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EDITED TRANSCRIPT

MRNA.OQ - Q4 2022 Moderna Inc Earnings Call

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OVERVIEW:

Co. reported 2022 revenue of $19.3b, after tax net income of $8.4b and diluted EPS of $20.12. For 4Q22, reported after tax net income of $1.5b and diluted EPS of $3.61. Expects 1H23 sales to be approx. $2b.

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PRESENTATION

Operator

Good morning, my name is Kevin, and welcome to Moderna's Fourth Quarter 2022 Earnings Call. (Operator Instructions) Please be advised this call is being recorded.

At this time, I'd like to turn the call over to Lavina Talukdar, Head of Investor Relations at Moderna. Please proceed.

Lavina Talukdar - *Moderna, Inc. - Senior VP & Head of IR*

Thank you, Kevin. Good morning, everyone, and thank you for joining us on today's call to discuss Moderna's Fourth Quarter and Full Year 2022 Financial Results and Business Update. You can access the press release 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; Stephen Hoge, our President; Arpa Garay, our Chief Commercial Officer; and Jamie Mock, our Chief Financial 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 or results to differ materially from those expressed or implied in these forward-looking statements.

With that, I will now turn the call over to Stephane.

Stephane Bancel - *Moderna, Inc. - CEO & Director*

Thank you, Lavina. Good morning or good afternoon, everyone. Welcome to our Q4 2022 conference call. Today, I will start with a quick business review of 2022. Stephen will then review our clinical programs before Arpa gives an update on our commercial progress and plans. Jamie will then present our financial results, and I will come back to share some thoughts on where we're heading.

We are pleased to report today revenues of $19.3 billion for fiscal year 2022, GAAP net income of $8.4 billion and GAAP diluted earnings per share of $20.12. Cash and investment balances of $18.2 billion at the end of the year.

We continued our disciplined capital allocation policy. We're investing first in our company. In 2022, we invested $3.3 billion in R&D, our highest level of R&D investments ever. We invested $1.1 billion in SG&A and $400 million in capital investments. We made investments in Metagenomi for access to new gene editing enzymes and Carisma in oncology. We announced an investment in CytomX and the acquisition of OriCiro in Japan to continue to streamline our manufacturing processes. And just yesterday, we announced the collaboration with LifeEdit. $3.3 billion were returned to shareholders through a buyback of 23 million shares.

I am proud of the strong results by our team in 2022 as we made history with a number of outstanding accomplishment for patients. In respiratory vaccines, we developed new products with remarkable speed, getting the mRNA-1273.214 against Omicron B1, the strain recommended by WHO, and mRNA-1273.222 against Omicron BA.5, the strain [asked] by the U.S. FDA. We developed 1273.222 in less than 2 months. We're able to protect millions of people from potentially severe disease resulting from new COVID strains.

Our RSV vaccine went from Phase I start to Phase III data in 24 months, and met its primary efficacy endpoint in the Phase III trial. In oncology, our Personalized Cancer Vaccine was the first demonstration of positive results from an mRNA cancer treatment in the randomized clinical trial.

In rare diseases, our propionic acidemia program showed early positive clinical results in a repeat dose chronic disease setting in reducing metabolic decompensation events in patients. And we announced what we hope will become the first effective inhaled mRNA therapy in humans as our partner, Vertex, entered a Phase I trial using our technology in the therapy for cystic fibrosis patients who lack CFTR protein.

Finally, we had our first ESG Day and published our first ESG report, providing additional transparency in how we conduct our business.

I want to take a moment this morning to touch on transition the Moderna Executive Committee. As we announced in late 2022, Marcello Damiani decided to retire as Chief Digital Officer after more than 7 years with the company. Marcello joined Moderna before our first clinical trial, and we are today, a digital-first company, as a big testament of his ability to scale digital resources. I'm grateful to Marcello for his contribution during the early years of Moderna.

I am excited to have worked already with Brad Miller since early January. Brad brings a wealth of enterprise solution and platform organization experience in several of the top technology companies. This will be instrumental as Moderna scales into a fully-integrated biotechnology company.

I want to also share with you that Juan Andres, currently President of Strategic Partnership and Enterprise Expansion has informed me of his intention to retire and will be retiring at the end of May. Juan has played a tremendous role since joining Moderna in 2017 from Novartis, where he led all manufacturing for them. Juan served as Moderna's Chief Technology Operations and Quality Officer where he led the manufacturing from an early-stage clinical development company to a commercial company.

I believe Juan did a historic job with his team in 2020 and 2021 to scale Moderna for global commercial launch during the pandemic. It is literally unbelievable that he led the team from having made across our entire portfolio, less than 100 million doses in 2019 to more than 800 million doses in 2021, all during the pandemic. We, and hundreds of millions of people across the globe who received the Moderna COVID-19 vaccine, owe Juan our gratitude. I believe very few manufacturing leaders would have led such an achievement.

