Q3 2021 Earnings Call

Company Participants

- Aamir Malik, Executive Vice President and Chief Business Innovation Officer
- Albert Bourla, Chairman and Chief Executive Officer
- Angela Hwang, Group President, Pfizer Biopharmaceuticals Group
- Christopher Stevo, Senior Vice President and Chief Investor Relations Officer
- Frank D'amelio, Chief Financial Officer and Executive Vice President, Global Supply
- Mikael Dolsten, Chief Scientific Officer and President, Worldwide Research, Development and Medical of Pfizer Inc.

Other Participants

- Andrew Baum, Analyst
- Carter Gould, Analyst
- Chris Schott, Analyst
- Geoffrey Porges, Analyst
- Louise Chen, Analyst
- Matthew Harrison, Analyst
- Ronny Gal, Analyst
- Steve Scala, Analyst
- Tim Anderson, Analyst
- Unidentified Participant
- Vamil Divan, Analyst

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 Stevo {BIO 2560339 <GO>}

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 in Medical; Angela Hwang, Group President, Pfizer Biopharmaceuticals Group; Aamir Malik, our Chief Business 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 {BIO 18495385 <GO>}

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 third quarter of 2020. When excluding direct sales and the 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 nine months of 2021, our innovative medicines and vaccines reached nearly a 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 US for children five years to 11 years of age, the first patient dosed in our large Phase 3 RENOIR study for our RSV bivalent vaccine candidate, and the initiation of Phase 2/3 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 US 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-income and low-income countries.

In addition, our weekly market share of COVID-19 vaccines administered continues to increase. In the US, 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 two-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 two examples. First, top-line results from our Phase 3 randomized, controlled trial demonstrated that a booster dose administered to individuals 16 years of age and older who previously received the Pfizer-BioNTech primary two-dose series restored vaccine protection against COVID-19 to the high levels achieved after the second dose.

Second, the US Food and Drug Administration has authorized our COVID-19 vaccine for emergency use for children five 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 two-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 US government exercised its final purchase option under the existing US supply agreement to purchase 50 million additional doses of Comirnaty. This brings the total number of pediatric doses purchased by the US government to 115 million, which is enough to vaccinate every US child. Overall, the US 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 US, 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 US 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 US. Revenues outside of the US 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 saw 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 US. The US 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 six biosimilars approved in the US 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 US 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. US 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 a 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 two 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 PPSV23 vaccination. This recommendation recognizes for the first time the significance of helping protect more population under age 65 with comorbid and immunocompromising conditions who are at increased risk of disease against these 20 disease-causing serotypes. This new one-dose regimen option, once endorsed by the CDC Director, also will help simplify long-standing adult pneumococcal recommendations. As a reminder, Prevnar 20 is the only vaccine the FDA has approved not only for invasive pneumococcal disease but also for pneumonia.

In September, I'm sure 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 content 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, its currently approved indication in the US, 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 a final US 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 UK Medicines and Healthcare products Regulatory Agency and the Japanese Ministry of Health, Labour and Welfare in both doses. It also received a positive opinion in adults from the European Medicines Agency's 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 US and Australia.

Overall, we remain confident in the importance of the JAK inhibitor class for appropriate patients with inflammatory diseases, and 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 2 development, to a new company formed in collaboration with a partner that has a proven track record in late-stage Inflammation & Immunology drug development. The new company will direct all future development decisions, while Pfizer will have a 25% stake and retain certain ex-US 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 into in recent years, spanning four 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 one to two 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's 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 Valvena 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 born out of our companies' 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, in

advanced prostate cancer and relugolix combination tablet in women's health in the US 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/SIRP-alpha 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 three approvals, four 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 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 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'll 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 {BIO 16368411 <GO>}

Thank you, Albert. I appreciate this chance to share updates on Pfizer's robust R&D pipeline.

As a measure of the transformation that we have 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 high rates in '21.

Today, I will provide updates from our Vaccines, Rare Disease, Inflammation and 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 programs. Of course, head-to-head clinical trials would be necessary to support any comparative claims.

