Q3 2021 Earnings Call

Company Participants

- David W. Meline, Chief Financial Officer & Principal Accounting Officer
- Lavina Talukdar, Senior Vice President & Head of Investor Relations
- Paul Burton, Chief Medical Officer
- Stephane Bancel, Chief Executive Officer
- Stephen Hoge, President

Other Participants

- Cory Kasimov, analystA
- Edward Andrew Tenthoff, Analyst
- Gena Wang, Analyst
- Geoffrey Christopher Meacham, analyst
- Joseph Stringer, Analyst
- Mani Foroohar, Analyst
- Matthew Kelsey Harrison, Analyst
- Michael Jonathan Yee, Analyst
- NA
- Salveen Jaswal Richter, Analyst

Presentation

Operator

Good morning, and welcome to Moderna's Third Quarter Earnings Call. At this time, all participants are in a listen-only mode. Following the formal remarks, we will open the call up for your questions. Please be advised that the call is being recorded.

At this time, I'd like to turn the call over to Lavina Talukdar, Head, Investor Relations at Moderna. Please go ahead, ma'am.

Lavina Talukdar {BIO 19691239 <GO>}

Thank you, operator. Good morning, everyone, and thank you for joining us on today's call to discuss Moderna's third quarter 2021 financial results and business update. You can access the press release we issued this morning as well as the slides that we'll be reviewing by going to the Investors section of our website.

On today's call are Stephane Bancel, our Chief Executive Officer; David Meline, our Chief Financial Officer; Stephen Hoge, our President; and Paul Burton, our Chief Medical Officer.

Before we begin, please note that this conference call will include forward-looking statements made pursuant to the Safe Harbor provisions of the Private Securities Litigation Reform Act of 1995. Please see Slide 2 of the accompanying presentation and our SEC filings for important risk factors that could cause our actual performance and results to differ materially from those expressed or implied in these forward-looking statements. On Slide 3, please see the important indication and safety information from our COVID-19 vaccine, which has been authorized for emergency use in the United States and many other countries around the world.

I will now turn the call over to Stephane.

Stephane Bancel {BIO 15174250 <GO>}

Thank you, Lavina. Good morning or good afternoon, everyone. Welcome to our Q3 2021 conference call. Today, I will start by a quick business review of the quarter before David presents the key financials. Paul will then walk you through some real-world evidence update, and Stephen will provide a clinical development update. I will then come back to close to share some thoughts about where we are heading.

Let's start on Slide 5 with a holistic pipeline update. First, respiratory vaccines. We are pleased to have filed the BLA for COVID-19 vaccine to FDA and have now received a priority review designation. We received our first full approval for Spikevax back in Canada. We received EUA from the FDA for a 50-microgram booster and mix and match has been authorized. We also received authorization for boosters from other major geographies, EMEA, U.K. and so on. We were informed recently that the FDA may take until January 2022 to review the EUA request for 12 to 17 years of age.

Turning now to flu, mRNA-1010 is fully enrolled for the Phase I and we expect human data soon now. For RSV, mRNA-1345, after very positive data in the Phase I, with high neutralizing antibody levels after one dose, our teams are finalizing the preparation of a Phase II/III in all the adults. This study should start soon. We also announced our development candidate for COVID booster plus flu booster in a single dose, mRNA-1073, which we anticipate will be in the clinic soon.

Let me now turn to vaccine against latent viruses. As many of you know, latent viruses are a major cause of health problems. Latent viruses are made of DNA viruses, and once a human is infected by latent virus, that virus will stay in the body. You are familiar with some latent viruses like HIV and HPV. There are many others that harms humans. As a company, we are committed to developing the portfolio of first-in-class vaccines and therapeutics against these latent viruses. Our first programs are CMV vaccine, EBV vaccine and EBV therapeutic vaccine. We have also partnered to work on two HIV vaccines.

Last week marked a big milestone for Moderna. We started hosting in the clinic the first participants of our Phase III pivotal registration study for CMV vaccine mRNA-1647. This marks the second Phase III study that the company has started and brings us one step closer to getting another important vaccine to millions of people around the world. Our EBV vaccine, mRNA-1189 should start dosing for its Phase I very soon. And our new development candidate on the EBV therapeutic vaccine, mRNA-1195, is moving toward the clinic.

Let me now turn to therapeutics. Our personalized cancer vaccine is in Phase II, (inaudible) KEYTRUDA monotherapy is fully enrolled, and we expect data in the back end of 2022. Our regenetic programs continue to progress well in the clinic. PA has its Phase I dose cohort fully enrolled. MMA is dosing patients in its Phase I. GSD1a has an open IND and has received Orphan Drug Designation by FDA. So as you can see, we have three rare genetic disease programs in the clinic or soon to be in the clinic. So we look forward to sharing clinical data in the coming months.

We are very proud to have found the way to get Crigler Najjar type 1 of CN-1 to patients through a donation of IP and the assets to the institute for life-changing medicines. CN-1 disease is an ultra-rare disease with very few patients afflicted around the world. For ultra-rare disease, just because of clinical development will result in a very high price for a few patients around the world that could benefit. This model is not one that we support. So instead of developing the drug and charging the very high price, we decided to give the drug away and innovate through a creative partnership. We provide the drug to the institutes. We pay for clinical trial material, the institute pays for the clinical trial cost. If a drug is approved, we'll provide the medicines to the kids and their families for free. And we will not charge any royalty or milestone to the institutes. We believe this is the right thing to do to continue to contribute to society for ultra-rare disease where our mRNA platform can help.

One of the important news item announced today is the introduction of a new modality to our existing six modalities. We are very pleased to announce that Vertex and Moderna are now in GLP tox studies for the cystic fibrosis program, VXc-522. This marks our first inhaled pulmonary therapeutics program. I would like to congratulate and thank our scientific team as well as the Vertex team for having been able to develop a novel lipid formulation to allow inhaled pulmonary delivery. This is really exciting for patients.

As we communicated previously, in addition to doing therapeutics using mRNA coding for human proteins like the ones I just described, we want to use our mRNA plus lipid technologies to develop therapeutics using mRNA coding for gene editing enzymes. We are pleased to announce our first partnership in that field. We announced earlier this week that we entered into a licensing collaboration with Metagenomi based in California, to use their next-generation gene editing enzymes. We believe that their technology coupled with our mRNA plus lipid technologies, and our manufacturing infrastructure will produce some exciting new medicine to take into the clinic. I am very pleased with the progress of the company. We are increasing depth in vaccines and at the same time, increasing breadth of application with our seven modalities the lung and gene editing.

On Slide 6, you will find financial highlights. For Q3, we reported revenue of around $5 billion, enabled by delivering 208 million doses of our COVID-19 vaccine. Net income of $3.3 billion. Our cash and cash equivalents position was $15 billion at the end of September. Since the end of the quarter, we have been working to gain better visibility into those variables that will impact our full year results. And we have much better visibility today than we did a month ago. For fiscal year 2021, we are updating the range of doses we plan to deliver to 700 million to 800 million doses. The key variable of this update volume range are, first, longer lead time for exports to countries outside the U.S. and for international shipments in general. In Q3, we shipped more deliveries to new international market and expect Q4 to also have more international deliveries. As we deliver to these countries for the first time, we expect the process to become more routine and delivery time to short term. However, some Q4 deliveries may still move to early 2022 as a result.

Second, in Q3, we have expanded our fill finish capacity with our manufacturing partners, which has the temporary impact on our shipments. That work is complete now, and we should see a positive impact from this expansion very soon. Third, the bottleneck of production has moved down the manufacturing line to product release. We added additional resources, skilled personnel to the release and of the manufacturing line, and we expect to increase the weekly number of doses released. We believe resolution of these factors put us in a good position heading into Q4 and 2022.

Now if I turn to revenue for '21, the updated revenue range for 2021 is $15 billion to $18 billion. This range reflects updated delivery schedule with fewer doses delivered in '21, as some doses are pushed into 2022. And also, the pricing impact of prioritization delivery to COVAX and African Union that have a lower tier pricing.

On Slide 7, let me start by summarizing the scale of operational challenges that the team had to work through, as we scale for making less than 100,000 doses in 2029 [ph] to hundreds of millions of doses in 2021. Q1 scale-up challenges were around drug substance, making mRNA in lipid. To do scale-up challenges, we're on drug product and ensuring we could fill in our pipes. In the first half of the year, we made great progress in these challenges, as you can see from the numbers on the right. We now have 901 million doses of drug substance that have been formulated and then a large volume batch of mRNA product. And we have 770 million doses of drug products already in vials. To really scale-up challenges, we're on product release as the supply chain became more complex, we've increased deliveries to many countries around the world.