Most recently, Juan has focused on building out our organization to support Moderna's growing pipeline, leading our efforts in producing of personalized cancer vaccine. Jerh, who used to work for Juan at Novartis, has joined us since early fall and has been leading manufacturing since then. I am thankful to Juan, who has ensured a very smooth transition, helping Jerh every step of the way. Upon his retirement at the end of May,

Juan's responsibility will transition to Stephen Hoge, President of Moderna, to integrate PCV across all functions, with Jerh leading the manufacturing of PCV for multiple Phase IIIs, and of course, for getting commercial ready.

On behalf of the entire Moderna team, I want to thank Juan for his continued leadership and wish him and his wife, Marina, the best of a well-deserved retirement. I am deeply thankful to have counted him for so many years as a partner at Moderna, and more importantly, for more than 20 years as a friend and a mentor. We will miss him.

The company continues to expand at a rapid pace. We now have 3 commercial COVID-19 vaccine products. We have 4 development programs in Phase III. We have to expand our commercial portfolio very soon. Overall, we have 48 programs underway with a team of 3,900 team members, and now present on the ground in 16 commercial subsidiary across Americas, Europe and Asia Pacific. Our $18 billion of cash balance at the end of the year is enabling us to scale across research, clinical development, manufacturing, commercial and G&A.

With that, let me now talk to Stephen.

Stephen Hoge - *Moderna, Inc. - President*

Thank you, Stephane. Good morning or good afternoon, everyone. Today, I will review our progress against our key clinical programs.

I'll start with our respiratory vaccines. We have approved our Phase III development programs against the big 3 respiratory viruses, COVID-19, RSV and influenza. I'll share some additional data on these in a moment, including some presented this morning on our older adult RSV Phase III trial. We're also advancing a portfolio of next-generation programs against these viruses, including mRNA-1283, which is a next-generation COVID-19 booster that is referred to as rather stable. We also have multiple next-generation flu programs. We seek to increase the breadth of coverage against influenza by adding additional antigens that are not present in currently-available flu vaccines. Lastly, our respiratory portfolio includes a large number of combination vaccines to provide protection against multiple respiratory pathogens which has advantages for many stakeholders, including health care providers, payers and consumers. These include combinations of COVID, flu and RSV, as well as 2 pediatric vaccines that include additional viruses that are important in children, including hMPV and PIV3.

As we prepare for endemic COVID in 2023 and beyond, we wanted to briefly recap the recent VRBPAC committee discussions and recommendations. At the January VRBPAC meeting, the committee voted to harmonize the primary series and booster dose vaccines, which is an important step to simplify future guidance. The FDA also indicated that it expects to convene VRBPAC to determine vaccine strain composition for the '23-'24 season in the second quarter of this year. We believe that our mRNA platform has demonstrated its ability to deliver variant match vaccines on accelerated time horizons, and we believe we are therefore well positioned to deliver whatever composition of the FDA and other public health agencies recommend.

Now, moving to RSV. As you know, we shared the topline results from our Phase III RSV study in older adults earlier this year. And today, we shared additional data that was presented this morning at RSVVW. The top line results we've seen are incredibly encouraging, and we're grateful to the FDA for breakthrough therapy designation for mRNA-1345, which further emphasizes the significant health impact of RSV in older adults and the high unmet need.

In the top line data presented in January, the mRNA-1345 demonstrated 83.7% vaccine efficacy and the primary endpoint of lower respiratory tract disease with 2 or more symptoms. 1345 was found to be generally well tolerated, and there were no safety concerns identified by the Data and Safety Monitoring Board.

In the data presented today at RSVVW, we confirmed that 1345 was well tolerated and has an acceptable safety profile. Solicited adverse reactions were mostly Grade 1 or Grade 2, and to date, most solicited adverse reactions were mild to moderate, with the most common adverse reactions being injection site pain, headache, myalgia and arthralgia. Vaccine efficacy was consistently high across all age groups and in participants with pre-existing comorbidities that are at highest risk.

Please refer to the scientific and medical meetings section of the Moderna Investor Relations website to see the full RSVVW presentation. And we're very encouraged by these data, and look forward to file a Biologics License Application with the FDA in the first half of 2023, as things proceed. With the option of using a priority review voucher, we might see regulatory action on this filing in late 2023 or early 2024.

Now moving to flu. Last week, we shared with you data from our Phase III Immunogenicity and Safety study in the Southern Hemisphere, study P301. In this study, our first-generation vaccine, mRNA-1010, demonstrated superiority on 0 conversion rates for influenza A/H3 and H1 and superiority on geometric mean titers for H3 and non-inferiority on geometric mean titers for H1. MRNA-1010 did not meet non-inferiority on 0 conversion or titers for the 2 influenza B strains.