Last Friday, the FDA granted Emergency Use Authorization for five through 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 five through 11 compared to 30-microgram dosing in 16 to 25 year olds. 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 adults. 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 two to less than five year olds this quarter, and in six months to less than two year olds next quarter, with full data readouts to follow.

On the right, we show improved handling conditions that have been approved for vials to dose five through 11 year olds. 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 3 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 two-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 two doses versus unvaccinated is above 55% at this time point. We observe consistent efficacy in younger and older idled while the majority of cases where in the olderage group as would be expected, we recorded a relative vaccine efficacy of 100% in individuals aged 16 years to 30 years.

Data from Israel, shown at the bottom and published by Professor Marc Lipsitch of Harvard and others in Lancet, showed that a 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 suggests that their vaccine may not be available in the near term for younger populations. 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 3 study evaluating Factor VIII gene therapy, which we're developing with Sangamo, in order to implement a 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 interactions with the FDA, Pfizer no longer plans to conduct the interim analysis of Phase 3 data from our Hem A and B gene therapy programs. We anticipate pivotal data readouts to be based on full analyses 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 trial compared to our previous expectation. For Hem A, we are working to evaluate the impact of both the FDA feedback as well as the protocol amendment on timelines, 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 1b DMD study, in which 19 ambulatory boys in the US have been treated, and plan to represent the one-year dataset at a scientific meeting.

We recently shared information on muscle weakness, presumed myositis, in some cases with myocarditis, in three participants in Phase 3 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 assessments performed in the trial support the hypothesis that an immune response against the mini-dystrophin protein caused these cases [ph].

This type of reaction is a risk potentially inherent for any gene replacement therapies, 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 exon 30.

A few sites have resumed new patient activities, and we anticipate that nearly all ex-US trial sites will have restarted clinical activity by the end of this month.

These mutations are estimated to represent less than 15%, 1-5, of 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 3 study, including technical aspects 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 one to two First-in-Human study starts each year.

We'll now turn to a high potency PDE4+ immune modulator we're exploring in atopic dermatitis and psoriasis. Topical delivered high potency PDE4+ inhibition may offer a differentiated efficacy and safety profile compared to other mechanisms 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 had been seen with PDE4 topicals in other trials. We expect to initiate Phase 2b 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 six. Our asset showed stronger or similar efficacy at week six as compared to reported data from another study at week eight with the recently approved topical JAK 1/2 inhibitor ruxolitinib. There was no stinging observed at the application site.

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 six.

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 2a 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 2b 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 matched the populations based on the characteristics of those enrolled in our TL1A study using propensity score matching. The week-14 data for tofacitinib is interpolated based on week-eight 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 were 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 2 clinical trial, we have observed significant reduction in clinical disease activity in skin compared to placebo. We anticipate the readout of the full Phase 2 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 share the design and preclinical profile of our novel investigational oral protease inhibitor, including its in vitro pan-coronavirus antiviral activity, in vivo efficacy, cell activity and preclinical safety profile.

A robust program to study the breadth of both treatment and prevention in high risk, standard risk and household contact populations 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. difficile 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 3 results for our RSV adult and maternal vaccine candidates, a potential pivotal Phase 2 readout for elranatamab in relapsed/refractory multiple myeloma, a proof of concept readout for our mRNA flu vaccine candidate, a phase 2b 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 3 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 D'amelio

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 and 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 business 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, this results in essentially the same number of selling

days in 2021 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've provided some additional subledger 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 $81.0 billion to $82.0 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 end-point, 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. (Technical Difficulty)

The $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 costs, 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 20's 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 and $2.65 for the year, which represents approximately 12% operational growth at the midpoint. These growth rates are all consistent with 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 you 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 three more selling days in the US and four 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 four fewer selling days each in domestic and international, eight 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 zero 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 a Q3 conference call, I wanted to make a brief comment related to potential Comirnaty sales next year as we have 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 of 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 nine 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 Stevo {BIO 2560339 <GO>}

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

Questions And Answers

Operator

Your first question comes from (Technical Difficulty) from Evercore.