At the beginning of the year, we supplied just a few large countries. As mentioned before, we are working through these challenges, and as November 3rd, we achieved 566 million doses around the world. With the progress year-to-date, we expect to be able to deliver to 700 million to 800 million doses for the full year 2021. We were pleased to be named last week for the seventh year in a row as one of the top 20 biotech and pharmacal company in the world by Science. We continue to invest in science and the culture of our team. We aim at building the best mRNA science in the world in the culture of boldness, collaboration, curiosity and relentlessness. On Slide 9, you will find our usual summary slide, which describes some of the key high-level attributes of the company as of today.

Now, let me turn over to David.

David W. Meline {BIO 6397419 <GO>}

Okay. Thank you, Stephane. We're providing today the analysis of actual 2021 third quarter results, along with an updated view of key drivers of financial performance going forward. Turning now to Slide 11, starting with an overview of our sales performance before commenting more broadly on our financial results. Total product sales in the third quarter were $4.8 billion, representing 208 million doses delivered to our customers. This compares to sales of $4.2 billion and 199 million doses in Q2 and sales of $1.7 billion and 102 million doses in Q1 of this year. Sales to the U.S. government were $1.2 billion in the third quarter reflecting, 73 million doses delivered, compared to $2.1 billion and 126 million doses in Q2 and sales of $1.4 billion and 88 million doses in Q1.

Sales to the rest of the world were $3.6 billion in the third quarter, reflecting 136 million doses delivered compared to sales of $2.1 billion and 73 million doses in Q2 and $0.4 billion of sales and 14 million doses in Q1. This reflects the significant manufacturing ramp up outside the U.S. over the last two quarters. The relatively modest increase of delivered doses in Q3 versus Q2 was driven by the factors that Stephane just explained. We continue to scale our production network and are working to achieve an increased quarter-over-quarter improvement, starting in Q4.

Turning to Slide 12. The transformation of Moderna from an R&D-focused biotech, to a commercial company continues to be very apparent when reviewing our financial results. The comparison of the third quarter of 2021 to prior year is not meaningful due to our significant growth, which is why we will primarily focus on the quarter-over-quarter comparison relative to Q2 on this slide. Total revenue was $5 billion in the third quarter of 2021, compared to $4.4 billion in the second quarter and $0.2 billion in the prior year period. The increase of total revenue is driven by the sale of the company's COVID-19 vaccine. Product sales in Q3 were $4.8 billion compared to $4.2 billion in the second quarter, an increase of 15%. Cost of sales was $722 million or 15% of the company's product sales in the third quarter compared to $750 million or 18% of product sales in the second quarter.

The quarter-over-quarter percentage improvement is driven by higher average selling price, as a result of shifts in our customer mix and to a smaller extent, by favorable manufacturing cost. Research and development expenses were $521 million in the third quarter, up from $421 million in Q2 and $344 million in the same period in 2020. The higher spend versus prior quarter and prior year was driven by increased COVID-19 vaccine clinical development activities, including our announced efforts around booster variant-specific and multivalent vaccine candidates. Headcount increases as well as external costs to support our growing and maturing development pipeline beyond the COVID-19 vaccine activities also contributed to the expense increase.

Selling, general and administrative expenses were $168 million for Q3 compared to $121 million in the prior quarter, and $48 million for the same period in the prior year. The growth in spending was driven by the commercialization of our COVID-19 vaccine globally, with continued investments in personnel and outside services in support of the

accelerated company build-out. Provision for income taxes was $219 million in the third quarter, following $283 million in Q2 and an insignificant amount in the prior year. Our effective tax rate for the third quarter was 6%.

Let me remind you of the fact that we had a net operating loss carryforward of $2.3 billion at the end of 2020. This year, we started to release the valuation allowance against the related deferred tax assets, which results in an estimated nonrecurring full year benefit to our effective tax rates of about 5 percentage points. Our Q3 effective tax rate was lower than the U.S. statutory rate, primarily due to the just described benefit related to the release of the valuation allowance, the foreign-derived intangible income deduction and an excess tax deduction related to stock-based compensation. This last item drove the quarter-over-quarter reduction due to the increase in our share price in Q3 versus Q2. We recorded net income of $3.3 billion in Q3 compared to $2.8 billion in Q2, an increase of 20%. This compares to a loss of $0.2 billion in Q3 of last year. Diluted earnings per share for Q3 2021 were $7.70.

Turning now to year-to-date financial results compared to prior year on Slide 13. Total revenue was $11.3 billion for the first nine months of this year compared to $0.2 billion for the same period in 2020. The significant growth was driven by the sales of 510 million doses of the company's COVID-19 vaccine. Grant revenue of $473 million in the first nine months of 2021, an increase of $286 million compared to the prior year, was primarily driven by increases in revenue from BARDA related to the company's COVID-19 vaccine development. Cost of sales was $1.7 billion or 16% of the company's product sales for the year-to-date period as of September 30th, including third-party royalties of $400 million. A portion of the inventory costs associated with this year's product sales was expensed as prelaunch inventory costs in 2020. If inventories sold for the first nine months of this year was valued at cost, our cost of sales for the period would have been 17% of the product sales.

Research and development expenses were $1.3 billion for the nine months ended September 30th of this year, compared to $0.6 billion for the same period in 2020. The growth in spending in 2021 was mainly due to increase in clinical trial expenses and to a lesser extent, personnel-related costs, manufacturing expenses and consulting and outside services primarily driven by increased mRNA-1273 clinical development activities. Selling, general and administrative expenses were $0.4 billion for the first nine months of this year, compared to $0.1 billion for the same period in 2020. The growth in spending in 2021 was mainly due to increases in consulting and outside services, personnel-related costs and marketing expenses primarily attributable to the company's COVID-19 vaccine commercialization-related activities and increased headcount.

For the nine months ended September 30th, we recorded a provision for income taxes of $541 million compared to insignificant amounts in the same period in 2020. Our effective tax rate for the first nine months of this year was 7%. It was lower than the U.S. statutory rate, primarily due to nonrecurring benefits related to the release of the valuation allowance, the ongoing benefit of the foreign-derived intangible income deduction as well as a discrete item for excess tax deductions related to stock-based compensation. Net income was $7.3 billion for the nine months ended September 30 of this year,

compared to a net loss of $0.5 billion for the same period in 2020. Diluted earnings per share were $17 for the first nine months of 2021.

Turning to cash and selected cash flow information on Slide 14. We ended Q3 2021 with cash and investments of $15.3 billion compared to $12.2 billion at the end of Q2. The increase is driven by our commercial sales and additional customer deposits received in the third quarter for future purchases of our COVID-19 vaccine. Net cash provided by operating activities was $3.3 billion in Q3, after $4.1 billion in Q2. The quarter-over-quarter reduction is driven by a lower amount of cash deposits for future product supply received in Q3 compared to Q2. On a year-to-date basis, net cash provided by operating activities was $10.3 billion compared to $0.8 billion in the prior year. Cash used for purchases of property and equipment was $164 million for the nine months ended September 30th, compared to $44 million for the same period in 2020, reflecting continuous investments in our manufacturing infrastructure.

Now turning to Slide 15. Let me briefly expand further on our cash and investment position and the net balance of cash deposits for future product supply, as this is an important point when modeling future cash flows. The cash and investment balance reported as of September 30th was $15.3 billion, up from $12.2 billion as of June 30th. The increase is driven by our commercial activities, including cash receipts from product sales and customer deposits for future product supply. The net balance cash deposits for future product supply was $6.7 billion at the end of Q3, at a similar level to the balance in Q2 of this year.

Turning now to the 2021 updated financial framework on Slide 16. For the full year 2021, we expect a product sales range of $15 billion to $18 billion. We now expect to be able to deliver 700 million to 800 million doses at the 100-microgram dose level to our customers. This compares to the prior outlook of 800 million to 1 billion doses. Our total cost of sales includes the cost of goods manufactured, third-party royalties as well as logistics and warehousing costs. Given the favorability we have observed in the year-to-date period, we now expect total cost of sales as a percent of product sales between 16% to 17% for the full year 2021. This compares to our previous outlook of 18% to 20% of product sales. For 2022, we currently expect the cost of sales ratio to exceed 20%, driven by customer mix and multiple presentation types.

On the R&D and SG&A expense side, we continue to plan for an increase on a quarter-over-quarter basis and expect this trend to continue for the remainder of 2021 and beyond, driven by a maturing development portfolio and the scale-up of our commercial activities. Based on further increased visibility of the utilization of our accumulated net operating loss carryforward, expected global sales mix and the mentioned discrete benefits in the first nine months of this year, we now expect our all-in 2021 tax rate to be in the high single-digit range. This compares to our previous forecast of approximately 10%. Since we won't have a material benefit from our valuation allowance in future years, we expect our reported 2022 effective tax rate will increase relative to our 2021 rate. It's also too early to further comment on impacts from a potential tax reform.

Finally, regarding capital investments, we are now planning for approximately $0.4 billion of capital investment to fall into the 2021 calendar year compared to our previous range

of $450 million to $550 million. We are strongly committed to a further build-out of our manufacturing and general company infrastructure and hence, predict capital investment in 2022 will be meaningfully above 2021 levels.

