OVERVIEW:
PFE reported 1Q22 YoverY revenue growth of 82%. Expects 2022 total Co. revenue to be $98-102b and adjusted diluted EPS to be $6.25-6.45.
Operator

Good day, everyone, and welcome to Pfizer’s First Quarter 2022 Earnings Conference Call. Today’s call is being recorded. At this time, I would like to turn the call over to 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, operator. Good morning. Welcome to Pfizer’s first quarter earnings call. I’m joined today by Dr. Albert Bourla, our Chairman and CEO; Frank D’Amelio, our CFO; and Mikael Dolsten, President of Worldwide Research and Development and Medical. Joining us for the Q&A session, we will also have Angela Hwang, Group President, Pfizer Biopharmaceuticals Group; Aamir Malik, our Chief Business and Innovation Officer; Doug Lankler, our General Counsel; and William Pao, our new Chief Development Officer.
The materials for this call and other earnings-related materials are on the Investor Relations section of pfizer.com. Please see our forward-looking statements disclaimer on Slide 3 and additional information regarding these statements and our non-GAAP financial measures is available in our earnings release and in our SEC Forms 10-K and 10-Q under Risk Factors and Forward-Looking Statements. Forward-looking statements on the call are subject to substantial risks and uncertainties, speak only as of the call’s original date, and we undertake no obligation to update or revise any of the statements. With that, I will turn the call over to Albert.

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

Thank you, Chris, and good morning, everyone. Pfizer had a solid start to the year. Revenues were up 82% operationally compared with the first quarter of 2021. Key growth drivers for the quarter included COMIRNATY, PAXLOVID, Eliquis, VYNDACEL/VYNDAMAX globally, our Prevnar family of vaccines and our oncology biosimilars portfolio in the U.S. Overall, we reached an estimated 468 million patients around the world only in 1 quarter with our innovative medicines and vaccines, which represent a 140% increase from the prior year quarter, and it is a testament to our purpose, breakthroughs that change patients’ lives.

We continue to supply the world with COMIRNATY, which remains a critical tool in helping prevent severe illness, hospitalization and deaths from COVID-19. Today, we have shipped nearly 3.4 billion doses of our vaccine to 179 countries. COMIRNATY is the most utilized mRNA vaccine in the markets in which we operate and that report market share. Pfizer’s cumulative share of doses administered in these markets has increased in fact from 52% that used to be on January 1, beginning of the year 2022, to 62% on May 1, 2022. Just a few months, 10 points. In developed markets, our share has increased from 59% to 67% over that same period of time.

We also have had a strong start to the year with regard to regulatory milestones, including the Emergency Use Authorization from the U.S. FDA and Conditional Market Authorization from EMA for our 12- to 15-year old booster dose. We had an EUA from the FDA for a second booster fourth dose in patients 50 years of age and older and 12 years of age and older who are immunocompromised. And we had an extension to a 12-month frozen shelf-life label 12 months from both the FDA and the EMA. Our ambition is to eventually achieve a 24-month shelf life, which would help alleviate concerns that some governments may have about having expiring doses in stock.

In addition to the U.S. and the EU, we now have authorizations for the 5 to 11 age group in 44 other markets around the world. In addition, we have recently released new results from a Phase 2/3 clinical trial, demonstrating that the 10-microgram booster dose of our vaccine in healthy children 5 to 11 years of age increases geometric mean neutralizing antibody titer -- geometric mean neutralizing antibody titers, wild-type and Omicron variants. Based on this data, last week, we submitted an application to the FDA for an EUA of a 10-microgram booster dose for children in this age group, and we look forward to filing in other jurisdictions in the near future.

We also expect to share data on our ongoing study in children who are 6 months to under 5 years of age in the next few weeks. This study is looking at the safety and efficacy of 3 doses of the vaccine in this age group, and we hope to submit an application for an EUA soon, pending the results of the data readout, of course. Last, we stand ready to support boosting authorized populations today as well as in the fall ahead of the traditional flu season. Independent real-world evidence from several countries have demonstrated that our booster doses improve protection that may have waned from the primary vaccination or since the first booster.

Our market research shows that greater than 96% of health care provider respondents in key markets like the U.S. and the EU5 largest markets, continue to recommend a third dose booster to their patients. We also have seen an upward trend in uptake of a third dose booster in various developed markets. In these same markets that I referred previously, 74% of people who have received the initial 2-dose regimen reported that they have all already received third dose booster. And the remaining 13% of the respondents said that they are very likely to receive a booster. We believe this is an encouraging leading indicator for the potential uptake of a fourth dose. We also continue to evaluate potential next-generation vaccines, including variant vaccines to provide broad coverage for the fall, and we look forward to evaluating and sharing these data in the coming months.

We are also delivering on our commitments for PAXLOVID, which is already having a profoundly positive impact on the lives of patients around the world. Through the end of March, we produced more than 6 million treatment courses, all of which have been shipped shortly after they were produced. Because the financial calendar quarter for international markets ends in February and the majority of these 6 million treatments were...
produced in March, only a small portion of these shipments were recorded in our first quarter revenues. In fact, as of today, we have shipped approximately 8 million treatment courses.

Our manufacturing ramp-up is progressing as planned, and we are on track to produce 24 million courses in the second quarter for a total of 30 million in the first half of the year. All of these quantities have already been allocated to existing orders. In addition, we remain on track to produce 120 million courses for the full year, as previously stated. To date, PAXLOVID has received regulatory approvals for temporary authorization for use with certain populations in more than 60 countries. We continue to have discussions with governments and regulatory agencies around the world about bringing this potential breakthrough treatment to additional markets.

Some countries that have experienced recent outbreaks have come back to us to request additional treatment courses, which we are responding to with urgency. Others are taking steps to expand access. For example, the Italian government recently announced an expansion of prescribing into primary care. We believe this shift from having only specialists prescribe PAXLOVID will help ensure more patients get access at the right time.

In the U.K. PAXLOVID will now be included in the National Panoramic Study, which we expect will increase access and collect further data regarding how the therapy works in a market where the majority of the adult population is vaccinated. This is important because, to date, the U.K. has restricted PAXLOVID use to a very limited populace. And this study could lead the government to open up access to a much broader population closer to the authorized populations.

In Canada, we expect increasing supply and the lifting of COVID-19 restrictions will enable greater access for patients across the country. Quebec and Ontario, which represent the 2 largest provinces and are home to more than 60% of Canada’s population, have expanded distribution to eligible pharmacies, allowed pharmacists to prescribe and started a comprehensive direct-to-consumer and social media campaign to ensure all eligible patients are aware of the availability of PAXLOVID.

Here in the U.S., we have seen PAXLOVID utilization grow nearly 10-fold in recent weeks. PAXLOVID was administered to more than 79,000 patients in the U.S. the week ending April 22, 2022, up from approximately 8,000 patients for the week ending February 25, 2022. We will continue to work with the U.S. government and health care providers to appropriately drive even higher utilization. And based on data from IQVIA Xponent, PAXLOVID market share relative to molnupiravir in the retail long-term care and mail order channels grew from 44% in the week ending January 28, 2022, to almost 90% in the week ending April 22, 2022. Together, these channels represent an estimated 50% of PAXLOVID utilization in the U.S.

The number of locations in the U.S. with PAXLOVID supply continues to increase with more than 33,000 sites live as of today. This is more than a fourfold increase since late February, leading to easier patient access. The U.S. government declared its intention to double the size again in the coming weeks and making PAXLOVID available to any pharmacy who wishes to stock.

In addition, 77% of recent U.S. COVID-19 cases occurred within 5 miles of the closest retail point of care, which is up from only 23% since February. We expect this trend to continue to increase, driven by the U.S. government’s Test to Treat initiative. For example, nearly 1,100 more Test to Treat locations have been added since the beginning of April on. Today, there are more than 2,200 locations of Test to Treat open. Overall, we expect the recent trends to expand access as well as inquiries received from governments as the virus mutates and cause spikes in infections around the world to result in increased orders in the coming months as governments continue to help protect their citizens who are at high risk of severe disease, hospitalization and death in response to emerging variants and continuing outbreaks.

Now I will turn to our business development strategy. We leverage business development opportunities to advance our business strategies and objectives. We recently announced positive top line results from a year-long Phase 3 trial of etrasimod in moderately to severely active ulcerative colitis. These results underscore Pfizer’s ability to identify strong business development targets as this potentially best-in-class drug candidate came to us via our recent acquisition of Arena. We look forward to presenting this data and filing for approval later this year.

First quarter, we discussed how the strength of our balance sheet and cash flows gives us the ability to pursue new business development opportunities that, if successful, could add at least $25 billion of risk-adjusted revenues to our 2030 top line expectations. Our planned acquisition of ReViral is the first deal to be counted towards this ambition. ReViral is a privately-held clinical stage biopharmaceutical company focused on
discovering, developing and commercializing novel antiviral therapeutics that target respiratory syncytial virus. Basically, they target RSV. We believe annual revenue from these programs, if successful, has the potential to reach or exceed $1.5 billion. This is peak revenues.