Q - Unidentified Participant

Hi, guys. Thanks so much for taking my question. I have three 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 a longer-term booster usage. Do you expect the hospitalization efficacy to dip 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 two?

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 exon 13 or exon 29 to exon 30. I'm just trying to understand if there is 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. Thank you so much.

A - Albert Bourla {BIO 18495385 <GO>}

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

A - Mikael Dolsten {BIO 16368411 <GO>}

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 we have noted in our trials, and then you lose some protection but more staged 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, [ph] and even death. So, yes, there is just a shift in time and that's why we already now are preparing for re-vaccination 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 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 experience since from Tamiflu and other antiviral drug, that you are likely to get a good probability for even higher -- hopefully a very high antiviral effect.

On DMD gene therapy, we are 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 a 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 to wreck [ph] when they're given the full normal dystrophin transgene.

A - Albert Bourla {BIO 18495385 <GO>}

Thank you very much, Mikael. Let's go to the next question.

Operator

Your next question comes from Vamil Divan from Mizuho Securities.

Q - Vamil Divan {BIO 15748296 <GO>}

Great. Thank you so much for taking my questions. So maybe just a couple, if I could. So, one, I appreciate, Frank, the comment you made around 2022 in terms of the COVID vaccine sales. Can you maybe just 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 probably in '23, '24, '25.

And sort of connecting with that but maybe a broader question. About a year ago, you guys hosted an 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 patent expiration starting in 2026. At that point, you mentioned that the pipeline you felt was at least sufficient to replace that revenue stream. I'm curious, given 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. Thank you.

A - Albert Bourla {BIO 18495385 <GO>}

Yeah, thank you. Frank, if you want to take on this. And then also Angela, you can chime in on the revenue stream.

A - Frank D'amelio

Sure. Thanks, Albert. Hi, Vamil. So, Vamil, the way I would think about '22 is kind of a rhythm that is 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 for the COVID vaccine because of incremental contracts signed from one quarter to the next. We're using that same approach for around -- 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'll 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'll continue to be of 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.

A - Albert Bourla {BIO 18495385 <GO>}

Yes. Please, Angela.

A - Angela Hwang {BIO 20415694 <GO>}

Sure. Thank you. Maybe just one more add to that. Which 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 multi-year contracts. So, we already know that looking into '22 and 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 US sooner than the others because that's -- ex-US is where the multi-year 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 the 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.

A - Albert Bourla {BIO 18495385 <GO>}

Thank you, Angela. And what I will add in this question in addition to what Angela said, I will 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 will say is, as you've not just 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 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 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 who received and not-for-profit at the low-income countries were very severely discounted price for the middle-income countries, they need to place orders. That's including COVAX, and WHO and all of them. So, the 4 billion doses that we are going to produce, they are still highly negotiated by the high and upper-middle class countries. And I don't want to read [ph] the 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 regards the broader question of 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 the 6%. So when it comes to the 6% of all the year to after '25, we 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 are working, excluding COVID. So all of that is COVID vaccines. All of that I think are in a very, very good, let's say, state.

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 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 because the goal is to sustain the 6% growth of the second part of the decade as well if possible.

Thank you. Next question, please.

Operator

Your next question comes from Tim Anderson from Wolfe Research.

Q - Tim Anderson {BIO 3271630 <GO>}

Thank you. On the oral protease inhibitor is 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 2 programs in your pipeline versus this one where will 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? With that primarily be used in the study populations, which is really unvaccinated patients, or will it be used more broadly?

A - Albert Bourla {BIO 18495385 <GO>}

Yeah. Thank you very much. We are very bullish on the oral inhibitor. This is why earlier this year in during summer, I approved another billion-dollar investment at-risk, to start manufacturing at-risk. And of course, to start to run three studies in parallel; one for the high-risk population, one for the standard population, and one for the household, let's say, contacts population. 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 -- that 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 populations that 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 running. So just to make sure that there is no misunderstandings here, we are investing very heavily and 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 another 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 to Merck's product, they should be the ones to speak about it.