This concludes my remarks concerning the financial performance, and I now turn the call over to Paul Burton.

Paul Burton {BIO 22323763 <GO>}

Thank you, David, and good morning, good afternoon, everyone. With more than 150 million people worldwide now having received two doses of our vaccine, we are humbled to be able to see the positive impact it is having on people's lives around the world. We are reminded of the fact that almost 250 million people have been infected with COVID-19 globally and 5 million people have lost their lives. Our profound thanks, as always, go out to those on the front lines, working tirelessly to keep us safe in this ongoing fight. Through numerous independent studies, time and time again, we see consistent findings showing that mRNA-1273 is highly effective in saving lives, reducing hospitalizations and reducing the risk of COVID-19 infection. I will highlight a few of these independently conducted studies this morning.

In Slide 18, I will begin with some of the data from the United States government. These data come from the CDC and show through September of this year, the difference in COVID-19 cases between fully vaccinated and unvaccinated populations. An unvaccinated person has an 11-fold greater risk of dying from COVID-19, underscoring the importance of getting vaccinated plays in our protection and ending this pandemic. The data showed that vaccination with mRNA-1273 provides the greatest protection, not only against COVID-19 infection, but also death due to COVID-19. In fact, even during the surge of the Delta virus variant during the summer months this year, Moderna's vaccine had the lowest reported deaths associated with breakthrough infection as the CDC data demonstrated.

Approximately 160 million doses of the Moderna vaccine have been administered in the United States. And in the next slide, I want to show you some further government-generated data in a country where the Moderna vaccine has also had extensive use and that country is Switzerland. You can see here exposure data on the left. Approximately 3.6 million people have been fully vaccinated with the Moderna vaccine and 1.9 million people have been fully vaccinated with the Pfizer BionTech vaccine. These government-generated data from the Federal Office of Public Health in Switzerland, again, are clear and showed that vaccination with the Moderna vaccine is highly effective at reducing infections, hospitalizations and deaths due to COVID-19 infection. For every 1 million people vaccinated, use of mRNA-1273 would be expected to result in 643 fewer COVID-19 breakthrough infections, 78 hospitalizations and 38 fewer deaths.

Next, in Slide 20, our data from two other recent independent studies that build on the results I just showed you from Switzerland. The first study on the left side of this slide, followed 38 million vaccinated people in the United States, Iceland, and South Korea. And again, found that those people vaccinated with mRNA-1273 were at 53% reduced risk of a COVID-19 infection and 33% reduced risk of a COVID-19 hospitalization, compared to those vaccinated with the alternate mRNA vaccine. The data on the right hand of the slide

are from a recent publication by Nordstrom and colleagues in Sweden and Norway, showing that mRNA-1273 delivered 87% vaccine effectiveness during a time of high Delta variant circulation in those countries.

The data I've shared so far are all from the general population. Let me turn now to the effectiveness of the Moderna vaccine, in particularly vulnerable populations the immunocompromised. These data were published just two days ago, again, by the United States CDC vision network and examine vaccine effectiveness at preventing COVID-19 hospitalization, which is so critically important in individuals with a variety of immunocompromised medical conditions between January and September of this year. As the authors of this study note, with the exception of those individuals with rheumatic disorders, vaccine effective point estimates were generally higher for the Moderna vaccine than for the Pfizer/BioNTech vaccine and the difference in effectiveness in these hard to immunize populations is shown in the column on the right.

I want to turn now to the topic of myocarditis and to put it in the context of the clinical benefits of vaccination that I've just described with mRNA-1273. It is important to recognize that the cases of myocarditis reported to occur following mRNA vaccination of rare, generally mild, typically respond to conservative treatment and self-limiting. Health authorities have reviewed many data sets and the U.S. CDC and WHO have concluded that there is risk of myocarditis and pericarditis after receiving any mRNA vaccine. The WHO's Advisory Committee on vaccine safety notes that myocaditis can occur following SARS-CoV-2 infection or COVID-19 disease and that mRNA vaccines have a clear benefit in preventing hospitalization and death from COVID-19. Analysis from our global safety database show that the events of myocarditis are very rare. Overall, we observed 9.5 cases of myocarditis per million vaccinated individuals compared to an expected rate of 21 cases per million individuals.

Now in common with other reports of mRNA vaccines in individuals aged 18 to 24, we see an increased rate of myocarditis of 40 cases versus 17 expected cases per million individuals. These data from our own safety database are consistent with the findings from safety databases evaluated by the CDC and other global health authorities. And the link to the CDC analysis is provided on the slide below.

MRNA-1273 has been authorized for use in adolescents, aged 12 to 18 in multiple countries around the world. Moderna's global safety database has information on an estimated 1.5 million of them, providing us an opportunity to look at the rate of myocarditis in those individuals and those data are shown in this table. We see the small absolute well-described risk of increased myocarditis rates in males aged 18 to 24 that I just described to you. But we do not see an increased risk in adolescents neither in boys nor in girls. These data are reassuring and important as we continue to offer mRNA-1273 to adults, adolescents and as we file for authorization in children.

So in summary, the data I've shared with you today from independent government reports in the United States and in Switzerland, countries with high vaccination rates of Moderna's vaccine showed mRNA-1273 is associated with lowest breakthrough infections, hospitalizations and deaths due to COVID-19. Other independent studies in millions of individuals continue to show that mRNA-1273 is highly effective in reducing the risk of

breakthrough COVID-19 as well as hospitalizations and death. And importantly, this is also true in those vulnerable and hard to vaccinate immunocompromised patient populations. Moderna's global safety database of 151 million vaccinated individuals shows a rate of myocarditis in males aged 18 to 24 that is consistent with analysis by CDC and others. Moderna's global safety database does not show an increased risk of myocarditis in 1.5 million individuals below the age of 18 and vaccinated with Spikevax.

So these -- this concludes my quick overview of some recent analyses of mRNA-1273 effectiveness data and review of data from our global safety database. And I will now turn the call over to Stephen.

Stephen Hoge {BIO 17925815 <GO>}

Thank you, Paul, and good morning or good afternoon, everyone. Today, I'll review the progress we've made across our vaccines and therapeutics pipeline. Let me start with our COVID-19 vaccine, mRNA-1273, for adult ages 18 and above, where there are a number of important regulatory updates. First, we have announced that the FDA granted priority review to Moderna's COVID-19 vaccine BLA. In October, we also received an EUA from the FDA and the European Commission's approval for a booster dose of our COVID-19 vaccine at the 50-microgram dose level for the adult cohort, ages 18 and above.

Turning to the adolescents and pediatric settings. As a reminder, there are two clinical trials for each of these groups: TeenCOVE is our study in the adolescent population, 12 to 17 year olds; and KidCove is the study in the pediatric population, age 11 and younger. For the adolescent population, 12 to 17 years old, our vaccine is authorized in a number of countries worldwide, including the United Kingdom, the European Union, Canada, Switzerland, Japan, Thailand, Taiwan, Saudi Arabia and Argentina to name a few.

We've submitted data from our KidCove study to the FDA in the United States as well as to other countries. We're recently notified by the FDA that the agency will require additional time to evaluate our proposed amendment due to recent analysis of the risk of myocarditis after vaccination in some populations. The agency expects this evaluation may extend until January 2022. As Paul noted, Moderna's global safety database includes an estimated 1.5 million adolescents, who received the Moderna COVID-19 vaccine, most outside of the United States. And to date, we have not observed a rate of myocarditis from those younger than 18 years in our safety database that points to an increased risk of myocarditis in that population. We continue to believe the benefits of vaccination significantly outweigh the risks.

In the pediatric setting, our study known as KidCove is ongoing and is focused in three age groups, a group with children six to 11 years of age; a group of two to less than 6; and a group of children six months to less than two. The trial consists of a dose escalation phase for each group, followed by an expansion phase once the dose has been selected. Last week, we shared positive top line data from the oldest of the age groups in KidCove, the six to 11-year-old cohort, showing the 250-microgram doses of mRNA-1273 were generally well tolerated and that the primary immunogenicity endpoints were met. We will submit our results soon to the EMA and other global regulatory agencies. For the

other two age groups in KidCove, the two to less than six years old group and the six-month to less than two-year old group, our dose selection studies are ongoing.

On the next slide, let me share with you some of the data we have in children ages six to less than 12 years of age. This data is after dose one as we are waiting for additional follow-up time to share the post-dose two data. As a reminder, the study was randomized 2:1 for vaccine versus placebo. Based on the case definition of COVID-19 that we used in the Phase III adult study, the observed interim vaccine efficacy was 100% in this analysis, starting two weeks after the first dose and using that case definition. Vaccine efficacy against SARS-CoV-2 infection was also high at 80%, and vaccine efficacy against symptom -- asymptomatic SARS-CoV-2 infection was 65%. Both endpoints that we think are incredibly important as we seek to end the pandemic.