We also are excited about the prospect of adding several experienced virologists to our team. Building relationship within the growing biotech ecosystem remains a priority for Pfizer. We continue to pursue new creative ways of partnering with biotechs to increase our access to cutting-edge innovation and to bring our resources to help drive for patients. We believe our scientific expertise, our end-to-end development and manufacturing capabilities makes us an extremely attractive partner. I see, for example, through our relationship with BioNTech, and we are confident that we have the financial resources to support business development opportunities that will complement and enhance our internal R&D efforts and add capacity and flexibility to support our growing clinical portfolio.

Next, I would like to discuss some of our recent ESG highlights. First, we announced in February the results of Pfizer’s third annual pay equity study in which a recognized compensation expert confirmed equitable pay practices for employees at Pfizer. The results indicated that Pfizer compensates female colleagues at a level that it is greater than 99% of what male colleagues are paid across the globe. Additionally, in the U.S., minorities are paid at dollar-for-dollar parity of what non-minorities are paid.

When you look at Pfizer’s median pay for women globally, it is in high 102.3% for the median pay of males. However, when you look at the median pay for minorities in the U.S. workforce, it is 85.5% of the median pay for our non-minorities. This median rate pay gap is an area we are actively addressing and that we expect to narrow.

Second, I want to reiterate that Pfizer stands with a unified global community in opposition to Russia’s invasion to Ukraine. While Pfizer is maintaining our supply of medicine to Russians, as we should, we will be donating all profits of our Russian subsidiary to causes that provide direct humanitarian support to the people of Ukraine. Additionally, we will no longer initiate new clinical trials in Russia and will stop recruiting new patients in our ongoing clinical trials in the country.

Pfizer will work with the FDA and other regulators to transition all ongoing clinical trials to alternative sites outside Russia. And consistent with our commitment to putting patients first, we will continue providing needed medicines to the patients already enrolled in clinical trials in Russia. Lastly, we are ceasing all future investments with local suppliers intended to build manufacturing capacity in Russia.

Third, further demonstrating our commitment to equitable access, we have made the decision that for as long as the pandemic lasts, Pfizer will not profit from sales of our COVID-19 treatment to the world’s poorest countries. In March, Pfizer announced an agreement with UNICEF to supply up to 4 million treatment courses of PAXLOVID to 95 low- and middle-income countries. Under the agreement, all low and lower middle-income countries will be offered the treatment courses at a not-for-profit price, while upper middle-income countries will pay a price defined in Pfizer’s tiered pricing approach.

Lastly, I’m pleased to share that Pfizer continues to be recognized as an ethical patient-focused company that calls itself in its employees and its business partners to high standards. In March, Pfizer was recognized as one of the world’s most ethical companies by Ethisphere, a global leader in defining and advancing the standards of ethical business practices. And just last week, and we are so proud about it, for the first time ever, Pfizer ranked first among big pharma companies in the PatientView Global Survey in 2021. This ranking is based on feedback from more than 2,000 patient organizations and associations worldwide. As recently as 2018, we were ranked fifth, and we have steadily climbed in the rankings ever since but we are so proud that we are #1 right now.

Now I would like to welcome 2 new members of Pfizer’s Executive Leadership Team. Dr. William Pao joined us on March 21 as Executive Vice President and Chief Development Officer. Throughout his 25-year career as an oncologist and scientist, William has amassed extensive clinical and deep scientific expertise that make him the ideal partner to continue our pursuit in breakthrough medicines and vaccines for the benefit of patients and society.

Just yesterday, David Denton joined us as Chief Financial Officer and Executive Vice President. Dave brings with him more than 25 years of finance and operational expertise, including more than 20 years in the health care sector. As a result, he brings to Pfizer a unique perspective on the role
of payers, the needs of patients and the rapidly evolving health care landscape. We are thrilled to welcome these 2 highly effective and visionary leaders at this critical time for our company in global health.

And now before I hand it over to Mikael, I want to take a moment to thank Frank D’Amelio, my best friend in Pfizer, for his many contributions to Pfizer. In addition to helping ensure Pfizer’s financial strength and discipline, Frank has been an incredible mentor to many of Pfizer’s current leaders, helped shape our long-term growth strategy and worked tirelessly to ensure Pfizer has the resources it needs to help improve the lives of patients around the world. Frank, on behalf of all Pfizer colleagues and I’m sure all the analysts on today’s call and not only, I wish you continued good health and success.

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

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

Thank you, Albert. I’d like to start by highlighting 2 recent external acknowledgment of Pfizer’s R&D turnaround. Pfizer was ranked first for innovation in the 11th Annual Pharmaceutical Innovation and Invention Index and first for what Forbes termed Total R&D Productivity over 20 Years in a paper published in by Discovery today. This is a testament not only to the work of our scientists over the past year but our purposeful efforts to improve our R&D engine over the past 10 years.

Today, I will share updates on COVID-19, inflammation and immunology, RSV, oncology, Lyme disease and hemophilia. In some cases, I may reference publicly available data on other agents so that you can understand our enthusiasm about what we’re seeing in our development programs. Of course, head-to-head clinical trials would be necessary to support any comparative claims.

We continue to pursue a comprehensive and data-driven clinical strategy for COMIRNATY, focused on evaluating real-world vaccine effectiveness, demonstrating higher immunogenicity with boosters, expanding access to pediatric population and addressing emerging variants of concern. On the left, in the Phase 2/3 trial of COMIRNATY administered to children age 5 to 11, we have shown that the third 10-microgram dose demonstrated a sixfold boost in utilizing wild-type SARS-CoV-2 and a 36-fold boost neutralizing the Omicron variant. Last week, we submitted an EUA request to the FDA for a third-dose boost in this population.

On the right, we show that the third 30-microgram dose administered for adults in the landmark clinical trial effectively neutralized the Omicron sublineages, including BA.2 1 month after dose 3. We have also now received EUA for a second booster in people aged 50 and older and for individuals 12 years of age and older who have certain kinds of immunocompromise. This expanded authorization was based on data from Israel, generated while the Omicron variant was dominant, an approximately 11-fold increase in geometric mean neutralizing antibody titers against wild-type virus, Delta and Omicron variants, respectively, were reported at 2 weeks after the second booster as compared to 5 months after the first booster.

Here, we show recently published real-world data from Israel that the fourth dose of COMIRNATY lowered rates of hospitalization, severe illness and death amidst the Omicron outbreak. A fourth dose is now recommended for certain high-risk populations in more than 15 countries. There’s been a notable increase in the number of pediatric infections and hospitalizations in the last few weeks. And we recognize that the parents of younger children and health care providers have been waiting for an effective vaccine. We have been working with urgency to generate data.

We began the rolling submissions for EUA in children aged 6 months to 4 years in February, while continuing to evaluate the third 3-microgram dose, which may be optimal to deliver high degree of protection against Omicron. We expect to analyze and submit the 3-dose data by late May, early June and anticipate both FDA and CDC Advisory Committees to meet soon after to consider the submission.

Turning to PAXLOVID. Following EUA in December for both high-risk adults and high-risk children 12 and older weighing at least 40 kilograms, we expect to file soon and anticipate an FDA decision on the New Drug Application in these populations in the second half of ’22. Recently, the WHO strongly recommended PAXLOVID for people with mild-to-moderate COVID-19 who are at the highest risk of hospitalization because they’re
unvaccinated, older or immunocompromised. We expect pivotal readouts of the standard risk study in the second half of ’22 and reported top line results from the household contact prophylaxis study last week.

In March, we initiated a study in children and expect to have data in the second quarter of ’23. We are first enrolling children aged 6 to 17 years and working to develop an age-appropriate formulation for children younger than 6. A new study in immunocompromised patients is planned to start in the second half of ’22. Some immunocompromised patients were enrolled in the EPIC-HR study. However, given the high unmet need, we believe EPIC-IC will allow us to further evaluate PAXLOVID’s efficacy in this population and ensure the treatment duration is optimized, given their more limited natural immune response to help clear infection.

With the close of the Arena acquisition in March, I’d like to highlight the potential for etrasimod as a best-in-class oral medicine for ulcerative colitis and its strategic fit within our overall inflammation and immunology pipeline. First, etrasimod is differentiated. It’s a once-daily pill with rapid onset, no anticipated required titration and a promising benefit-risk profile. In the Phase 3 ELEVATE studies, etrasimod demonstrated robust clinical remission in patients with moderate-to-severe active ulcerative colitis. In March, we reported that the ELEVATE UC 52 trial met the co-primary endpoints of clinical remission at both weeks 12 and 52 and all key secondary endpoints.