Our separate Phase III efficacy study in the Northern Hemisphere, study P302, has now accrued over 200 confirmed cases of influenza-like illness, almost all of which are influenza A. Which is expected -- this was expected as the overwhelming majority of influenza burden in older adults is caused by influenza A, including over 95% of hospitalization in the most recent season.

Now based on the case accrual in P302, we now expect the independent DSMB will review the first interim analysis of efficacy in that study in the first quarter of this year.

Now let's take a look at our latent vaccines on Slide 14. Our CMV vaccine is in an ongoing Phase III study, and we've begun dosing participants in the Phase I/II adolescent dose-ranging study. Our EBV vaccine to prevent infectious mononucleosis is in Phase I, while our EBV vaccine to prevent long-term sequelae of EBV is in pre-clinical development. We have 2 HIV Phase I trials ongoing, and our HSV vaccine is in preclinical.

And finally, our VZV program has begun dosing in participants in a Phase I/II study, which I will discuss further on the next slide. The VZV study is a Phase I/II randomized safety and immunogenicity study evaluating mRNA-1468 against Shingrix. This is a relatively large study, enrolling 500 0 negative older adults in multiple doses and dosing intervals, and a 12-month study follow-up. Over 35% of participants will be 70 years and older, which is in line with the largest disease burden of shingles.

Now, let's take a look at our therapeutics portfolio on Slide 16, and I'll highlight a few of the programs. We recently reported strong top line data for our personalized cancer vaccine, which I will talk to in a moment. In Immuno-oncology, we are working to address disease burden beyond PCV with our checkpoint and triplet programs, both of which are in Phase I trials in various tumor types.

In rare diseases, our Phase I/II PA program continues to enroll patients and we are looking forward to selecting a dose of the expansion arm. I'll provide a brief update on that in just a moment.

Earlier this year, our partner, Vertex, announced an initiation of a Phase I trial in cystic fibrosis patients, which is our first inhaled pulmonary mRNA therapeutic program. And in Cardiovascular, we announced Relaxin has initiated dosing in the Phase I study. Both of these study initiations represent important milestones for Moderna as we expand our modalities in therapeutic areas.

Now in December, we shared exciting top line data from our Phase II personalized cancer vaccine program, testing the combination of PCV and KEYTRUDA against KEYTRUDA alone in the setting of adjuvant melanoma. KEYTRUDA is the standard of care in that setting.

In this study, we showed the addition of our personalized cancer vaccine treatment mRNA-4157 to KEYTRUDA reduced the risk of recurrence or death by 44% compared to KEYTRUDA alone. This was the first demonstration of efficacy for an investigational mRNA cancer treatment in a randomized clinical trial, and we are pleased to announce that 4157 has received breakthrough therapy designation from the FDA. Along with our partner, Merck, we are excited about these results and expect to launch multiple late-stage confirmatory studies for PCV in 2023, starting with melanoma and then moving to non-small cell lung cancer.

We are planning to explore additional indications for 4157, where we believe there is a strong biologic rationale for immune-stimulating approaches. These include early-stage and metastatic settings and will include indications where KEYTRUDA is not yet approved.

Finally, we expect to release full data from our Phase II study at an oncology meeting this spring and in an upcoming publication.

Now moving to PA. Since our update with our -- at our R&D Day, the PA Paramount study has made good progress. Our fourth cohort is now fully enrolled, and we're currently enrolling patients in our fifth cohort which doses at 0.9 milligrams per kilogram every 2 weeks. We are encouraged that to date, we have not observed any dose-limiting toxicities. And we're also encouraged that all patients and families have opted to continue treatment electively in our Open-Label Expansion study across all prior dose cohorts.

Now, the next step in this trial will be to review available data and determine a dose for expansion.

I'll now hand the call over to Arpa Garay, who will provide an update on our commercial activities. Arpa?

Arpa Garay - *Moderna, Inc. - Chief Commercial Officer*

Thank you, Stephen, and good day to everyone. I will start with a review of sales on Slide 20.

In the fourth quarter, total product sales were $4.9 billion. In the U.S., our sales were $1 billion, sales in Europe approximated $2.2 billion, and sales in the rest of the world were $1.6 billion. We ended the full year strong, with total product sales for 2022 of $18.4 billion. Sales in the U.S. for the full year were $4.4 million, sales in Europe were $6.7 million, and in the rest of the world were $7.3 billion. We are reiterating approximately $5 billion in COVID sales for delivery in 2023 from our currently-signed advanced purchase agreements and deferrals. And we do expect additional sales from key markets such as the U.S., EU and Japan.