Turning now to our booster and next-generation COVID-19 vaccine programs on Slide 28. As a reminder, we are evaluating multiple COVID-19 vaccines as potential boosters to provide the broadest range of countermeasures to the virus, as it continues to evolve. We were granted EUA for the 50-microgram dose of our current vaccine as a booster, as mentioned previously. And we are currently evaluating two variant-specific vaccines and two multivalent vaccine candidates, which are combinations of different variants of concern in an effort to stay ahead of the evolving virus.

In addition, we're also evaluating mRNA-1283, as a next-generation refrigerator stable vaccine, which is in a Phase I study. The interim analysis of that Phase I data has been completed at three different dose levels and indicates that a lower dose of mRNA-1283 can achieve similar neutralizing antibody responses as a primary -- in primary series as our authorized vaccine mRNA-1273. mRNA-1283 also had an acceptable safety and tolerability profile and we're moving forward towards a Phase II booster study for that candidate. This will also evaluate even lower doses of mRNA-1283 given the strong boosting performance seen in Phase I. While the start of our booster strategy in late January of this year was in response to the threat of newly identified variants at that time, our booster strategy has continue to evolve as the pandemic unfolds.

Slide 29 is a slide we shared at our Vaccines Day in April of this year. At the time, the graph on the left was illustrative of our view of the likely path for the pandemic, based on our perspective on respiratory virus evolution and epidemiology, including prior coronavirus pandemics. Today, it's becoming clear that the SARS-CoV-2 virus is following the footsteps of other respiratory viruses, and is on its way to becoming a seasonal epidemic/endemic threat.

So where are we now? With Delta and the potential for other variants, the winter of 2021, 2022 still looks to be a time of moderating but persistent variant epidemic waves. Infection and reinfection continue to cause morbidity and mortality during this phase, but hopefully in fewer people. The focus will remain on suppressing the rate of viral evolution and emergence. Primary vaccination is critical. But given the high rate of background transmission, booster vaccines will also be important in all countries.

Looking ahead, we expect 2022 will be the beginning of the seasonal endemic phase, reinfections in individuals who are at high risk, including older adults, the immunocompromised or healthy adults with more rapidly waning immunity due to under vaccination with potentially less effective vaccines will be at the greatest risk for severe outcomes. As with the recent Delta wave, this will include some risk of hospitalization and unfortunately, some risk of death as well as social disruption. We believe this will become the primary population for whom seasonal boosting will provide a significant enduring benefit.

In summary, as we described earlier this year, we believe SARS-CoV-2 is following a familiar path that will ultimately become a seasonal threat to a large population of higher risk adults. Perhaps the biggest unknown in the near term is the extent to which further viral evolution in the coming Northern Hemisphere winter and Southern Hemisphere winter in 2022 will create hurdle ground for new -- newly transmissible and immune-evading variants to emerge. If so, rapid boosting may become necessary. We will need to remain vigilant throughout this time as we fight the pandemic, and we are ready to advance updated boosters rapidly if they become needed.

Now moving from COVID onto Slide 30. We announced in September that the Phase I portion of our quadrivalent seasonal flu vaccine, mRNA-1010, is fully enrolled, and we look forward to sharing data from that trial and moving to Phase II soon. We also announced positive Phase I interim data from our RSV vaccine in older adults in September, and we plan to start pivotal Phase II/III RSV vaccine trial before the end of 2021. Separately, the pediatric RSV program continues to move forward with cohorts enrolling well in our Phase I study. Our hMPV/PIV3 study in pediatrics is also currently enrolling in toddlers.

We were very excited to announce last week that our Phase III CMV vaccine trial has dosed its first participants. The start of the Phase III trial, CMV -- CMVictory is an important step in evaluating our CMV vaccine against congenital CMV. As a reminder, CMV is the number one cause of birth defects in the United States, and we are evaluating the safety and efficacy of mRNA-1647 in women ages 16 to 40 at the 100-microgram dose level. The trial is starting in the U.S. and will include approximately 150 sites globally, and will enroll on approximately 6,900 women of child-bearing age. Importantly, including criteria of the trial includes women at high risk of CMV exposure through direct exposure in the home, socially or occupationally to children under five years of age.

Diversity in our clinical trials is also extremely important to us, and we're proud to continue our commitment from last year on clinical trial diversity. We believe setting targets and measuring ourselves against them remains one of the most important ways we can work to address the health care inequity in clinical research. For the CMVictory Phase III study, our goal is to have 42% of the trial participants in the United States come from communities of color, many of which are disproportionately impacted by the CMV virus.

Moving on from vaccines. This slide highlights our mRNA therapeutics pipeline. At R&D Day, we described how our modalities and therapeutic areas overlap. In oncology, our PCV Phase II trial is now fully enrolled, and we expect to readout for that as early as the fourth quarter of next year. Separately, an expansion cohort in head and neck cancer in

our Phase I trial is ongoing. We also have Phase I trials ongoing for our KRAS vaccine, which is partnered with Merck, the triplet program; and the IL-12 intratumoral program, which is partnered with AstraZeneca. In cardiovascular, our VEGF program, is also partnered with AstraZeneca, has completed the enrollment of a low-dose cohort in its Phase II study and AZ will be providing updates at a presentation of the data at the American Heart Association meeting in two weeks.

Within autoimmune, our IL-2 program is in a Phase I trial in dosing. And within rare diseases, our PA and MMA trials are ongoing in Phase I, and our GSD1a program has an open IND and is expected to start a Phase I study soon. I'm also very excited to announce that our first cystic fibrosis program has moved into preclinical development with IND enabling studies now underway. We and our partners at Vertex are pleased to announce that development candidate, VXc-522. This program marks our first program in a brand-new modality inhaled therapeutics. As a reminder, Moderna modality encompasses a new method for utilizing our proprietary lipid nanoparticle technologies and mRNA technologies to bring forward medicines.

Now double-clicking for a moment on the CF programs in research. Recall that we have two partnerships with Vertex. Our first collaboration targets the CFTR protein in trying to produce it using mRNA and LNP technologies. This is where we are advancing our candidate, VXc-522. We also have a collaboration with Vertex using mRNA for gene editing and gene therapy. Both collaborations are focused on treating this 10% of CF patients with disease that unfortunately is not addressable with current CFTR modulators. For this 10% of the CF population, alternative purchase are absolutely necessary. And the exciting update today, as I said a moment ago, is that we're announcing the first development candidate to move into development from that collaboration described on the left-hand side of this slide.

In this collaboration, we're delivering messenger RNA that encodes for CFTR protein that is missing or nonfunctional in patients who suffer from cystic fibrosis. We plan to target that 10% that I mentioned a moment ago. We've been working incredibly hard with Vertex to advance the candidate, and we are very excited that, that has now moved into IND-enabling studies. As Vertex announced recently, they expect to submit an IND in 2022, paving the path for clinical studies in these patients.

In the close, I'd like to just highlight our pipeline on the following three lines, starting on Slide 35, which includes our respiratory vaccines in development. Slide 36 summarizes our large portfolio of latent virus vaccines and vaccines against other viruses. And on Slide 37, you will see the extensive mRNA therapeutics pipeline that we have in development.

With that, I'll hand it back to Stephane to close.

Stephane Bancel {BIO 15174250 <GO>}

Thank you, Stephen. Slide 39 is from September 9th R&D Day and summarizes the product franchise we focus on at Moderna. Priority number one is our pan-respiratory

annual boost of franchise. Priority number two, is our first in-class vaccines for latent viruses. Priority number three is our therapeutics based on mRNA-encoded proteins. And priority number four is the therapeutic space on mRNA-encoded gene editing enzymes. As we have said for several quarters now, SARS-CoV-2 is here to stay and will evolve from a pandemic to endemic setting. We believe that 2022 will see pandemic in low-income countries throughout the year, but at high income countries, the year would be of two halves, pandemic priming for children and boosting for others with an endemic boosting campaign in the fall of '22.

On Slide 42, you can see the revenue drivers that we anticipate will pay out in 2022. We believe there are three components that will drive our COVID-19 vaccine revenues for next year. First, signed APAs. We have already signed around $17 billion of advanced purchase agreements or APAs for delivery in 2022. Second, APA options. They are up to $3 billion of APAs that are in options. Some options have been converted in Q3 from options to FIM order. Third, the fall of '22 commercial market. We also believe that the fall of '22, assuming that BLA is granted for boosters, will drive the commercial booster market of up to $2 billion. So in total, at this point, we believe that 2022 revenues could be between $17 billion and $22 billion. We, of course, continue to have discussions of 2022 APAs with governments and international organizations, including COVAX, the Pan American Health Organization or PAHO, and the African Union.

For this pan-respiratory franchise, our goal is to evolve the COVID-19 vaccine primary series into fall of '21 boosters, which is happening as we speak and then fall of '22 boosters and then add to a COVID booster of two booster in a single dose and then added to COVID and flu and allergy booster in a single dose. Our flu vaccine human data should be out soon. And the team is already preparing the Phase II/III for flu, and RSV is moving fast to Phase II/III.