Looking at the totality of data across Phase 2 and Phase 3 studies, we see a 12-week remission rate of 25% to 30% compared to placebo at 6% to 15%. We are projecting a filing in ulcerative colitis in the second half of ’22. This candidate also has broad potential beyond UC. The adaptive Phase 2/3 study in Crohn’s disease is ongoing, and we expect to start Phase 3 in atopic dermatitis in the fourth quarter. The potential expansion into Crohn’s and eosinophilic esophagitis strengthen our gastroenterology pipeline. Overall, given that immuno-inflammatory diseases have heterogeneous disease drivers which require multiple options for effective treatment and the continuing significant unmet need of patients in achieving long-term remission, we are excited about the portfolio of diverse and promising candidates from Arena that nicely complement our existing I&I pipeline.

Ritlecitinib is our unique cytokine modulator. It’s a potent family inhibitor which spares IL-10 protective cytokines and spares dominant activity of existing effective oral agents. We have seen promising Phase 2 efficacy demonstrated across alopecia, vitiligo and ulcerative colitis. The Phase 2 study in Crohn’s disease is ongoing. Ritlecitinib received FDA Breakthrough Designation for alopecia and we expect to file in the second quarter. We are finalizing potential Phase 3 study protocols for vitiligo and exploring paths for ulcerative colitis.

In Phase 2b, ritlecitinib demonstrated robust efficacy in both facial and total Vitiligo Area Severity Indexes, or VASI. Here, we showed a facial VASI improvement. On the left, ritlecitinib demonstrated up to 66% improvement from baseline through week 48. Efficacy was observed across light and dark skin types. On the right, you see 2 visual representations for significant improvement in facial VASI at 48 weeks.

Last month, we announced our intent to acquire ReViral and its respiratory syncytial virus therapeutic candidates. RSV remains a significant unmet need globally with no approved treatment, and the proposed acquisition will strengthen our capability in infectious disease R&D with a complementary strategy to help improve patient outcomes through treatment and prevent illness through vaccination. This mirrors our COVID-19 strategy, establishing leadership across vaccines and therapeutics for RSV to deliver potential breakthroughs.

Our RSV candidate elicited high RSV A and B neutralizing titers in preclinical animal models and in Phase 1/2 clinical studies and has received FDA Breakthrough Designation for the maternal and adult programs. We anticipate total readouts of the maternal and adult studies in the second half of ’22. ReViral’s pipeline include a lead candidate, sisunatovir, which has received Fast Track Designation and the second program focused on the inhibition of RSV replication targeting the viral N protein.

Sisunatovir is an orally administered inhibitor designed to block fusion of the RSV virus to the host cell. In our Phase 2 health adult challenge study, sisunatovir significantly reduced viral load. The data are shown on the right. There’s also an ongoing 3-part adaptive Phase 2 study in hospitalized infants. Successful completion of Part A was achieved in June ’21 with favorable safety and pharmacokinetics. Part B is ongoing.

We now turn to oncology and encouraging data on the Phase 3 trial of LORBRENA. 3-year follow-up data presented at AACR confirmed prolonged progression-free survival in first-line ALK-positive non-small cell lung cancer patients. There was a 73% reduction in risk of disease progression of test versus cristotinib. The 3-year PFS rate in the LORBRENA arm was 63.5%. 3-year rates for second-generation medicines are generally 20% points
Revenue increased 82% operationally in the first quarter of 2022, driven by COVID-19 vaccine and PAXLOVID sales and strong performance for a number of our other key growth drivers. And looking at the revenue excluding the COVID-19 vaccine direct sales and alliance revenues and PAXLOVID contribution, it increased by 2% operationally. The effect of fewer selling days year-over-year decreased revenues by about 1%, and losses of exclusivity negatively impacted revenues by 2%. Operational growth would have been approximately 5% without these.

Now I’d like to highlight our robust portfolio of investigational therapies to potentially treat all people with hemophilia. We expect a number of clinical trials for our hemophilia portfolio to read out in ’23. Marstacimab is our novel nonfactor treatment candidate with the potential to address a broad patient population. As a new subcutaneous prophylactic treatment for patients with hemophilia A or B, including those with inhibitors, we anticipate the pivotal readout in second quarter ’23. Marstacimab has FDA Fast Track designation for heme A and B patients with inhibitors. If successful, we predict submitting for the non-inhibitor indication in both heme A and B in the third quarter of ’23.

Turning to our gene therapy candidates. Last year, at ASH, we presented updated Phase 1b/2 data from the largest cohort of persons with hemophilia B, who have had at least 3 years of follow-up with AAV gene therapy. 93% of participants achieved Factor IX activity in the mild or normal range between 3 to 5.5 years of follow-up. We expect a pivotal readout in the first quarter of ’23. In heme A, we also presented updated Phase 1b data at ASH. Factor VIII activity was 25% of normal after 2 years in the highest dose cohort. The FDA has lifted a clinical hold on our Phase 3 pivotal study, and we anticipate study resumption in the third quarter of this year with a pivotal readout estimated in the second half of ’23.

Finally, here are the top 25 key milestones achieved and anticipated for the rest of the year, 6 in the regulatory space, 12 pivot to readout and 7 early-stage readouts. I’d also note that last week, we announced the planned opening of the first U.S. sites in our Phase 3 trial evaluating our investigational mini-dystrophin gene therapy for ambulatory patients with Duchenne’s muscular dystrophy. The trial also has received regulatory approvals to restart in several other countries. Pending regulatory feedback, we anticipate that nearly all sites will open by the end of June.

In addition, the European Medicines Agency’s Committee for Medicinal Products for Human Use granted Prime Designation for GBS6, our maternal vaccine candidate against streptococcal infection. It’s currently being evaluated in an ongoing Phase 2 study. Thank you for your attention and I look forward to your questions. Now let me turn it over to Frank.

Frank D’Amelio - Pfizer Inc. - Chief Financial Officer, Executive VP

Thanks, Mikael. I know you’ve seen our release so let me provide a few brief highlights regarding the financials. Turning to the income statement. Revenue increased 82% operationally in the first quarter of 2022, driven by COVID-19 vaccine and PAXLOVID sales and strong performance for a number of our other key growth drivers. And looking at the revenue excluding the COVID-19 vaccine direct sales and alliance revenues and PAXLOVID contribution, it increased by 2% operationally. The effect of fewer selling days year-over-year decreased revenues by about 1%, and losses of exclusivity negatively impacted revenues by 2%. Operational growth would have been approximately 5% without these. Also, please...
remember that Q1 2021 grew 8% operationally, excluding COMIRNATY versus the prior year quarter, resulting in a very difficult comparable. This was broadly as expected and is embedded in our current guidance.

The Adjusted cost of sales increase shown here reduced this quarter’s gross margin by approximately 10 percentage points as compared to the first quarter of 2021, with 14 percentage points attributable to the impact of higher COVID-19 vaccine sales year-over-year, partially mitigated by an unfavorable product mix for other products, primarily driven by higher sales of PAXLOVID and higher alliance revenues.

Adjusted S&A expenses in the first quarter decreased primarily due to lower spending on corporate-enabling functions, partially offset by increased spending for COMIRNATY and PAXLOVID. The increase in Adjusted R&D expense this quarter was primarily driven by increased investments in multiple late-stage clinical programs as well as additional spending on programs to prevent and treat COVID-19. The growth rate for reported diluted EPS was 59% while Adjusted diluted EPS grew 76% operationally for the quarter. Foreign exchange movements resulted in a negative 5% impact to revenue as well as a negative 4% impact or $0.04 to Adjusted diluted EPS.

Now let’s move to our updated 2022 guidance. We expect total company revenue to be in a range of $98 billion to $102 billion, representing an operational growth rate of 27% at the midpoint. The revenue range absorbs an additional $2 billion of anticipated negative impact from changes in foreign exchange rates as the U.S. dollar continued to strengthen against other currencies since we last updated our exchange rate assumptions.

Regarding our COVID-19-related revenues, we continue to expect the vaccine revenue for the year to be approximately $32 billion, unchanged compared to our prior guidance provided on February 8, despite the impact of $1 billion of incremental negative foreign exchange. For PAXLOVID, we expect sales of approximately $22 billion, keeping the guidance unchanged despite an incremental $500 million headwind due to foreign exchange. This means that excluding the COVID-19-related revenues, we expect sales to be approximately $46 billion at the midpoint, representing operational growth of 5% and absorbing the increased negative impact of about $500 million for foreign exchange. While this is slightly below the 6% CAGR that we continue to expect between 2020 and 2025, we continue to be confident in our ability to achieve that 2025 target.

Now let me give some detail on our cost and expense guidance. We slightly improved our guidance for Adjusted cost of sales, reducing the entire range by 20 basis points, the new range being 32% to 34%. We’ve separated the former R&D line into 2, R&D and a new line for acquired IP R&D to isolate the IP R&D charges, which are driven by business development transactions.

