoints that we look at the 2 different groups. And I do think if the vaccine efficacy is what we hope -- sorry, the treatment efficacy is what we hope, that should be within our reach to get claims on both vaccinated breakthrough and all-comers that includes unvaccinated.

And as I said, it would be, to the best of my knowledge, the only trial on the standard risk that are not vaccinated. But it has this unique opportunity where antibodies are difficult to use in vaccinated, and there is no other oral running it. This is a growing population and in countries that may be late with re-vaccinations, of course, this is a really interesting drug profile.

Also for new variant, please remember, I didn't emphasize it that much, our oral PI today has shown robust activity against all variants of -- from Delta to Alpha variants, all variants we have tested. We believe it's going to be active against many different coronavirus. So Angela spoke about stockpiling. It also has a stockpiling opportunity for new things coming up in the coronavirus family even if they're quite remote from SARS-COV-2. So it's a really important drug for the world and fingers crossed as we look forward to readout.

Operator

Your next question comes from Geoffrey Porges from SVB Leerink.

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

A few quick questions. First, on Prevnar. Could you give us a sense of whether you believe Prevnar will return to growth next year? And have -- what is the supply that you expect to have in terms of number of doses for next year?

Secondly, on the question of overall guidance, it seems to me that next year should be another growth year for Pfizer given what you're saying about the many opportunities for both the COVID vaccine and the antiviral. I know you haven't given guidance, but can you give us a sense of whether that's your expectation as well?

And then lastly, on capital, it seems pretty clear that you'll almost be in a net positive cash position by the end of this year given the cash that's coming in for the COVID vaccine. There have been some suggestions that you might redeploy that capital into returning to the consumer business. Is that of any interest? Or are you going to maintain the focus on strictly innovative biopharma?

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

Angela, on Prevnar?

Angela Hwang - *Pfizer Inc. - Group President of Biopharmaceuticals Group*

As we think about the Prevnar adult revenues, I think we have to look at it at the different sort of age ranges. For the 65 plus, the opportunity will be obviously those who are aging and the newly 65s that are becoming every year as well as the opportunity, and we're waiting for -- we're actually waiting for the CDC and the MMWR to give us guidance as to whether those who have been previously vaccinated with PCV13 will be candidates for revaccination. So that's how we think about revenue on the 65 plus. And then in addition to that, one, what is completely new is the 18 to 64 age group. This is a whole new population. It is a large population. And this will be the other opportunities that we'll be looking to for PCV20 in '22 and beyond.

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

Yes. Jeff, look, on the guidance, first of all, this year, we have a record -- recorded record sales. And I'm very happy that you are predicting that last year, we may grow. We will provide guidance, as always, in the first month of the year in our fourth call earnings, which I think is late January.

As regards to capital allocation, Frank has spoken multiple times about our priorities in capital allocation. We are maintaining a growing dividend. That's very clear. And then our second priority is clearly to invest in the business, to invest in developing the business. And actually, I will turn to Aamir Malik, who this is his first call here, to speak a little bit about the opportunities in business development and how he sees them.

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

Thanks, Albert. Thanks, Geoffrey. We see business development, frankly, as a very important part of our strategy, and we plan to be very active in dealmaking. Specifically, we're going to be interested in compelling later-stage assets that can contribute positively to the top line growth in the back half of the decade. And we're also going to be interested in accessing medical breakthroughs that are in earlier stages of development. And we, frankly, see focusing in these areas as being much more value-creating than synergy-driven deals that require lots of resource-intensive integrations that can take a long time to complete. Obviously, we don't speak in absolutes, and we never say never. But right now, our focus will be, as I described, on compelling later-stage assets and earlier-stage medical breakthroughs in biopharma.

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

Thank you, Aamir. We are rightly -- as you can understand, we are very active, as we speak, in a lot of these discussions.

Operator

The next question comes from Andrew Baum from Citi.

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

A couple of questions. As you look at the competitive environment for oral antivirals for COVID, could you talk to how you're thinking about the probability of either your compound or the competitor having a REMS program. I know that ribavirin did at one point, but I don't think it has REMS now and your protease shouldn't demand one from a teratogenicity point of view. If you care to comment on the competitive outlook for those 2 drugs from a regulatory side, that would be interesting.

And then second, you've spoken previously, Angela, about the Xeljanz rebate providing sufficient ammunition against AbbVie to ensure that abrocitinib is not disadvantaged when you launch in securing positions on formulary. When I look at the totality of the rebate that AbbVie's products generate, it would seem to be a multiple of what Xeljanz does. So doesn't that still mean that you're potentially going to be disadvantaged as you seek to win share in the atopic dermatitis indication?

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

Andrew, thank you for, as always, very good questions. Angela, I will give both of them to you.

Angela Hwang - *Pfizer Inc. - Group President of Biopharmaceuticals Group*

Okay. So Andrew, I think on the abro one, as we have learned, and we've talked about this in the past as well, we're just in a really different place now. We have a tremendous number of contracts that we have in place. You see that in the gross to net when you look at Xeljanz. And our work with the various payers is continuing. And with all new products, when you launch, access and getting access is always a critical issue. And so we'll continue to do that as we have with all of our products for abro. Not to forget that obviously, the profile that we have, the value that we can bring to patients as well as organizations is a big part of what's going to help us to be able to get that access. So I think that we'll do what we've always done, and that access will build through time. And we believe that we do have a competitive profile that will allow us to play a role in this very, very big market. On your other question, which was related to the protease inhibitor, Andrew, do you mind just repeating that again?