A - Mikael Dolsten {BIO 16368411 <GO>}

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 sometimes with polymerase inhibitors and require longer follow-up before you know about their potential impact. So that's why we think their 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 its results. Thank you.

A - Albert Bourla {BIO 18495385 <GO>}

Thank you, Mikael. Next question, please.

Operator

Your next question comes from Ronny Gal from Bernstein.

Q - Ronny Gal {BIO 15022045 <GO>}

Good morning, and thanks for taking m question. I have three, if I may. First, regarding your adalimumab biosimilar, you kind of noted the SWITCH trial has been successful. You've not commented specifically on filing for interchangeability. Can you clarify that point?

Second, it's kind of going across the wire there's some comments from DC about negotiating drug prices for 30 drugs by 2028 as part of the negotiated agreement. Is this something that the drug industry can live with or not, is this something you're objecting to, or is this something that within a great bargain they will settle drug prices with -- drug price legislation for the next three 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 a higher side effect profile for the efficacy delivered. Can you discuss what is your view here?

A - Albert Bourla {BIO 18495385 <GO>}

Thank you very much, Ronny. I will answer the drug pricing and Angela, I will pass you the biosimilar question and then 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, I've said multiple times, with drug pricing, but the issue is not the cost to the healthcare system. The issue it is the cost out-of-pocket for the patients that are taking their medicines. The cost of drug pricing to the overall healthcare system, it is 12%. So by definition, it cannot be the big problem. And this cost is going down. In the US in the first quarter, it was minus-5, in the second quarter was minus-5, in the third quarter is minus-5 in our audited numbers of Pfizer but -- in fact, of price. Problem is that none of our patients that are taking our medicines are experiencing minus-5 in what they pay, actually 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.

Not 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 is price-fixing. What they're suggesting as negotiation it is that we will be -- tell the price that 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. That, I think, is going to be a very big mistake to see that happening, and we are objecting.

But what I want to emphasize here is not if we're 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.

A - Angela Hwang {BIO 20415694 <GO>}

So for the biosimilar for adalimumab, we will have interchangeability studies and we're filing that in December 2021. (Multiple Speakers) Over to you, Mikael.

A - Albert Bourla {BIO 18495385 <GO>}

Thank you, Angela.

A - Mikael Dolsten {BIO 16368411 <GO>}

Yeah. 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 seen with oral-delivered peptide. 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 peptides. We'll later, next year, have an obesity readout. And the drug class 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 these 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. Thank you.

A - Albert Bourla {BIO 18495385 <GO>}

Thank you. Next question, please.

Operator

Your next question comes from Steve Scala from Cowen.

Q - Steve Scala {BIO 1505201 <GO>}

Thank you. A couple 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 3 study in obesity alone generate results? Thank you.

A - Albert Bourla {BIO 18495385 <GO>}

Thank you. Very good questions. 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'll give a range of Q4 to Q1 of next year, but still this is the expectation that it's very highly chance that we'll have it by the end of the year.

Again, things are moving nicely in all three 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?

A - Mikael Dolsten {BIO 16368411 <GO>}

Yeah. Just wanted to echo what you said, Albert. We have 300 sites, enrolling well cross all the ORAL PI, and we have used these target date 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 optimized 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 GLP-1 class injectable, and some reports have shown much above 10% body weight with metabolic gains. So that's really the purpose to get the right titration, staged titration. And this is a small molecule that we have developed manufacturing processes. So pending data and dialogues with regulators, I think this is a study that could progress quite fast to Phase 3 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.

A - Albert Bourla {BIO 18495385 <GO>}

Thank you. Next question, please.

Operator

Your next question comes from Louise Chen from Cantor.

Q - Louise Chen {BIO 6990156 <GO>}

Hi, thanks for taking my question. 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? Thank you.