If we looked at the health damage of latent viruses, it is profound. EBV is a major cause of infectious mononucleosis. EBV has been reported to increase risk of multiple sclerosis. EBV is associated with certain cancers and autoimmune diseases and EBV is associated with a higher risk of long COVID. CMV associated will be the leading cause of birth defects. CMV is a major driver of immune dysfunction with aging, CMV associated with cardiovascular diseases, CMV associated with cancer and cognitive impairments. For now, our focus is CMV, EBV and HIV, but we are developing in a labs vaccine against all the latent viruses which short human health. Our goal is to eliminate these viruses.

As we discussed earlier, several cancer and regenetic programs are in the clinic and should provide clinical results soon. On November 15th, AZ will present Phase II data in patients from the VEGF program at the American Health Association. And we are pleased to announce the new modality with Health Pulmonary therapeutics.

Modernizing is our effort, we expand the use of our platform to create more innovative drugs to help patients. Our strategy to invest internally under the leadership of Dr. Eric Huang with a dedicated team and to set up licenses agreements with next-generation gene editing companies. The Metagenomi partnership is a first step in that direction. The strategic part of the company is very clear and exciting. We want to stop people getting hospitalized from respiratory infection. We wont stop until this goal is achieved.

We want to stop for human beings from suffering from these latent viruses. We want to bring to market mRNA protein therapeutics in oncology, cardiology, rare genetic disease, autoimmune. We want to bring therapeutics using gene-editing enzymes. We believe Moderna could become the most impactful drug company in the world. As we scale, we realized that we needed to go further in setting the right framework for our team to understand what has made Moderna, Moderna. So we worked through Q2 and Q3 to articulate our mindset, how we behave and make decisions at Moderna. There is more information on our website, and we'll be happy to spend time with those of you who want to learn more about them.

Let me just summarize them at a high level. At Moderna, we act with urgency. Action today compounds the life saved tomorrow. We'll pursue options in parallel to make the best choice later. We accept risk as the only path to impact. We're obsessed over learning. We don't have to be the smartest. We have to run the fastest. We pivot fearlessly in the pace of new data. We question convention because proven models don't always fuel the future. We push psst possible. We behave like owners, the solutions we are building go beyond any job description. We act with dynamic range, driving strategy and execution at the same time and at every step of the way. We will remove viscosities to encourage collective action. We prioritize our platform over any single product. We digitalize everything possible using the power of digital information to maximize our impacts on patients.

We want to be the most impactful drug company in the world, we care deeply about doing it the right way. It means being a great company to work for, as exemplified by our seventh consecutive year ranked as the best company to work for by Science. But it also means building a company that is responsible and minimizing our impact on the planet. We are proud to have announced earlier this week that we will work to achieve net zero carbon emission for operations globally by 2030. I want to thank the Moderna team for their commitment to our mission, and their relentless work to build the best Moderna over the next 20 years.

Before we jump into Q&A, we wanted to share the dates of our annual investor events for 2022: Vaccine Day on March 24; Science Day on May 17; and R&D Day on September 8. Operator, we will now be happy to take any questions.

Questions And Answers

Operator

Thank you. (Operator Instructions) Our first question comes from the line of Salveen Richter from Goldman Sachs. Your line is open.

Q - Salveen Jaswal Richter {BIO 15151450 <GO>}

Good morning, thanks for taking my question. For 2022, can you walk through the supply aspects. Are you still guiding to up to 3 billion doses here? And can you also speak to demand dynamics? Is there upside to the guidance that you've commented on today for

future signed APAs. And then secondly, how confident are you that you can fix these supply issues and over what time frame?

A - Stephane Bancel {BIO 15174250 <GO>}

Great, Salveen. So let me take those different questions. Let me start with the short term. Yes, we really believe we can fix those short-term supply issues. As I tried to explain in my remarks, those are what I would qualify as teething problems of scaling up so fast. In Q1, it was all about making enough drug substance, and we are literally now waiting to have enough drug substance to fill vials. And the teams scaled very nicely. In Q2, the challenge we had internally was all about filling vials. And the complexity of Q3 has really moved to the, I would say, the back end of the supply chain, which is releasing product and shipping products.

And the complexity has been around just a number of markets we have to serve. Beginning of the year, it was mostly shipping to CDC in the U.S. and Europe, and that was it. But then as we increased the number of countries to many dozens by now, that the complexity is just increasing and it's even further now that we are serving COVAX, we need to go country by country. So that's just the type of teething problems that we are experiencing right now. We have increased personnel. We have invested in digital to help the teams. So I already expect this to be resolved like we resolved the drug substance strategies in Q1 and the drug product strategies in Q2.

The 2022 -- in terms of drug substance, yes, we could see make up to 3 billion doses in terms of material. As you know, that number was really depending on the booster dose. And now that we're on the other side of that decision with the 50-microgram dose, we confirmed we could make up to 3 billion doses, if there was a need for it. The challenge in 2022 is going to really be around product form because as the market moves to an endemic market, you're going to need basically vials to be able to go to less number of dose per vile. Again, in the pandemic setting, as you know, we launched with 10 dose per vial, which we think was really an update in low-income offer, where we will add more into vials now. But as we think about the endemic market, and we're trying to serve pandemic and endemic at the same time, we just need to keep adding presentation to be relevant to health care workers and health care systems around the world.

So drug substance will not be an issue. There's, of course, as I described, potential upside to those numbers. We still have quite a number of APAs being discussed with countries around the world. We don't know what will happen in terms of epidemiology. Is there a new variant coming? Is it a variant where the current vaccines is still helpful is still helpful or we need, as Stephen described, a new booster. There is, of course, a big question mark here that we'll follow in epidemiology literally on a daily basis.

And then there's so many for boosting people around the world that have had non-mRNA vaccines. As everybody knows, there is a prime of waning immunity over time. So time is not our friend as people see the levels antibody going down. And as we have new variants like Delta or potentially others, but we should not forget that most people around the planet have not had an mRNA vaccine injected in their body to date. And so we believe there is an important need to boost people with mRNA vaccines. And as Paul

showed the real world evidence securing the data from CDC and Switzerland, the more we get data and the more time is helping to see, we see a net differentiation between products. And this doesn't go unnoticed by governments around the world, who are working really hard to preventing hospitalization and death.

And so, there is upside to that. Again, it's a very unpredictable environment. None of us has worked for pandemic before thankfully. But you will be assured that we will keep scaling up manufacturing, we keep in getting with government, so that we can maximize how we can help people and the revenue should follow from that.

Q - Salveen Jaswal Richter {BIO 15151450 <GO>}

Thank you.

A - Stephane Bancel {BIO 15174250 <GO>}

Thank you, Salveen.

Operator

Your next question is from Matthew Harrison with Morgan Stanley. Your line is open.

Q - Matthew Kelsey Harrison {BIO 17603148 <GO>}

Great. Good morning, thanks for taking the question. Two for me this morning. So first, can we just spend a moment on myocarditis. And I think the overlying question here is, why do you think the regulator is more concerned with your vaccine in younger age groups compared to Pfizer, which has obviously already been approved in younger age groups. And then -- and related to that, how much of an impact is this having on uptake and distribution of your vaccine given that we see Pfizer continue to highlight potential differences and bringing that to government's attention?

And then secondly, on flu, can you just comment on how you're going to interpret these results? Obviously, we're just going to get titer results. But I think it's your premise that you can achieve a much higher efficacy flu vaccine compared to traditional flu vaccines. So do you think there is a clear correlation in titers to efficacy? And what level of titers would demonstrate very high efficacy? Thanks.

A - Stephen Hoge {BIO 17925815 <GO>}

Thank you, Matthew. So this is Stephen. I'll take -- try and take those questions. So first, look, I think it's most important to say that what we communicated and desired to be maximally transparent last week was that the FDA, unlike other regulators, has asked for some more time to review emerging recent data. And that might take until January. I think your question is how is that different vis-a-vis what happened with the Pfizer vaccine. I think the most important thing to recognize is that the Pfizer adolescent vaccine was authorized prior to any substantial discussion about myocarditis as a benefit or as a risk. In fact, the signal emerged a few weeks later just before we made our filing. And I think a prudent approach there was to -- the Vertex conducted, there was ongoing discussions.

But what we've continued to see over the course of the -- over the last four or five months is that for both mRNA vaccines, there's a question of whether there's an increased rate of myocarditis above background in 18 and 24-year-old males, a relatively small population, but an important one. And I think it's -- in the face of those continuing emerging questions, that the FDA is being diligent and appropriately conservative in their approach and making sure they have the time to review those. And they have continued to come out over time. And so I think, principally, what we're seeing here is -- the difference is a function of timing, which is that the other vaccine had been authorized prior to this concern, and there has been continued emerging data around that.