Our guidance includes $900 million of this expense for 2022 based on business development transactions which have either already closed or are already signed as of mid-April, of which only $100 million was previously assumed and our R&D guidance for adjusted results. We will not forecast acquired R&D for transactions which are not closed or signed. We’ve also increased our Adjusted R&D expense guidance by $500 million to reflect incremental life cycle spending for COVID-19 vaccines and antivirals and investments in other projects.

In addition, as noted with fourth quarter results, we’ve made a decision to modify our adjusted results treatment of amortization of intangibles. Previously, we only excluded amortization related to large mergers and acquisitions, but we will now exclude all intangible asset amortization expense. This is anticipated to contribute $0.06 to our 2022 Adjusted diluted earnings per share and improves comparability with our peers. This $0.06 was previously included in our 2022 guidance.

These assumptions yield an Adjusted diluted EPS range of $6.25 to $6.45 or 61% operational growth at the midpoint compared to 2021. This updated EPS guidance includes a $0.10 operational improvement, offset by a negative $0.11 due to foreign exchange and another $0.11 due to IP R&D. Together, these impacts led out to an Adjusted EPS range, which is $0.10 lower than our initial guidance. 2022 guidance once again assumes no incremental share repurchases beyond the $2 billion of share repurchases we completed in March. Going forward, we will continue to be prudent in our capital allocation activities with the opportunities for deployment shown here on this slide.

So before I turn the call back to Chris to start the Q&A session, I wanted to make a personal comment. This conference call will mark my last as Pfizer’s CFO, and I wish Dave and Pfizer all the success in the world. It has been my immense pleasure and privilege to serve as Pfizer’s CFO for nearly 15 years. I’ve always enjoyed my interactions with you, our investors and our analysts and I will miss it. To my Pfizer colleagues, I am so proud of what we have accomplished together. I look forward to you achieving yet more success in the future. And as a large Pfizer shareholder, you can be sure that I’ll be watching. With that, let me turn it over to Chris for Q&A.
Christopher J. Stevo - Pfizer Inc. - Senior VP & Chief IR Officer

Thanks, Frank. With that, let's start the Q&A session. We will answer as many questions as time permits. And as always, Investor Relations will be available after the call to answer any questions you weren't able to ask. Operator, first question, please.

QUESTIONS AND ANSWERS

Operator

Your first question comes from the line of Louise Chen with Cantor.

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

Frank, thank you for all your contributions to Pfizer, and we will really miss working with you. So first question I have for you is William, what are your initial impressions of Pfizer, having come recently from the outside? And then the second question I had is, what is the opportunity for a potential EU PAXLOVID contract and sales potential in China?

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

William, why don't you start with your impressions?

William Pao - Pfizer Inc. - Executive VP & Chief Development Officer

Sure. Louise, thanks for the question. Yes, I would say I've been -- my expectations have been exceeded. Many reasons I came to Pfizer but one of them was the great science that's going on, the real dedication to breakthrough innovation but also the pace with which things have been done. And seeing Pfizer accomplish PAXLOVID and the vaccine were really inspiring, and I came to further build upon that and really transform how we do drug development.

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

Angela, you want to take a little bit the EU PAXLOVID contract?

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

Yes. Thanks for the question, Louise. So in Europe, I would say that we're really taking a sort of a two-pronged approach to our contracting. One, we have bilateral agreements that have actually either been secured or about to be secured with many of our countries. But in addition to that, we're also looking at an EU-level contract. So I think more on that to come as we -- whenever we're ready to share what the outcome of that is, but just suffice to say that we're using both approaches in Europe.

On China, what I am able to share is that we are working with a local distributor called Meheco to distribute and to ensure access to PAXLOVID in China. And that's what I'm able to say right now. I'm not really able to share more about the terms of the agreement or the volumes or anything related to that. So thanks.
Operator

Your next question comes from the line of Evan Seigerman with BMO.

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

So I have 2 on COVID: one, when we think about the evolution of the booster market, how do you see this going? We’ve seen some data suggesting that we’re kind of walking blindly into recommending boosters every so often. What’s the ultimate goal of vaccination? Is it to prevent mild, symptomatic disease? Or is it really just to prevent the severe disease and overloading at the hospitals?

And then my second question is when we think about the evolution of the commercial model for PAXLOVID, can you talk to that? When do you expect to maybe file an NDA and transition away, at least in the United States, from kind of government contracting to more traditional commercial model?

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

Yes. Thank you for your questions. Let me see if I can answer and then I will ask our scientists if they have something to add. On the evolution of booster, I think all authorities, they are not moving blindly. We are moving based on data. And the reason why they recommend what they recommend is because data are supporting according to their opinion. I believe that right now, the effort it is to be able to stay ahead of the virus and the virus mutates and the most serious mutation that we have seen was the Omicron, one, because there was the one that was able to evade the new protection of us.

Until then, I think the vaccines were offering very, very good protection against disease and, of course, an excellent protection against hospitalization and death. With Omicron, we saw that while we keep a very good protection against hospitalization and deaths, the protection against the disease is going down. So we have seen that with our data that a fourth dose of the current vaccine protects significantly folds, many folds, the patients from either hospitalizations or death and, of course, also protects the infections but not to the degree that it used to be.

Everybody is working also for new vaccines that will be able to protect better against Omicron while maintaining the same protection against the wild types. We are very advanced with our studies. And we are waiting to hear from FDA what basic combinations they would recommend, what they would like to see at the EMA, and we will be ready day 1 with our vaccines, both in terms of filing and both in terms of manufacturing. As regards PAXLOVID, right now, we are completing the studies and I will ask Mikael to comment when we think that we can file for a full NDA.

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

Yes. We will file NDA quite soon, this half of the year, and look forward to, as soon as possible, pending review, getting it approved, which would allow even more engagement with the medical and other communities. So we think that would be very helpful in order to increase education and access to the medicine.

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

And anything to add on the booster and how we are looking at it?

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

You described very well how this has been science-driven, and Pfizer is proud to have been leading, often the first, for whether it is primary series, a boost or new age group. So I just wanted to add that we expect, pending the VRBPAC, starting the fall season with a vaccination campaign, a
new boost, which will be critical then to regain, and as Albert alluded to, possibly further strengthen versus new evolution that we’re seeing in Omicron. And it’s likely going to be an annual procedure with this type of public recommendation about strains.

And for some more vulnerable patient groups, immunocompromised, older, we have learned that it may be even in between an extra dose. So we are on top of the science, and we expect every year to be able to incorporate new science. We’re doing multiple learnings on how to further evolve the vaccine and see us as a natural leader as we have established such deep insights.

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

William, anything to add?

**William Pao** - Pfizer Inc. - Executive VP & Chief Development Officer

No.

**Operator**

Your next question comes from the line of Mohit Bansal with Wells Fargo.

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

Maybe 1 question regarding PAXLOVID. So it seems like you have mentioned 6 million courses with sales is about $1.5 billion. So discount rates are about $250 per course price. So am I calculating it right? And number two, it seems like you’re suggesting that all 20 million courses in 2Q would be shipped. So is that correct, and the pricing should be lower or higher than $250 per course?

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

Thank you very much, Mohit. No, there is a disconnect. Let me try to explain it. We did produce 6 million doses in -- by the end of March. From them, only 4.2 million or 4.3 million were shipped outside in March. The remaining were shipped in the first week of February basically. But also from the 4.2 million that were shipped, the very small proportion -- a smaller proportion was recorded as revenues in this quarter. Why? Because most of them were shipped in March, and everything that were shipped in the U.S. in March accounts for Q1, but everything that were shipped internationally in Q1 counts for Q2 in the accounting calendar that we have.

So the doses that are made, this $1.5 billion of sales, is way smaller than the 6 million doses that you referred. In terms of what we expect, we expect in this quarter to have 24 million doses, so by the end of June, we have been able to produce 30 million doses altogether. Clearly, some of that again will be shipped in July. Clearly, some of that will be shipped in June in international markets. So you should not be calculating as it have in the first quarter, that everything will go into, let’s say, the second quarter of all this volume.

**Operator**

Your next question comes from the line of Terence Flynn with Morgan Stanley.

**Terence C. Flynn** - Morgan Stanley, Research Division - Equity Analyst

I know it’s a little too early to give 2023 guidance, but maybe Angela or Frank, could you just help us think about the puts and takes for COMIRNATY for next year, and if you think consensus is in the right range at $17 billion to $18 billion. And then my second question relates to etrasimod for
ulcerative colitis. Mikael, based on your comments, it seems like the placebo response rate in the Phase 3 trial might have been slightly higher than Phase 2. Just wondering if that’s accurate and any additional insight you could share there.