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

I'm happy to say a few words that you were asking about the different profiles there of protease inhibitor and polymerase and how that could play out and the need for REMS. Well, as always, we are -- pending positive data, we are extremely experienced in pharmaco-vigilance programs, and we'll discuss with regulators what they see as appropriate. For the high-risk group, we'll have a 5-day study and there could be then options for polymerase or a protease inhibitor. And there could be an upside to even look at combination between those in the future.

For the standard risk, to the best of my knowledge, we are the only one that will be completing that study in the relative near term and actually the only one running it. And for the household exposure study, there, you are treating potentially healthy, uninfected individuals. And as a physician, I would just say that the protease inhibitor class has been -- and is known to be addressing a unique viral product and not really affecting the human cells.

So I would think it would be a very much preferred drug class if the profile comes out as we hope. Polymerase inhibitor, nucleoside based, you're always concerned in healthy individuals whether they could incorporate into the genome, whether their germ line or the mitochondria genome. So I would think that's something you need to keep in consideration. But that's why we were keen to be working on an oral PI because it has broad utility for SARS-CoV-2 future variants and future coronaviruses.

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

Thank you, Mikael.

Operator

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

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

I guess to start, I just wanted to come back to the 2022 guide. Can you first, I guess, clarify that, that 1.7 billion doses is inclusive of the 700 million that was sort of left over from 2021? And I guess sort of regardless, your 4 billion capacity far exceeds the doses you expect to deliver? I appreciate Frank's comments on the projected doses to be distributed will likely may and likely will evolve. But is it safe to assume you're done increasing capacity and/or '22 could be a peak on capacity? And then on the TL1A inhibitor, this is the first time I think we're hearing you guys talk about this kind of publicly, which presumably leads me to believe you have a better understanding of what drove the immunogenicity in TUSCANY or that you don't view the rate of ADAs as a problem or that you have confidence it will decrease with the subcu formulation. Any insight on this front? And then finally, still plan to hold that Analyst Day this year? Or has the thinking changed on that front?

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

All right. So many questions. So Angela, explain a little bit the 1.7 billion.

Angela Hwang - *Pfizer Inc. - Group President of Biopharmaceuticals Group*

Sure. I think the way to think about it is that the 1.7 billion doses that we talked about for '22 are those that we have line of sight for contracts for. And as Frank said, as contracts continue to be confirmed and finalized, we'll add to that. The spillover that you mentioned, which is the end of fiscal year but really not the end of calendar year, and so there is some -- there are some doses that were contracted for in 2021, but the revenue will be collected in 2022, so somewhere between December and January. So I think the way to think about it is just that we have to look at contracts as well as revenue recognition, and those are 2 slightly different things.

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

Frank, capacity?

Frank A. D'Amelio - *Pfizer Inc. - CFO & Executive VP of Global Supply*

So Carter, 3 billion doses this year, 4 billion doses next year. Quite frankly, I think as demand requires, we can continue to expand on our capacity. Just as an example, given some of the improvements we've made, when we first started making the other vaccine, it took us 110 days from, I'll call, start to vial ready. We've taken that 110 days down to 31 days, so over a 70% improvement in terms of the process. And quite frankly, I think we continue to make more improvements. So I don't think capacity is going to be a challenge for us. I think it's just a matter of our making sure we're meeting the demand that's being generated by patients and, obviously, by the contracts we generate and the like. But I don't see capacity as some sort of a constraining factor for us.

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

Well said, Mikael -- Frank. Mikael, TL1?

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

Yes. Thank you for -- Carter, for asking about TL1A. Yes, it's a novel member of the TNF superfamily. It actually had some genetic association with IBD, Crohn's disease and more severe Crohn's disease. We are, by far, the most advanced with a biological. And so far, we have not seen any meaningful impact of ADAs on activity of the drug in patients. So we think we'll be able to manage that. Of course, we're waiting for the final readout of the study. We think it could be a drug given conveniently subcutaneously. We are reporting data on a biomarker first, to my knowledge, to have a biomarker for selecting of high responders that captures the larger patient group.

And if you look at the efficacy in the biomarker group, it's really above where any other agents have reported so far, and that's what we want to report and reproduce in the extended study. And this TL1A is highly applicable, not only to Wilson's colitis but also to Crohn's. So that's another indication where we'll aim to go, which is supported also by genetic studies. So thank you very much for your interest in it and look forward to keep you updated as we generate more data and move on with this exciting program.

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

Thank you, Mikael. And Chris, maybe you answered the question about the analyst's -- I think there was an R&D day, I think, the question, right?

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

Sorry about that -- yes.

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

Yes. Sorry, that is our plan, correct.

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

All right. So you heard that. I think, Chris, that's the end of our call, right? So maybe I'll make just one closing comment. Clearly, we are very happy and very excited for, first of all, I'm proud for the impact that we had on global health and public health across the world with 150 countries receiving our vaccines, more than 1 billion people. We have touched their lives with our medicines and products. I think that's the record, not only for us, but for any pharmaceutical company so far. Also, that came with very strong financial rewards also. Our $80-plus billion of revenues that we will record this year likely sets a new record on the sales of any pharma, clearly for Pfizer. We are looking with lot a of optimism in the future because our pipeline is having very exciting projects that are moving very nicely. And we are utilizing our learnings in our development from COVID-19, so that we can accelerate even further and create new standards not only for us but for the industry. Thank you very much for your support, and I wish you a nice day.

Operator

Ladies and gentlemen, that concludes Pfizer's Third Quarter 2021 Earnings Conference Call. You may now disconnect.