We are very grateful to the FDA for that diligence. I would note that the same information are available to other regulators. And as I have said before, we are authorized for that population internationally. And fortunately, as Paul characterized, we have not seen an increased rate of myocarditis in 12 to 17 years. And we think, over time, the substantial benefits of our vaccine will ultimately win out here. And so we look forward to continuing to work with the FDA. So that's my best version of what I think we heard from them last week.

The question about how we see that evolving over time. Obviously, internationally, we are participating in the market. In the United States, adolescent vaccinations have substantially tailed off, as we all would note. And so the extent that there is an ongoing need in the United States for vaccination, it is a diminishing market for sure. And again, this is a primary series vaccine. And so we do hope that most people in the world will zero convert and not need a primary series moving forward.

The question then of what is that endemic market going forward that is of greatest importance. And I tried to summarize that in our view of the evolution of this virus and what that need will be. It is, we believe, in the future, a booster market. And for booster market, targeted at those populations that are higher risk of respiratory disease. Those populations tend to be older adults and immune compromised. Places where we think mRNA-1273 is demonstrating really remarkable efficacy differentiated perhaps. But public data -- publicly-reported data is really encouraging on that dimension. And I would note that it's not a population that's associated to-date with any of the vaccines that have an increased rate of myocarditis. And so the benefit risk there, we think, even swings more favorably to 1273, but we'll allow data to continue to develop and ultimately drive this behavior. So we are quite encouraged by the performance of the vaccine in the population that we think is going to be most important in the years ahead.

The last question was on flu, which is what do we think about that data? Obviously, as you pointed to, there are correlates of protections that have been used previously with HAI titers in influenza vaccine. We will be looking at that as I'm sure everybody will as well as other responses in the immune system as we continue to try and identify the optimal dose. I'm not going to put out there a view of what I think our view of success will look like. I would just say that we have very high expectations for our platform.

Now, we do believe that our performance in older adults, including with the COVID vaccine, but also more recently with the RSV booster study in Phase I demonstrates that our platform does incredibly well in those at highest risk of these respiratory viral

diseases. And so we're optimistic that we will continue to show strong performance, hopefully, strongest performance in those populations. But I won't give you a specific titer number today.

Q - NA {BIO 19970485 <GO>}

Yeah, And maybe just to add to Stephen's point, Matthew, I think we should not forget the company's strategy, which is a long combination. We believe that combining flu and COVID booster in a single dose and then adding RSV is the critical central part of our strategy. We think it has tremendous value for compliance, for protection. It has a tremendous value in terms of convenience to the consumers. I don't believe that most people will want the flu shot and the COVID shot and the RSV shot every fall. And as we heard from the (inaudible) and health care worker, that's the value of a product. So we believe the combination is really a critical success factor.

Q - Matthew Kelsey Harrison {BIO 17603148 <GO>}

Thank you.

Operator

Next question is from Ted Tenthoff with Piper Sandler. Your line is open.

Q - Edward Andrew Tenthoff {BIO 1880164 <GO>}

Great, thank you very much and congratulations on all the progress. My question has to do with the emerging Orphan disease pipeline. And I've been really impressed by the progress that you guys are making there in these important patients. And I think the mRNA technology just suits ideally here. So what do you see as sort of the plans over the next couple of years. Kind of take us forward a little bit, what could this pipeline look like? And maybe you can just give us a sense of where you think Moderna will be in the Orphan disease setting in a couple of years? Thank you.

A - Stephen Hoge {BIO 17925815 <GO>}

Thank you, Ted. I'll take that too. So first, I think we're very excited about the programs that are already in the clinical space, either already dosing patients or about to start. And so I think the most important thing is looking forward to next year, the demonstration, we would hope, of proof of concept in that rare disease modality. As you know, we are dosing quite a large number of folks in propionic acidemia, and we've been dosing in methylmalonic acidemia, and with the opening of the; GSD1a IND, we'd hope to be following a short order there.

So all three of those are potentials for us to demonstrate the real proof that this technology can be used to correct in more in areas of metabolism in these populations. I'll also note that there's a quite a wide range of disease going down as young as two years of age in some of the organic acidemias and not the older adults in some of the GSD1a program. So we're going to be demonstrating quite a lot there. Crigler Najjar presents another opportunity for that proof-of-concept as well as the PKU program when that moves forward, but those are still in preclinical, as I said.

So the question is what do we do on the back of that proof-of-concept from any one or all of those programs. What you've seen us do in respiratory vaccines and in vaccines generally is probably the best predictor of how we will respond, which is, as you know, there are a very, very large number of metabolic diseases that could be addressed to deliver through mRNA therapy. We have -- we could list off large groups, but urea cycle disorders, other organic acidemias, so many beyond that. And even in moving into more broadly present metabolic diseases. So what we would do is we would define that systemic intracellular therapeutic modality as a core modality, just like we did with vaccines a couple of years ago. And that would cause us to dramatically expand that pipeline.

Now I can assure you we're looking at those programs in research right now, but we will -- we have held back on moving them into preclinical development and putting them on our pipeline until we've seen the modality perform. So that is probably the most important thing for me, looking at the rare and orphan disease space over the course of the coming year is when do we cross that threshold? And then ultimately, when do we expand dramatically that pipeline of programs.

Q - Edward Andrew Tenthoff {BIO 1880164 <GO>}

That makes a lot of sense, and I really appreciate seeing the new pulmonary disease areas. So thanks for all the updates.

A - Stephen Hoge {BIO 17925815 <GO>}

Thank you.

Operator

We have a question from Michael Yee from Jefferies. Your line is open.

Q - Michael Jonathan Yee {BIO 15077976 <GO>}

Hi, good morning, thanks for the questions. Two questions. One is just trying to clarify guidance. I think there's some confusion around guidance. So I would love to understand some clarification. You lowered 2021 a little bit, I think, by $5 billion, but raised 2022, 2022 by $5 billion. Is that a timing shift of deliveries? And how much of that is just option contracts as you think about 2022 because you've talked about APAs as firm commitments. I'm just trying to understand how much our commitments versus acceptances and how to think about those two.

And then on flu -- following up on the flu question, I think people are looking at labels and looking at fall in increases and seroconversion rates of four to seven times and 50% to 60% seroconversion rates. Are those accurate numbers? Are those numbers we should be looking at and comparing to? Maybe you could just help us qualify that because I think that's what people are trying to do. Thank you so much.

A - Stephane Bancel {BIO 15174250 <GO>}

So, good morning, Mike, it's Stephane. I'll take the first one and give it through to Stephen. So I think you already highlighted some of the other drivers. So on '21, so there's two things I think that is driving, first is, of course the lower volume. And the second one is price. As you know, we are working very hard with several governments to send products that they have bought for high-income countries like the U.S. to low-income country this side of Christmas.

And so when you think about just the U.S., the U.S., we see that publicly. When we announced our African Union partnership, the U.S. decided to delay to Q2, the delivery over December quarter. That volume is going to African Union at a low tier price. So do you have an impact on the turnover just by doing the math of a lower price on the same volume right there? And some orders that are moving from December to January on the supply volume side of things. So when you're on to '22, where you have the increase of volume moved from December to January. That is one. We've signed new APAs since the last numbers. And as I said, some options have been exercised. One of them was a COVAX option. That was exercised at the end of Q3. That is now counted as a full APA because I've seen those firm commitment and some prepayments and so on. And so those are the dynamics that are happening.

The team also is starting to spend a lot of time to commercial team on focusing on the fall of '22 because we think that's going to be an important moment. The mix and match, we think, is critical. That is now allowed in most places. In some countries, that isn't just mix and match for a long time. But the U.S. market, of course, is important, is allowing mix and match. And as Paul just shared, we believe that as time will go, the data will show that what we believe is that we have a longer duration efficacy vaccine on the market.

And today, if you look at data and market research, very few consumer in the U.S. know that. People that are listening to this call now that because you read papers in on a daily basis, a few people in the U.S. We believe there is an opportunity for us between now and let's say next summer to make sure that people understand the facts, understand the real-world evidence so that they can make an informed decision and that includes the health care workers, the pharmacies, the doctors, the nurses, that include the consumers directly.

And so this is why, as we're starting to sharpen our pencils and probably spend a lot of time working towards the fall of '22, we believe that's another piece that was not if you go back to our previous numbers. We only disclose APAs and options of APAs, the commercial opportunities for fall of '22, we think is going to be an important vector to the '22 sales.

Stephen, answer?

A - Stephen Hoge {BIO 17925815 <GO>}

Sure. So I'll try and clarify that answer on conversion rates. So we -- it is a Phase I study. And so we are looking at a range of doses, and I have not got access to the data. So just don't -- I don't want to presuppose the specific answer yet. As soon as we have the data, we will provide our thorough interpretation of it. However, as you point out, generally seroconversion is defined as a fourfold rise in titers above baseline, and we've done that

in some of our other studies. And we will be looking at that from the percentage of people who achieve that seroconversion.