Albert Bourla - Pfizer Inc. - Chairman of the Board & CEO
Thanks so much, Terence. Look, I will ask Frank, but good luck, he will not give you guidance for a product and she will not give you guidance for ’23. But let’s see how he responds to that question. And then Mikael, can you speak about etrasimod?

Frank D’Amelio - Pfizer Inc. - Chief Financial Officer, Executive VP
So I’m not going to provide 2023 guidance. But obviously, what we did for 2022 guidance, we reiterated the guidance on PAXLOVID. We reiterated the guidance on COMIRNATY. By the way, $54 billion approximately of revenue while absorbing $1.5 billion of foreign exchange. And if you listened to the commentary we’ve had so far on PAXLOVID, we remain bullish on PAXLOVID if you look at some of the recent trends and you look at some of the charts that Albert provided in terms of tenfold growth from the end of February to mid of April, the number of sites that we’re at, 33,000 sites now. So the rhythm of that product looks very good and we remain very bullish.

Albert Bourla - Pfizer Inc. - Chairman of the Board & CEO
And those I will say that for 2023, there are going to be a lot of puts and takes because there will be likely new innovation that is coming that we need to see how that plays and also changes in the business models, right? There is a chance that the U.S. will go to private market in the next year. I think likely international, they will continue with governmental purchases, and we do have a contract for these purchases that goes ’23 and beyond at ’24. So there are a lot of puts and takes that will be in play here. But let’s move to something that is very interesting, etrasimod.

Mikael Dolsten - Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical
Yes. Thank you for your interest, Terence, there. And I think, of course, the I shared was based on the pivotal studies that will be filed. And noted that one of them did have a placebo rate slightly higher. The more extensive of the Phase 3 had a traditional placebo rate and a very nice delta between treated and untreated. As you know, for great drugs, you would like to see in the range of maybe a 20% delta. And while we won’t give you all details as we’re expecting data soon to be presented this year at the proper conference, I can assure you that we saw a very nice favorable delta for etrasimod treated.

We talked about 12-week remission rate in our earnings talking point. The drug did very well in the 52-week maintenance phase and all secondary endpoints are looking very favorable. So that’s really why we think it can be both best-in-class and, in some way, a best-in-disease, given its convenience, its rapid onset of action, its well-tolerated profile.

Operator
Your next question comes from the line of Vamil Divan with Mizuho.

Vamil Kishore Divan - Mizuho Securities USA LLC, Research Division - MD
Maybe just shifting gears a little bit to the quarter and some of the core products here. So what I'm curious about Ibrance, especially in the U.S. because we -- I know you mentioned again in the release it was down 5% and some of this was through the Patient Assistance Program. And I guess I assume I thought that was more of a 2021 dynamic kind of going through the pandemic. And by this year, it may actually be more of a positive pricing benefit that you see. So maybe you can just kind of share a little bit more color on what you're seeing in the market there.
And then the second 1 is on Xeljanz, which is obviously down quite a bit. We all know about the safety issues and label updates and all that. I'm just trying to get a better sense of how you see that product sort of going forward. You obviously have a good immunology pipeline and a lot of other assets to leverage here, but do you see sort of Xeljanz stabilizing here? Do you see (inaudible) continue to climb? So how would you sort of view that price outlook over the rest of the year and in the next year or 2 going forward?

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

Thank you, Vamil. Very good questions, both of them. So Angela, start with Ibrance and then you go to Xeljanz.

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

Sure thing. So let's talk about Ibrance first. Just from a performance perspective, I just want to emphasize that Ibrance is still, by far and away, the undisputed leader in the CDK class. Actually, in ex U.S., it grew 12% this quarter. And as you mentioned accurately, it did have a negative 5% growth in the U.S., and this was largely due to the PAP. In fact, if you strip that out, TRx volume actually grew 3% in the U.S. for Ibrance. So it's really this high proportion of unpaid RXs that led us to this revenue growth that you saw.

Just to give you a sense of the scale of the PAP, compared to a year ago, we have seen a 32% increase in PAP applications. And however, Q1 was similar to where we were in Q4 in terms of the number of enrollees. But maybe if we step back, it may be not so surprising that Ibrance would have such a high proportion of PAP because it is the market leader. More than 75% of all the scripts in the CDK class belong to a part of Ibrance. And so if you link that to the financial hardships that are still in the economy, and you link that to the fact that there are reduced alternate sourcing of financial assistance, which is driving more people to the Ibrance PAP.

Also, just from an annual perspective, patients enrolled in January, most of them and that they stay for the year, so I think what we're seeing is approximately what we're going to continue to see for the remainder of the year. But maybe the important message here is that this does not mean that there is no growth opportunity for Ibrance even in 2022. We know that there is tremendous growth opportunity in the CDK class. And our ability to make this pie bigger is going to be great for patients as well.

We saw, just in the last year, an increase of the CDK class from where we were in Q1 of 2021, which was just 48% to where we are now, this quarter in '22, which is 54%. So this positive momentum of the growth of the class is something that we are very focused on, in addition to the fact that, of course, over the pandemic, we did see some lag in new patient starts and new diagnosis of metastatic breast cancer patients or delays in putting them on treatment. And so that's another area of focus for us as well that will help to drive the increased momentum around Ibrance. So that's Ibrance.

So let's spend a minute talking about Xeljanz and your question around sort of where are we with Xeljanz and what do we see. And we definitely see 2022 as a year of transition for us. Why? Well, first, when you step back and look at Xeljanz performance, you have to look beyond Xeljanz. It's not just about the product, it's also about the class. And so just to give you some numbers on what has happened in the class, over the last year, so between this quarter and same quarter last year in 2021, the new-to-brand prescriptions in the JAK class actually went down 40%.

Now Xeljanz went down 50% but we also saw products like of the product in the JAK class go down by 35%. So when we look at growth, it's important that the class returns to growth as well. I'd say that '22 is going to be a year of transition for Xeljanz because we finally have a clear label. And with this label, we're going to be able to focus on the post-TNF segment as our place and it's the place where Xeljanz can play. And this market is also significant because we know that many patients don't respond to TNFs and most will need options beyond TNFs.

Finally, we're seeing some nice signs of stabilization compared to where we were over the last year. For the first time, our new-to-brand Rxs are stable versus declining. We're also seeing that there are switches back into Xeljanz versus just purely away from Xeljanz. In our market research, we see an increase in the intention to prescribe by health care professionals. And then finally, also in the market research, we see that the safety perceptions of Xeljanz are equivalent to that of Rinvoq. So it demonstrates the playing field in the JAK class is now leveling. So we're really focused
on education. We have massive education efforts behind Xeljanz to reestablish where and how Xeljanz should be used, and that’s what gives us confidence that we can return Xeljanz to growth.

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

Thank you, Angela. As always, a very comprehensive answer.

Operator

Your next question comes from the line of Kerry Holford with Berenberg.

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

A couple of questions, please. Firstly, on COVID vaccine. I noted in your 10-K that you expect to recognize at least $11.8 billion of revenues in 2023. Should we think about that as a floor for next year based on the contracts you’ve already signed? And if so, have you signed any further contracts for delivery in 2023 and beyond since you published that 10-K in February?

Secondly, on the RSV vaccine, I saw in Slide 36 you’re now confirming the Phase 3 data readout for RSV vaccine now in the second half of the year. Does that totally reflect the expansion of the patient population was in the study? Do you need to run into another RSV season? Or are you also evaluating annual RSV vaccinations in this study? And lastly, when do you aim to file and launch that product in the U.S.?

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

Thank you very much. Frank, do you want to give the answer on the...

Frank D’Amelio  - Pfizer Inc.  - Chief Financial Officer, Executive VP

Yes. Just in terms of 2023, we’ll talk about 2023 in detail when we provide 2023 guidance, which will be on our fourth quarter earnings call. We’ll talk about the puts and takes. We’ll explain where we are this year, where we are next year, what the growth drivers are. And obviously, that will include what the revenues will be for the COVID vaccine. So that’s to come.

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

And then Mikael, do you want to take the RSV question about the seasonal filing, and then William, if you have anything to add, please?

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

Yes. As I spoke in the introduction, Pfizer is very excited about the portfolio of the RSV vaccine and the RSV therapeutics. And I think we have had very strong data in the Phase 2 CHALLENGE study, complete protection and also in the MATERNAL study where we actually, with small numbers, had 85% efficacy and very strong immunity across the A and B strains. I believe we are the only 1 with such a comprehensive data set.

Starting with the MATERNAL, to the best of my knowledge, we are really the only advanced RSV vaccine there. We took the opportunity as we had sites opening up in Latin America to also capture from that region of the world and in this now, 2022 season, more cases to add to our study. And we expect in a couple to a few months to have the readout based on (inaudible) for the MATERNAL. And relatively shorter thereafter this year, the adult trial is expected based on a comprehensive set of sites also in the Southern Hemisphere. So it’s really a perfect composition of RSV cases from different parts of the world. And I look forward very much to the readouts and remain very optimistic. It’s one of my favorite programs.
Albert Bourla - Pfizer Inc. - Chairman of the Board & CEO

Mine as well. William, anything to add?