A - Albert Bourla {BIO 18495385 <GO>}

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 analog to the durability of the vaccines 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're 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?

A - Mikael Dolsten {BIO 16368411 <GO>}

Yeah. 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-haul flights. So it has a lower binding to CD-47 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 who 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 datasets coming out in links with 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 lifecycle 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.

A - Albert Bourla {BIO 18495385 <GO>}

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.

A - Angela Hwang {BIO 20415694 <GO>}

Well, the market that we're looking at, we estimate to be about 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 Pfizer population that we're looking at. So, I think that this opportunity will allow -- 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.

(Multiple Speakers) 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.

A - Albert Bourla {BIO 18495385 <GO>}

Thank you. Thank you, Angela. Next question, please.

Operator

Your next question comes from Matthew Harrison from Morgan Stanley.

Q - Matthew Harrison {BIO 17603148 <GO>}

Great. Good morning. Thanks for taking the questions. I have three, 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 is -- 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? Thank you.

A - Albert Bourla {BIO 18495385 <GO>}

Thank you. The 2022 revenues are mostly from countries in the -- for COVID, that Frank spoke, this $29 billion that we have already in 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 the second because you 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, you might say, the protocol changes. Mikael?

A - Mikael Dolsten {BIO 16368411 <GO>}

Yeah. We are very intrigued by the use of mRNA for flu as it can generate both an antibody response against hemagglutinin and a 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 products 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 dataset 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 gene 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've 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 allow much longer gene therapy benefits than if you were on the lower end of the spectrum, particularly for Factor VIII patients. Thank you.

A - Albert Bourla {BIO 18495385 <GO>}

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, there are primary doses. But also I forgot to mention the pediatric, and pediatric will be predominantly in the next year's revenues. Keep in mind that in Europe, in 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 US, we will have also some pediatric booked this year.

So with that, next question, please.

Operator

Your next question comes from Chris Schott from J.P. Morgan.

Q - Chris Schott {BIO 6299911 <GO>}

Great, thanks so much. Just two from 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, and I guess you mentioned in the call a few times, going to emerging markets and lower-priced geographies where the vaccine is sold closer to 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. Can you 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? Thanks so much.

A - Albert Bourla {BIO 18495385 <GO>}

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

study. Angela?

A - Angela Hwang {BIO 20415694 <GO>}

Yeah. 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 realized. So, I think that there is still opportunity in 2022 for the developed world to acquire additional doses.

A - Albert Bourla {BIO 18495385 <GO>}

Frank?

A - Frank D'amelio

And then, Chris, on the IBT as a percentage of revenue for the COVID vaccines, remember that 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 20's. For next year, you should assume the same thing. And then obviously, we will provide updated guidance on all of the P&L line items on our next earnings call when we close out Q4 and provide guidance for 2022.

A - Albert Bourla {BIO 18495385 <GO>}

Mikael?

A - Mikael Dolsten {BIO 16368411 <GO>}

Yeah. 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 two 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 commerce that includes unvaccinated. And as I said, it will be, to the best of my knowledge, the only trial on standard risk that are not vaccinated, but it has this unique opportunity where antibodies are difficult to use in vaccinated and there's 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 it 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 corona family even if they're quite remote from SARS-CoV-2. So it's a real important drug for the world and fingers crossed as we look forward to readout.

A - Albert Bourla {BIO 18495385 <GO>}

Thank you, Mikael. Next question, please.

Operator

Your next question comes from Geoffrey Porges from SVB Leerink.

Q - Geoffrey Porges {BIO 3112036 <GO>}

Thank you very much. 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 will 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? Thanks.

A - Albert Bourla {BIO 18495385 <GO>}

Yeah. Angela, on Prevnar?

A - Angela Hwang {BIO 20415694 <GO>}

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 in, the newly 65 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 would be -- will be candidates for re-vaccinations. 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 adults. 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.