And most important to me will be looking at the consistency of that percentage across ages. In particular, the older adults where you often don't achieve the type of the same level of immunogenicity, but we believe with our platform well. There are other endpoints as well in terms of seroprotection defined as absolute titers, again greater than 40 is accepted. We will look how high that goes because that can also be reassuring. But I don't think right now we're ready to guide on a specific target that we will declare a success other than looking again at that fourfold rise for measuring seroconversion across the range of agents that we'll be studying in the study.

Q - Michael Jonathan Yee {BIO 15077976 <GO>}

Got it. Thank you.

A - Stephane Bancel {BIO 15174250 <GO>}

Thank you, Michael.

Operator

Next question is from Gena Wang from Barclays. Your line is open.

Q - Gena Wang {BIO 18848097 <GO>}

Thank you for taking my questions. I have two regarding the COVID vaccine. And the first question is that given the supply restraints, do you see 100-microgram doses being used as 250-microgram doses? And then also any hesitance due to safety concerns, and we did see a few countries put a cautionary action on Moderna vaccine. And my second question is, in the U.S., if we do the math, you completed delivery of 300 million doses and then U.S. exercised total doses of 410 million for 2021 and then 90 million doses in first quarter 2022. So just wondering how much of the remaining 110 million doses in 4Q '21 will flow through next year?

A - Stephen Hoge {BIO 17925815 <GO>}

So I can try and take the first question, I'll then invite Paul as well. So I think in terms of -- you referenced some of the more recent communications that happened from public health officials, for instance, in the Nordics and elsewhere, I would note that those same communications, literally often the same documents and include reference to the fact that there's very strong efficacy for the Moderna COVID-19 vaccine. And in fact, some of those Nordic country communications include reference to the fact that it looks to be potentially greater in terms of protection as emphasis for why the vaccine, not only is still recommended in many of those jurisdictions, but ultimately, provide very favorable benefit risk. And so we continue to believe that whole picture looking at the benefit and quantifying that benefit, which we think is substantial and larger than any risks contemplated here is really important. And we, again, look to those communications that clearly state that.

Paul, anything you would add to that?

A - Paul Burton {BIO 22323763 <GO>}

Only, Stephen, that recently, I think last week, the WHO gave updated guidance, continuing to endorse the vaccines in mRNA-1273. And I think as they are doing their analysis of these data sets -- subsets that they need to think about potential biases that occur in general practice, looking at the primary vaccination schedule, the difference in timing, we know that vaccines are used differently sometimes, and that may account for these. But I think clear standing behind the data.

Stephen?

A - Stephen Hoge {BIO 17925815 <GO>}

Yeah, I mean just as a closing comment, I would just reference, we have entered in some of these markets into a very interesting phase of the pandemic, which is that we are in the lower risk population and we are providing vaccination to them as is appropriate. But -- so as we do that, we're looking at benefit risk in the most -- increasingly cautious ways, and that's appropriate. But as we look forward to next year and we start thinking about boosting and particularly, the seasonal markets are protecting those at our highest risk, I think that calculus obviously changes pretty dramatically. And so I think we are in a period of time where we are, again, looking at the lowest risk populations. And I think that is transient period time ultimately because it is high risk populations that are of greatest concern looking forward from 2022.

A - Stephane Bancel {BIO 15174250 <GO>}

Yeah, maybe just to add just a bit of color, I've had a chance to speak with a couple of health ministers across the world in the last week or two. And I think people are very clear that the risk is low. That it's very manageable, as Paul said, and it's only in the male 18 to 24. And those health ministers were -- they care about going back to the risk profile that Stephen just mentioned, take care of about having the winter where they don't have hospitals exploding again. And this is driven by the 50 and above, the 40 and above, where they know the vaccine, as Paul mentioned, with the data from the U.S. or Switzerland or many other countries that 1273 vaccine seems to be a vaccine providing the longest protection of efficacy, and that's what they care about.

And so I think that people are getting educated and looking at the data. They're just trying to look at the facts and figure out in a very practical way, how they keep the economies running, how they keep people out of our hospitals and very focused on the high population. As in many countries, the boosters are not approved in the younger population whereas they are being really advertised and promoted in the older population, so that people get boosted and don't get sick and hospitalized this winter.

On the U.S. government, Gena, we don't comment on volume. U.S. government is a private contract to the government. But indeed, there are some shift from Q4 to next year, both Q1 and Q2.

Q - Gena Wang {BIO 18848097 <GO>}

Okay, thank you.

Operator

Next question is from Cory Kasimov with JPMorgan. Your line is open.

Q - Cory Kasimov {BIO 3009346 <GO>}

Hey, good morning guys. Thank you for taking my questions. Two for me as well. So first of all, in terms of the 2022 APAs that you outlined, are there $17 billion worth of existing contracts constructed as firm commitments or do countries have -- the contracts have optionality embedded in them where in countries don't necessarily have to take the full amount depending on the evolution of the pandemic. And then my second question is, given your comments on the call about potentially moving into the endemic phase by the second half of next year, should we think about 2022 revenue as being weighted toward the first half of the year? Thank you.

A - Stephane Bancel {BIO 15174250 <GO>}

Thank you, Cory. So let me take this part. The APAs do not have options. When we say 17 billion of APAs, those are firm orders, signed orders and all our APAs have upfront payments. Now, David did a nice job walking you through the cash upfront we are receiving for those contracts. It's one of the way that we are conducting our business. We want people to be very committed and to have a material upfront of the total value of the deal when they sign. The options components that we characterize is up to 3 billion as of today.

Those are true options, meaning people are reserving capacity. And sometimes it's for financing rhythm because, again, as I said, we do not do APAs without upfront. And one of the best example today probably is COVAX. We had to do a quarterly option with COVAX. As I said, it just exercised our Q2 option at the end of Q3. But Q3 2022 and Q4 2022 COVAX still options and it's mostly because of the funding issue. They don't have the cash. They get cash from their different funders, which are mostly government and foundation on the kind of a month-to-month basis. And so we did that to help COVAX and to do the right thing to help the planet. As you know, we don't have to do options. We say, if you want the vaccine when you sign a contract and you pay an upfront. But with COVAX, we have to do so.

We thought it was the right thing to do. And so we expect, if they want their Q3 volume, that in Q1, they will exercise the options -- sorry end of Q4, they will exercise the options, and that you will go like this. On the endemic and the ventilation of the sales over the year, I think it will be dangerous to assume at this stage one way or other in terms of first half and second half because of volume and also pricing. As you get a sense, the COVAX, the African Union and some BARDA deals we have lower prices and David mentioned that, fewer pricing. And so there might be a large volume, but the product might be way lower than what the commercial market could drive, which we believe is going to be above what has been the pandemic price again because of volume. And so we are so

people stocking ahead of when they need to inject in pharmacies. I would be cautioned that assuming Q1 to be lower and Q2 is a bit too early.

Q - Cory Kasimov {BIO 3009346 <GO>}

Okay, thank you. That's helpful.

A - Stephane Bancel {BIO 15174250 <GO>}

Thank you, Cory. Next question is from Geoff Meacham from Bank of America. Your line is open.

Q - Geoffrey Christopher Meacham {BIO 21252662 <GO>}

Hey guys, thanks so much for taking the question. I just had one more on the flu program, maybe for Stephen. It's highlighted that you'll see an increase in antibody titers. I was just thinking for the combo study though with 1273, what other factors do you need to address to derisk that study? And just I guess I'm trying to determine how to optimize the regimen by things like dose titration or even selecting the population by more urgent need for the COVID booster side of things. Thank you.

A - Stephen Hoge {BIO 17925815 <GO>}

Thank you for the question, and it's a great one. So what we're going to be looking at in the combinations are actually the things that you just pointed to. And so in particular, we do believe the most of the value of respiratory vaccination in the near term boosting will be in older adults, 50-plus or 60-plus depending upon how you want to look at it, very similar to the RSV population, certainly for the flu population and recommendations globally. And we think COVID moves that direction as well.

And so as we look to the first part of the question, where do we intend to optimize that ratio in immunogenicity, it really is towards those higher risk populations that do need, we think, a respiratory booster every year. When it comes to looking at the -- what are the combination of things that we're going to be doing in selecting that ratio in dose, obviously, it's mostly going to be immunogenicity and the tolerability profile. Fortunately, these vaccines have been very safe to date in these older adult populations. None of the concerns that we're having about myocarditis really exists in the 50 plus, 60 plus populations.

And so we feel very confident on the overall safety profile. But the question will be, where are we in optimizing the immunogenicity against endpoints that are pretty well validated now in COVID, and where are we against the immunogenicity against endpoints that are also broadly accepted in influenza. We will be doing this for a range of different -- it's a four-strain, seasonal strain vaccine. And so we want to make sure there's no interference between those and that we're able to achieve strong balance immunity across the four flu strains plus the COVID vaccine.