William Pao - Pfizer Inc. - Executive VP & Chief Development Officer

Yes. I would just add that you mentioned already, Mikael, that both programs got Breakthrough Designation. And so we're very excited about that.

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

Of course, everybody recognizes that it's apparently the favorite program of FDA as well.

Operator

Your next question comes from the line of Steve Scala with Cowen.

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

And thank you, Frank, for everything, and all the best to you in the future. I have a follow-up on the RSV vaccine. In which ACIP meeting in 2023 would the Pfizer vaccine most likely be considered? And I assume, of course, you have not seen premature birth in the maternal study, but do you have a theory as to why you haven't when your competitor has? And then a question on Eliquis for Angela. To what degree has bleeding risk limited prescribing of Eliquis? And if a drug came along that was associated with less bleeding, do you think that would be a significantly preferred agent?

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

All right. Angela, why don't you take the ACIP meeting and then also the question about the bleeding and then we can go to Mikael?

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

Sure. ACIP, the schedule for ACIP is just closely held by the ACIP, the working group and the CDC. So it's a really difficult thing for me to be able to predict. But typically, it's sort of within the 2- to 3-month period of -- from launch, right, because you know that it only happens several times of the year. So you really need to be able to catch it right to be able to meet whatever their next meeting is. So I honestly think that's a very difficult question to answer. But suffice to say that, of course, we will work as rapidly as possible to ensure that it gets on the schedule of the very next one post launch.

On your question around bleeding, it has not been one that has come up actually for Eliquis, in large measure, I have to say. Our performance continues to be really strong. We're the #1 NOAC in 24 markets. We're the #1 oral anticoagulant in 21 other markets. So I'd say that the uptake of Eliquis outperformance, which as you can see this quarter, continues to be double digit, I think it's the tenth year in a row that we've had double-digit growth on Eliquis. And we continue to see tremendous market share and utilization. So I would say that, that has not been an issue that we have seen.

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

Frank?
Frank D’Amelio - Pfizer Inc. - Chief Financial Officer, Executive VP

And if I could just punctuate, if you look at the revenue number this quarter for Eliquis, the revenue number is $1.8 billion almost, up 12% operationally. Continued, continued strong performance by that product.

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

Exactly, exactly. And also, I wanted also to add to Angela’s comment, of course, we can’t predict when ACIP will do whatever they think is appropriate to do. But we do know that RSV is considered by CDC as a major disease threat. And I’m sure that, as always, they will demonstrate the appropriate urgency to deal with a vaccine if it is registered. Mikael, there was this question about premature births that we do not have, and if you can provide some why we don’t and why others may.

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

Well, we have a very deep and long experience how to design vaccines and for different patient groups. As this is for maternal, we obviously developed a very well-tolerated vaccine, and we were able, without the need of any harsh adjuvants, to get very high immune responses, that included that we use both RSV A and B antigens. I believe we’re the only one that have that going.

I can’t really be certain on the other vaccine you’re referring to, but certainly, it’s not an advantage to use an adjuvant that was known to give very significant local and systemic adjuvant actions for a fragile patient group like maternal. So we feel very bullish that we are the main vaccine in the maternal. We’d only that have a bivalent model, strong data behind it and look very much forward to the readout.

Operator

Your next question comes from the line of Colin Bristow with UBS.

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

And I wanted to say all the best to Frank. So a couple on my side. On the business development front, could you comment on how large a deal you would be willing to consider? And is there a preference for marketed assets or pipeline or some combination of the 2? And then just in terms of disease spaces, yes, I’d be curious to hear how you view the rare disease category as an area of potential business development from here.

And then just a quick one on PAXLOVID. I understand your prior comments, but I just want to get a sense here on what is the risk that we end ‘22, and obviously, the doses have been purchased but are essentially stockpiled or not utilized, which could subsequently impact ‘23 onwards.

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

Thank you very much. Why don’t we start with the BD questions and I will ask Aamir Malik to speak about it?

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

Colin, thanks for your question. On our BD focus, I think we’ve been very clear that compounds that have the potential to be breakthroughs is where our focus is. And these can be in the form of late-stage clinical development, they can be in earlier medical innovations as well as, as well as early launches. We’re going to bias to the TAs where we have scientific and commercial expertise because we can add value. We’re going to be flexible on deal structures.
And on your question on size, we've been very clear in the past that we're agnostic to size. But we're not going to focus on deals where cost synergies are the primary source of value creation. We're going to focus on deals where we can add value, we have a scope to have impact and where there's going to be revenue impact in the '25 to '30 time period. So that is our current focus.

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

Thank you very much, Aamir. And as we said also multiple times, it is important to see Pfizer as a partner of choice also. So it is important to see Pfizer as the company that can add value, either by acquiring or by partnering molecules, with companies to the same extent that we have proven with other biotechs that we can provide benefits to patients by putting our capabilities into work. And that's, I think, it is the way moving forward. And clearly, we are focusing on filling the gap between '25 and '30. We started this call again by making -- myself making comments that we reiterate that we plan to have $25 billion of risk-adjusted revenues with analyst expectations by the year 2030. And we feel that we are moving as per plan to achieve that goal. Now let me turn to Angela to speak a little bit about PAXLOVID and the question about is there any risk that the quantities will be purchased will not be utilized.

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

So I think when we think about our contracts and what has been purchased, we also think a lot about demand, right, like generating demand and utilizing the product. And I think that the U.S. gives us a good example of what you can see when utilization and adoption picks up. You heard from Albert's opening presentation that just in the last few weeks, we saw the prescriptions of PAXLOVID grow 10x. And just in 1 week alone, you've got as high as 80,000 prescriptions that were dispensed.

You also heard that there are 30,000 sites that are available now in the U.S. that dispensed PAXLOVID and that is increasing. Deep dive to those Test to Treat sites, which were only 1,100 at the beginning of April and now have doubled to 2,000. And you add upon that, the U.S. government's announcements around their focus on increasing more sites. All of this is showing us that momentum around PAXLOVID is real and that there are a few sort of key levers that open up this access. One is the number of sites and the proximity to patients. And two, it's the education around how to use PAXLOVID and who are the patients that are eligible.

And so when you think about what has happened in the U.S., you now are beginning to see that happen around the world as well. We see that demand is increasing. You heard Albert speak about how countries that have purchased from us are now coming back with reorders. You're also seeing in, across many countries, how they are changing their eligibility for criteria for PAXLOVID as well as the number of sites where PAXLOVID can be accessed, much like what we're seeing here in the U.S.

So I think when you add all of this up, what we are seeing is the fact that there is demand for this product. We also see that the social -- the removal of the mask mandate, the social distancing requirements that have been removed. You also know that in the EU that just in the last week, they've removed the emergency period of the EUA. That means that people are going to get out there. We know with all of that, infections are going to increase, and that's the role that PAXLOVID can play.

So we're intently focused on working with national governments, state governments, in helping them to educate, to take great lessons learned from around all the different countries to help them to utilize PAXLOVID. And importantly, what we're also seeing is that it's not as -- we don't have any inventory on hand. Every dose that we produce is being shipped out and is being ordered. So I think all of these give us a lot of confidence that there is a demand for PAXLOVID. We know what we need to do to support the utilization of PAXLOVID, and we'll continue to drive that throughout the year as we anticipate further surges in COVID infections.

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

Thank you, Angela. And also what Angela said, I want to reiterate that I like what we have seen with the partners of vaccines that the governments were trying because of lack of manufacturing capacity to build stocks. Right now, the orders that we are coming are orders not for the entire year.
They are orders for the immediate needs of the countries. And this is why we have repeated orders of COVID. That’s across many all countries that we see internationally.

Operator
Your next question comes from the line of Carter Gould with Barclays.

Carter Lewis Gould - Barclays Bank PLC, Research Division - Senior Analyst
Best of luck to post-Pfizer endeavors, and I appreciate all the color on PAXLOVID right there. Maybe moving to the pipeline. In highlighting your UC franchise in the slides, you focused on etrasimod and ritlecitinib, notably didn’t mention your TL1A program. Has your enthusiasm there shifted now that you have the induction data in-house? And on the IRAK4 side, I saw the discontinuation in HS. Has that changed in any way how we should think about development in RA? I believe that got removed from your early-stage readout calendar?

Albert Bourla - Pfizer Inc. - Chairman of the Board & CEO
Thank you very much, Carter. Mikael, the floor is yours.

Mikael Dolsten - Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical
Yes. I did speak about that etrasimod creates a very rounded and comprehensive pipeline. I think the TL1A data that we have in our hands, and it will be -- I shared earlier at previous earnings calls, some of it, it’s very strong. Actually, to the best of my knowledge, in the biomarker selected group, it’s probably the strongest or among the very strong that I have seen.