A - Albert Bourla {BIO 18495385 <GO>}

Yeah. Geoff, look, on the guidance -- first of all, this year we have a record recorded 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 regard the 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 opportunities in business development and how he sees them.

A - Aamir Malik {BIO 22440053 <GO>}

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 deal-making. 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.

A - Albert Bourla {BIO 18495385 <GO>}

Thank you, Aamir. And we are rightly, as you can understand, we are very active as we speak in a lot of these discussions. So next question, please.

Operator

Your next question comes from Andrew Baum from Citi.

Q - Andrew Baum {BIO 1540495 <GO>}

Thank you. 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 a 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 two 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 Avi [ph] 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 Avi's products generate, it would seem to be a multiple of what Xeljanz does. Doesn't that still mean that you're potentially going to be disadvantaged as you seek to win share in the atopic dermatitis indication? Many thanks.

A - Albert Bourla {BIO 18495385 <GO>}

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

A - Angela Hwang {BIO 20415694 <GO>}

Okay. So, Andrew, I think on 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 and -- is continuing. 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?

A - Albert Bourla {BIO 18495385 <GO>}

I think -- yes?

A - Mikael Dolsten {BIO 16368411 <GO>}

I'm happy to say a few words, you were asking about -- (Multiple Speakers)

A - Albert Bourla {BIO 18495385 <GO>}

Yeah. Okay, Mikael, please.

A - Mikael Dolsten {BIO 16368411 <GO>}

-- the different profiles there of protease inhibitor and polymerase and how that could play out and the need for REMS. Well, as always, we -- pending positive data, we are extremely experienced in pharmacovigilance programs and we'll discuss with regulators what they see as appropriate.

For the high-risk group, we have a five-day study and there could be then options for a 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 the germline or the mitochondrial 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 oral PI because it is broad utility post-SARS-CoV-2 future variants and future coronaviruses.

A - Albert Bourla {BIO 18495385 <GO>}

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

Operator

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

Q - Carter Gould {BIO 21330584 <GO>}

Great. Good morning. Thanks for squeezing us in. 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 to 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 (inaudible), or that you don't view the rate of ADA as the problem, or that you have confidence it will decrease with the subcu formulation. Any insight on this front?

And then finally, you still plan to hold that Analyst Day this year or has the thinking changed on that front? Thank you.

A - Albert Bourla {BIO 18495385 <GO>}

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

A - Angela Hwang {BIO 20415694 <GO>}

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 -- at 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 two slightly different things.

A - Albert Bourla {BIO 18495385 <GO>}

Frank, capacity?

A - Frank D'amelio

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, I'll give you some of the improvements we've made. When we first started making the vaccine, it took us 110 days from our call [ph] start to viral 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.

A - Albert Bourla {BIO 18495385 <GO>}

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

A - Mikael Dolsten {BIO 16368411 <GO>}

Yeah. Thank you, Carter, for asking about TL1A. Yeah, it's a novel member of the TNF superfamily. It actually had some genetic association with the 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 a 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 ulcerative colitis, but also to Crohn's. So that's another indication where we will 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 your updated as we generate more data and move on with this exciting program.

A - Albert Bourla {BIO 18495385 <GO>}

Thank you, Mikael. And Chris, maybe you answer the question about Analyst -- I think there was an R&D Day, I think, the question, right?

A - Mikael Dolsten {BIO 16368411 <GO>}

Sorry about (Multiple Speakers) -- Yeah.

A - Christopher Stevo {BIO 2560339 <GO>}

Yeah, sorry. That is our plan, correct.

A - Albert Bourla {BIO 18495385 <GO>}

All right, so you heard that. I think, Chris, that's the end of our call, right? (Multiple Speakers) Maybe I'll make just one closing comment. Clearly, we are very happy and very excited for, first of all -- and proud for the impact that we had on global health, on public health across the world with 150 countries receiving our vaccines, more than a billion people who 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 from the sales of any pharma, clearly for Pfizer.

We are looking with a lot of optimism the future because our pipeline is having very exciting projects that are moving very nicely. And we're 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.