I think we have approximate targets based on the immunogenicity we saw from Phase III and the immunogenicity we're seeing in the booster studies. But the open question is are

we going to need all of that for the COVID portion of our vaccine going forward. And so we'll continue to follow over time whether we see more durable protection and therefore, you might be able to optimize further that dose, if there was a reason to do so. And then the second part is with the seasonal annual flu component. We just want to understand, particularly in the older adult population where flu vaccines have had less clear efficacy every season, is maybe the way of say it. And there is an opportunity for improvement by raising those titers. We're going to want to look to whether or not we need to get those titers above what have been achieved by others. And I'll note that there's a precedent even for high-dose flu vaccines in that market that have been differentiated on price and grabbing market share.

And so it could cause us to look in that 60-plus or 50-plus population at really indexing more to those flu antigens and making sure that we exceed or at least achieve that similar high degree of seroconversion there. So those are the factors that we'll look at around the 1073 program that we've announced. We're looking at a range of ratios. Fortunately, we're going to have experience -- we already have experience in flu and COVID from our prior work, and it will be a demonstration we hope, of the ability to combine vaccines. I will note as a final comment, we have done combination respiratory vaccines in the past, including in adults with the 1653 program. And so we do have a basis we're beginning to think about how we might combine those antigens going forward. But ultimately, we'll let the 1073 study and the early clinical experiences there be confirmatory around this.

Q - Geoffrey Christopher Meacham {BIO 21252662 <GO>}

Great, thank you very much.

Operator

We have a question from Joseph Stringer from Needham. Your line is open.

Q - Joseph Stringer {BIO 19776403 <GO>}

Hi, good morning. Thanks for taking our questions. Two from me. Just curious on the guidance for -- the $2 billion guidance for the US fall 2022 booster market. Can you help us understand what assumptions are sort of built into that number? Is that based on sort of your internal expectations around relative percentage of individuals that would -- fully vaccinated individuals that would get a booster or just trying to handicap what the variance could be around that. And then for CMV, the -- can you give us a sense for the relative time lines for enrollment of that Phase III trial and when we could see the initial data from that? Thank you.

A - Stephane Bancel {BIO 15174250 <GO>}

So on the fall of '22, so the commercial team has spent quite a lot of time modeling different assumptions in terms of volume of people who will want the boost, market share and, of course, pricing. I cannot comment further for competitive reason right now, especially on the pricing piece, but we will do that in due time. But indeed, I mean, it's typical commercial analysis that the team that has done many times before in other companies have run through for the last few months.

A - Stephen Hoge {BIO 17925815 <GO>}

Great. And on the enrollment of CMV, thank you for the question. So we're -- the answer from our target perspective is as fast as we can, because we ultimately think there's just such a huge unmet need here, and we're excited to get the study going. There are some caveats that I should put around that, which is it probably won't be as fast as we did in COVID, which was obviously in a couple of months, because we are targeting a population at high risk of disease. And in this case, we're looking for women of child-bearing age who are exposed to seroconversion of COVID-19 -- with CMV. And that is often those that are exposed to children because that's the primary vector for those infections. And so we want to make sure that we get the right population. And that matters because this is a case-driven study, as we're kind of familiar with based on COVID-19, the number of cases we achieve that will ultimately dictate those interim analyses that we're looking for in the time ahead.

And so it makes sense to try and enrich for the at-risk population. So you might see a slower enrollment curve or it might go really fast. We're going to work as hard as we can go very fast. But the most important thing is that we need to be enrolling those that are at highest risk because we think that will ultimately generate the cases that accelerates the interim readout. We won't -- because it is an interim readout that's driven on the cases, I can't predict when that will happen. What I can do is I can try and enrich for those cases in the way I just described.

Q - Joseph Stringer {BIO 19776403 <GO>}

Great, thanks for taking my questions.

Operator

Next question is from Emmanuel Papadakis from Deutsche Bank. Your line is open. Emmanuel Papadakis, your line is open.

A - Lavina Talukdar {BIO 19691239 <GO>}

We can go to the next question, operator.

Operator

Okay. And next is from Mani Foroohar with SVB Leerink. Your line is open.

Q - Mani Foroohar {BIO 20015167 <GO>}

Hey guys, thanks for taking my questions. A couple of quick ones. Can you give us a sense of when we might see, if any, the impact on pricing shift to increase deliveries to low and middle income countries that Stephane mentioned. Is that something that we'd start to see a little bit of early next year? Is that more of a 4Q phenomenon in terms of the budgetary timing and sort of quarterly contract that Stephane talked about.

Secondarily, I have a few small piggy back question on the numbers. You -- on Slide 15, the $6.7 billion in deposits, that was on all for APAs for '21 or '22? Or does some of that applied to APAs for delivery -- for contracts for 2023? Thirdly, your CapEx guidance is a little lower than it was last Q. Is that $50 million to $150 million that you took out of that, is that absolute savings? Or is that just going to get pushed into next year as some of the contract revenues were? And then finally, a little more substantive of the question. How much perspective can you give us on you're able to potentially compete for share on contracting in EU, the competitor Pfizer/BioNTech locked in pretty large contracts on volume for the next two years? Is there an opportunity for you guys to start capturing more share returns or relevant to the EU? And last -- and finally, we talked on the last quarter about potentially access to China market where you guys are essentially not existing at this point. And you have mentioned going to via JV, can you give us an update on status of your ability to access that market, discussion of the JV to compete with BionTech, frozen? Sorry for the barrage of questions, and thanks for taking the questions.

A - Stephane Bancel {BIO 15174250 <GO>}

So I'll take a few and David, if you can take the financials, that would be great.

A - David W. Meline {BIO 6397419 <GO>}

Sure. Yeah.

A - Stephane Bancel {BIO 15174250 <GO>}

So on Q4, we already actually picked COVAX products. And the African Union will be in December, as we communicated in the press release, and it's going to be a big ramp into next year, obviously. In terms of European share, which was one of your questions, so if you look at this, there's a few things. First, in Europe, if you remember, we had a late and slow launch in Europe because we had no manufacturing capacity in Europe. If you recall, when we -- at the start of the pandemic, we had Norwood that we converted, and we were not allowed to export or serve the US market. So Lonza came online a bit later in Norwood because we have nothing in Lonza too, we were just updating some time in the summer to just get machines and get the facility ready.

And so indeed, in Europe, we have a lesser share than we have in the US, except for example, for Switzerland like you saw earlier. And so as the country gets more and more of an understanding first that mRNA vaccines are superior, the other vaccines that other than mRNA, I'm not sure, they're used anymore as my understanding, they're mostly given through COVAX. I think we have an interesting opportunity because as I shared, as you talk to health care leaders, health minister, as you get more and more data that Paul shared, we have a better and better understanding that the two mRNA vaccines are not the same. And so again, as we look into 2022, we already have a contract with Europe for '22. And we are discussing also with country by country on the data and also seeing the benefit of the Moderna vaccine versus the other one. And then the other question is going to stay in Europe, which is today, contracts are done at the European level because this was organized and agreed by Europe because of the pandemic.

The big question that's going to be out there is when do countries start to be buying by themselves because they have to make guesses of supply when they set up '21 and '22 agreements that might not meet the needs that they have, as they understand that they have a different profiles of a vaccine. And so I think it's going to be quite interesting to see the share opportunity that we have in Europe. Also as we build our teams, you remember, we had no infrastructure in Europe, zero, not one Moderna employee in commercial. We have now teams in several countries in Europe, in the U.K., in Spain, New France, in Germany, building the Italian team as we speak. So I think that also helped because we get feet on the ground to be able to get the message that -- of the real world evidence data. David, do you want to take the capital financial questions?

A - David W. Meline {BIO 6397419 <GO>}

Sure. Yeah. So in terms of the deposits of $6.7 billion we have in hand, I would just say that preponderance of those deposits are for deliveries either in '21 and in '22. There may be some small amounts in '23, but it's pretty early in terms of the contracting there. Secondly, in terms of CapEx, I think the answer is yes, you can expect, as I said, we're going to see a notable increase in our CapEx next year. But generally, in terms of the reduction this year, it's a combination of things moving into the first quarter of next year and also we're running, in some cases, at or below the estimated investment requirements. So it's a combination of those two.

Q - Mani Foroohar {BIO 20015167 <GO>}

Great. And on potential China JV. I know you guys have mentioned it in the last call, I don't know if there's been any progress?

A - Stephane Bancel {BIO 15174250 <GO>}

Yes. So nothing to announce today, but we do have valets [ph] of people in China.

Q - Mani Foroohar {BIO 20015167 <GO>}

Right. Thanks for taking the questions. I'll let you guys on check on a manual.

A - Stephane Bancel {BIO 15174250 <GO>}

Thank you.

Operator

There are no further questions at this time. I would now like to turn the conference back to Mr. Stephane Bancel.

A - Stephane Bancel {BIO 15174250 <GO>}

Well, thank you very much for joining us. And if you have any further questions, you know where to reach Lavina and the team. Have a great day. Bye.

Operator

This concludes today's conference call. Thank you for joining. You may now disconnect.