I think it can be a very much complementary drug to etrasimod. And we also know that the TL1A principle, not just as anti-inflammatory but also play a role in fibrosis. We didn’t have much time to speak about ritlecitinib beyond our real exciting data that we shared in vitiligo. We also have additional inflammatory drugs that are coming to readouts with strong data behind them for potential start of pivotal, such as interferon beta in inflammatory muscle diseases.

So I would just say we have the advantage of a richness now of inflammatory drugs and really building a pipeline with complementary approaches. And we hope to share more which of the ones that will be kicked off soonest from the many options that we now have in our hands, but TL1A clearly a very active drug.

Operator
Your next question comes from the line of Andrew Baum with Citi.

Andrew Simon Baum - Citigroup Inc., Research Division - Global Head of Healthcare Research and MD
A couple of questions, please. Firstly, Pfizer is the leader in cardiology thrombosis and hemostasis. Four of your competitors have Factor Xla inhibitors in clinical development. There’s still significant unmet needs in thrombosis despite the NOACs. I’m curious as to why you’ve passed on the opportunity and what data would make you change your mind or review your decision.

And then the second question is going back to the barriers that PAXLOVID adoption that have existed historically. You’ve addressed, addressing the access barriers. But in terms of physician education and holding back prescribing because of supply, patient awareness, how would you delineate
the percentage contribution of those to the current underutilization of PAXLOVID? And what do you think are the timelines for knocking down the separate reasons?

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

Mikael, why don’t you take the cardiology question?

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

Yes. First of all, we think the breakthrough with Eliquis, the NOACs, was so dramatic for patients and physicians from warfarin, which had many issues of significance, including a very complicated dosing and risk for bleeding. While we monitor new drug classes, including the one that you have mentioned, we really want to see a similar step-up in breakthrough potential as we saw with Eliquis. And we haven't yet been convinced about that step-up, but we are carefully monitoring. And internal medicine and cardiometabolic diseases is an area that we think are very interesting. And you, of course, heard us speak about oral GLP-1 as another very important growth area.

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

Thank you, Mikael. And then Angela, what about the education that we plan to do alone or with governments to address other barriers of PAXLOVID, like the perception that it’s not available or other stuff that Andrew spoke about?

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

Well, education is key, and it underpins the promotion of all of our products. But I think the first comment I have to make is that you all know, we're under an EUA. And in this EUA, we're really -- we are limited by what we are allowed to talk about and also limited by the level of promotion that we would typically do. And that's why you see that much of the education that is occurring right now is coming from the government, whether that's the CDC or at the state level, state departments of health and how they've chosen to roll out the messages regarding antiviral treatments.

Of course, we're supplementing that by what we can do. We've put public service announcements out there. We've utilized our field force in the appropriate way to convey, when we're able to, through an EUA. And there is just a significant amount of medical education as well that we are doing, again, also in an EUA-appropriate way to support our brand. But of course, this doesn't look anything like what we would typically do if we had a full commercial launch where we would have the ability to really deploy the entirety of our promotional engine towards education and towards support of both patients and physicians. So I would say that the education is happening and we are doing our part, and I think that there is a lot more that can be done.

But I think the second part of your question was also around how much does this contribute to the bigger issue. And I want to say that truly, the ability to access product quickly is one, that even though there's been great improvements, I think that there's still a long way to go. Even with all the improvements that we have had recently, we're still a fraction, I would say, under half of all the possible retail locations where PAXLOVID could be found. So it's tremendous that we're seeing this uplift, but I would say that we need to continue on the path of where we've been and continue to do more because there's still a lot more that can be done.

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

Thank you, Angela. And of course, I wanted also to add that I have also never seen the government being so active. They truly believe that it is a way to control hospitalizations and deaths. And we see that their own educational campaigns are working because as we have seen, there is a tenfold increase just in a few weeks, and I think that comes together with all the measures that they are taking, I think will yield even more impressive results. I'm confident.
Operator

Your next question comes from the line of Chris Schott with JPMorgan.

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

Just 2 additional PAXLOVID ones. I think it was a question of kind of contracting. It seems like we saw a lot of activity late last year, early this year. But it’s been a bit more quiet, I guess, more recently on the contracting front. So I know you’re expecting more contracts for PAXLOVID, but just qualitatively, can you just give us a sense of how broad of a swath of the market has already entered in contracts, they're going to satisfy demand this year relative to how large a portion of, I guess, a realistic global market are still in negotiations and still need to come up to some agreements? I'm just trying a sense of like what does the TAM look like versus what's been contracted.

And then my second, just one on PAXLOVID was there seems like there's been several data points of kind of PAXLOVID like kind of COVID rebound occurring in some patients. Is that something you're seeing in your data? And just how are you thinking about kind of addressing that as we kind of learn more about the longer-term outcomes in some patients there?

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

Thank you very much, Chris. Excellent questions. Angela, what about our contracting?

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

Well, I would have to say that I'm really pleased with how our contracting has gone. You heard Albert talk about the 100 countries that we are engaging with. And actually, compared to where we were last quarter, we've made some really nice and significant progress. In terms of the number of countries, just to give you a sense, we've actually -- when we think about the $22 billion in guidance, right, plus the $500 million that we're absorbing from foreign exchange, when you think about that part of revenue, it really consists of countries that we have finalized contracts with as well as countries that we anticipate to close shortly. So there are sort of 2 buckets of countries in there.

And what I'm happy to say is that compared to where we were in the first quarter, we are 3x larger in terms of the number of countries that have actually finalized contracts. So that's the first thing. But in addition to that, we have bilaterals that have either been completed or about to be completed with 60 countries, and that doesn't count the multilateral agreements that we're also having. You heard about UNICEF earlier today from Albert. We have others as well in the works. So I think when you think about the total addressable market, as you say, I think that we are not done, but we have combed through a large proportion of them, and that gives me great confidence in our ability to meet the guidance that we've provided you.

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

And also, I want to reemphasize that what is different with PAXLOVID contracts is that we signed a contract with -- typically they start with smaller volumes and then they keep ordering and reordering. It's very important to have the legal framework so that a country can order first, which we have done, but they are ordering based on the needs rather than based on the anticipation to build stocks, which that also, by itself, shows that with the signed contract you expect more because it's not to cover the whole year. But of course, all will depend on the usage in the field. We're optimistic, but we need to see how the usage in the field will go. William, you want to take the COVID rebound?
William Pao - Pfizer Inc. - Executive VP & Chief Development Officer

Sure. So we take very seriously the case reports that have been anecdotal so far in terms of potential rebound and (inaudible) PAXLOVID. To respond to that, we've taken some preliminary look at our EPIC high-risk data. And so we've seen, for example, that we -- about an incidence about 2% of that viral load rebound. But we also see the same or close to the same percent in the placebo arm. So it's something that's not particularly associated with PAXLOVID but may have something to do with the virus itself.

We've also looked for patient characteristics and potential recurrence of severe symptoms, and we haven't seen any association with patient characteristics or severe symptoms developing in these patients who rebound. And then finally, we haven't seen any association with mutations in Mpro, which is the target of PAXLOVID. So it's preliminary data so far. We again take it very seriously, but it's occurring at a very low incidence. And we continue to learn as we go along.

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

Mikael, anything to add there?

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

It was a very good response from Will. So I'll just add as we do surveillance of patients in very large databases, and we have access to more than 300,000 PAXLOVID treated. In one of the databases, we have reports of this happening in less -- in about 0.005% or less, which is less than 1 out of 3,000 treated patients. So overall, it's quite uncommon. But as Will spoke about, it's not really related to PAXLOVID but more to the individuals that then need to clear the virus. And it is a virus that can either reinfect patients or that can be reservoirs left in the patients.

Now what we also learned is that for some patients, immunocompromised, they may carry this virus for a very, very long time. And we see that area as a real new opportunity growth area for PAXLOVID to do very well, where you may need to take multiple courses over a year or even treat with extended duration, and that's something we're now planning to study in order to expand the use of PAXLOVID where it may be the most appropriate and life-saving drug.

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

And as Mikael said, the work of PAXLOVID is to reduce the viral load and, as a result, help your body overcome the disease faster and without serious consequences. It could be that in some cases, there is a rebound. That was why the label speaks about a second treatment that can be given. And also we need to think that if by reducing, and it seems in all these cases that have reported that actually did what they're supposed to do, which is reduce the virus load because they became negative.

So then they came back. I can only imagine if without the help of PAXLOVID, what will be the clinical symptoms of the patients that is coming back. So let's not forget that this is for people that they already sick and we help them go easy with their disease, easier than without PAXLOVID. And so far it's working extremely well.

Operator

Your next question comes from the line of Tim Anderson with Wolfe Research.

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

I have a couple of questions. Prevnar 20 in pediatrics, important franchise, peds is 75% of current usage. It looks like the readout of your peds trials has slipped from first half to second half. I'm wondering if you can explain why and if that impacts your confidence in the readout at all. Second
question, your biosimilars are growing. Your press release mentions interchangeable HUMIRA. We have no real precedent with Part D biosimilars in the U.S. My view has been that AbbVie is going to hold on to more share than what they've been guiding for. But as you’re on the other side of this, I'd love to get your perspective. I know your launch is a year away, but what are your expectations for uptake in the U.S. for biosimilar HUMIRA, whether it’s yours or anyone else’s? And how do you think that will compare to what we've seen with biosimilars with Part D drugs like Avastin?

Albert Bourla - Pfizer Inc. - Chairman of the Board & CEO
Thank you. Mikael, Prevnar 20?

Mikael Dolsten - Pfizer Inc. - Chief Scientific Officer and President of Worldwide Research, Development & Medical
Yes. It’s a very minor shift. We’re predicting earlier, mid of the year and we now see it will come in the second half. Not too far away from our original prediction is what I believe and it was just affected by COVID and the ease with which we could get infants vaccinated. So overall, it’s on track for readout. We had a very good readout with adult. I have no reason to believe that we won’t have also a very good performance in the clinical trial for the pediatric.

Albert Bourla - Pfizer Inc. - Chairman of the Board & CEO
Thank you. What about the uptake for biosimilar HUMIRA? Angela?

Angela Hwang - Pfizer Inc. - Group President of Biopharmaceuticals Group
So we are optimistic about the uptake of biosimilars. I think we’ve learned a lot over the last several years. And if you look at our experience with Inflectra, you look at our experience recently with our 6 biosimilars in oncology, I mean, they’ve just -- they’ve gained tremendous market share. I think that physicians and institutions have become extremely comfortable with the use of biosimilars.

If I compare my experience with Inflectra when that was first launched infliximab and I compare that to what I see now with the 6 biosimilars we just launched in oncology, very different experiences in terms of willingness, in terms of uptake and comfort for a physician to use it. So I think we’re very far from where we were when we first launched our first biosimilar here in the U.S. That, coupled with the interchangeability data, should mean that we would be able to gain a fair market share.

Operator
Your next question comes from the line of Geoff Meacham with Bank of America.

Alexandria Hammond - BofA Securities, Research Division - Associate
This is Alex Hammond on for Geoff Meacham. Maybe to follow up on the previous response. What’s the PAXLOVID capacity like? To what extent is guidance potentially constrained by any limiting factor, whether in terms of production or potentially distribution? In other words, if the contracts were there, to what extent do you think they could address the near term? And then can you maybe comment on the pace of business development? As we think about some of your longer-term growth targets and where you sit now, those gaps, are you still comfortable with the current trajectory?

Albert Bourla - Pfizer Inc. - Chairman of the Board & CEO
On the PAXLOVID capacity, we are on plan. So we will make 30 million treatments available this year -- excuse me, this June, the first half of the year. And we have already built our capacity, we can make 120 million by the end of the year. I don't think, given this very high ramp-up, that
capacity will become a limiting factor to governments to place orders. And anyway, as we see, we don’t have situations that they are placing orders that they keep in their warehouse. So they are placing orders so that they can use it so it’s always manageable reordering.

And we will be able to meet this demand. Particularly, we are cognizant that waves are coming so far not necessarily in terms of seasonality, but everybody expects that when you come after mass gatherings in the summer or as we are entering into the flu season, there will be, let’s say, dramatic uptake. So in that period of time, we have really a lot of PAXLOVID available. So I don’t foresee any issues on that. And then on the -- what was the second part?

**William Pao - Pfizer Inc. - Executive VP & Chief Development Officer**

Pace of business development.

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

The pace of business development. Aamir, do you want to take that?

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

Sure. Alex, thanks for the question. You heard Albert very clearly reiterate our commitment to the $25 billion in risk-adjusted revenue by 2030, and we fully believe that we can and will get there. We’re going to be very active in BD and that also means being thoughtful and thorough and disciplined. So when we see a great opportunity, we’re not going to hesitate to move fast, and I think some of our recent deals are good examples of that. And our ReViral acquisition is a good example of our first move towards that goal. And at the same time, we’re not going to be hurried or cavalier just for the sake of doing deals quickly. So we will move fast, we’ll be thoughtful, we’ll be disciplined, and we are very confident in the aspiration that we’ve put out.

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

And I want to, once more, to reiterate. We think there is substrate to do good deals that will provide us $30 billion risk adjusted. But we are going to be very disciplined. We can accomplish that. It is -- I will accomplish all of that without compromising on financial returns that are expected. And we truly feel that we can accomplish both. And we will accomplish, of course, in the next few years we need to do to complete this activity so that we will be able to have an impact in the ’25 to 2030 period of time. But I reiterate, there is substrate to do good deals and we will do a lot, but only good deals.

**Frank D’Amelio - Pfizer Inc. - Chief Financial Officer, Executive VP**

$25 billion by 2030.

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

$25 billion by 2030. What did I say?

**Frank D’Amelio - Pfizer Inc. - Chief Financial Officer, Executive VP**

You said $30 billion.
Albert Bourla - Pfizer Inc. - Chairman of the Board & CEO

$25 billion by 2030, not $30 billion.

Operator

Your final question comes from the line of Robyn Karnauskas with Truist Securities.

Robyn Kay Shelton Karnauskas - Truist Securities, Inc., Research Division - Research Analyst

So just first on PAXLOVID contracts. You had mentioned that there’s a bucket of contracts where you’re further away from signing. Can you just give a little bit more color on what the rate-limiting steps are for signing in those countries or signing those contracts? Are they in areas where there’s less infection, for example? And then second, on the booster, just a follow-up question. It seems like there’s a lot of debate about how long the immunity lasts with the boosters. And so how far away do you think we are scientifically from a longer-lasting mRNA booster?

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

Fantastic questions. Angela, what about the contracts?

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

So they’re not infection-related. It literally is just time. We have many countries to get to, and each one of them have their own internal process to -- that they need to go through. So there really is nothing here other than just getting through at end time.

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

Thank you, Angela. On the booster, let me make also some final comments because we are out of time and also try to answer that one. Clearly, COVID, it is a main uncertainty for the world and for, let’s say, companies, but they are trying to make a difference with COVID. But I think we don’t know the future but there are some scenarios that are the most likely.

I believe that the most likely another you should be seeing right now, it is that the virus will be around and the virus will mutate. And we know that the characteristic of this virus, is in addition to mutations, it is that doesn’t produce long-lasting immune protection, not only through vaccinations but also through natural infection. People that are getting sick, they will get sicker because they can get again sick with different or with the same variant. We know that after some time.

The second thing that we know, it is that the social distancing measures that were the main way to control the disease spread in the first 2 years of the pandemic. The pandemic will ease. It is happening because now have authorities, they do have a treatment in their hand, which they can count so they can release, let’s say, the measures they are not as skeptical as before to see overwhelming of hospitals. But also, it is happening because the societies are pushing for that. So there is a tremendous pressure across the world to get our lives back. As a result of these things, it’s very clear that we will have waves, that we will be more and more going to be affecting people. And for that, we need to have constant vaccinations, compliance with the vaccinations and the effective treatment.

Right now, people, it’s clear that they are skeptical in vaccines that is not clear if they will be needed to take another one and another one. People are tired from the repeated booster. So it is extremely important to come to a vaccine that could be a yearly vaccine. And to that, it’s not technically easy to achieve. It is but we are having very good scientific leads on that. So we are working on that. So when it comes to vaccines, I think this is what needs to be the next steps to be able to stay ahead of the virus, which we are in terms of the new variants but also try to go to the next generation that will be vaccine.
And of course, when it comes to the treatments, we need to make sure that we go with the manufacturing and the availability because the usage, unfortunately, I expect the need, let me put that, with the need, unfortunately, I think will increase as we are moving to less social distancing measures and that’s our reality. So that’s how I wanted to answer the booster question in terms of a long-acting booster.

And I want also to thank you, everyone, for today’s call. We are seeing very strong signs of increasing demand for PAXLOVID as it remains one of the best tools we have. I’m proud to have been able to recruit some of the best and brightest external minds to add to our talented roster of people. I’m proud that we have been named the most patient-centric company based on feedback from more than 2,000 patient organizations and associations. It’s a testament to the important and innovative work our colleagues do every day in pursuit of our purpose.

And I want to close once more by thanking Frank about his tremendous contributions and his friendship to not only me but many of the executives at Pfizer, and wish him well in his after-Pfizer life, although as he said, he remains a major shareholder so he will be attending everything that’s happening here with a lot of attention. Thank you very much, everyone.

Operator

This concludes today’s conference call. Thank you for participating. You may now disconnect.