Slide 21 summarizes the current composition of sales for 2023. We have advanced purchase agreements from Canada, Kuwait, Switzerland, Taiwan and the United Kingdom. We expect these sales to be recognized upon delivery of vaccines in the second half of 2023. Additionally, we expect further sales from deferrals from 2022 contracts. These deferrals are from the countries listed on the slide, and are expected to be mainly recognized from deliveries in the first half of 2023. Together, these advanced purchase agreements and deferrals totaled approximately $5 billion in sales for 2023.

We do expect additional sales from key markets, including the United States, EU and Japan, as well as Australia and other countries in Asia and Latin America. In the U.S., contracting discussions with commercial customers are ongoing, and we will provide visibility into expected U.S. sales at a future date after we complete these discussions.

In our discussions with commercial customers in the U.S., it is clear to us that our customers recognize that COVID is still a substantial health burden. Throughout 2022, COVID continued to be a leading cause of hospitalizations and deaths.

If you look to the chart on the left-hand side, what you'll see here is data available through September of 2022, COVID was the third leading cause of death in the United States only after heart disease and cancer.

And if you look to the right-hand side, (technical difficulty) four months for the fall and winter season from October 1, 2022, (technical difficulty) 2023, hospitalizations from COVID in the U.S. are nearly 450,000, more than double from flu and nearly 3x higher than RSV in that same 4-month period. There continues to be a clear need to protect against severe COVID infections and our customers recognize that.

Given this need, we estimate the U.S. fall 2023 COVID market volume to be approximately 100 million doses. We base this assumption after looking at 2022 vaccination rates, and including potential recommendation for 2-dose booster series for high-risk individuals. Taken together, the doses administered represent roughly 30% of the U.S. population.

A few factors that can impact this volume include viral evolution, regulatory recommendations as well as vaccine understanding and uptake by consumers. Moderna's commercial organization is prepared for the transition to a commercial market in the U.S.

Let me now take you through how we have been preparing to go to market. First and foremost, we are committed to access, which I will explain in greater detail in just a moment. To ensure coverage of our vaccine, we are engaged in discussions with private customers as well as public entities such as the VA, CDC and the Department of Defense. We are increasing awareness and educating consumers as well as healthcare providers about

the benefits of booster vaccinations in alignment with public health agencies such as CDC and ACIP. We are reaching healthcare providers and consumers through innovative digital outreach programs. We have built the infrastructure needed to fulfill customer orders and shipments, and our commercial and medical organizations have been scaling to execute on this plan, and we are ready for the transition to a commercial market in the United States.

Very importantly, as we enter the commercial phase of the endemic COVID market, we want to emphasize our commitment to vaccines access for everyone in the United States regardless of their ability to pay. For all insured individuals in the United States, consistent with preventative health services requirements, current reimbursement rules will be sustained. As an ACIP-recommended vaccine, Moderna's COVID vaccine will continue to be available for 0 out-of-pocket costs for individuals with insurance. And we are proud to say that for uninsured or underinsured people in the United States, Moderna will be launching a patient assistance program that will provide COVID-19 vaccines at no cost.

Let me now summarize our COVID vaccine outlook. In 2023, we expect COVID sales of approximately $5 billion. In addition, we are expecting sales from U.S. commercial market orders, EU, Japan and other countries. We will provide visibility into these sales after we complete ongoing discussions with governments and with customers.

We recognize COVID continues to be a burden to healthcare systems, and this continues to be an important point as we discuss the value of booster vaccinations with our customers. In the U.S., we expect commercial market volumes to be approximately 100 million doses in 2023, and Moderna's commercial organization is prepared for the transition to a commercial endemic market. Last but not least, we are committed to patient access in the United States.

I now want to turn to another launch in the respiratory vaccine space that the commercial team is preparing for, our RSV vaccine in 2024. As you heard from both Stephane and Stephen earlier, we are very pleased by our Phase III RSV vaccine results. Stephen's organization will be filing for the approval soon, and we expect we may be approved in late 2023 or early 2024. With the potential approval fast approaching, I'm very excited for the RSV vaccine launch, and I want to provide additional color into the launch plans.

The RSV launch will leverage the existing commercial infrastructure that is already in place for COVID and we will continue to invest to support it, ensuring strong execution. Both COVID and RSV markets overlap considerably as we look at our target customers as well as potential target patients and audiences, and we will leverage this overlap between the 2 markets. We will ensure awareness of RSV disease and the associated economic burden of RSV in older adults across key stakeholders such as healthcare providers and payers. Upon approval of our RSV vaccine, we will educate consumers on key attributes of our vaccine. These planned activities will be initiated in 2023 and in full force upon approval. We have the added benefit of an in-place commercial infrastructure built for COVID. Many of these resources can be leveraged for flu as well into the future.

I look forward to keeping you updated on our progress throughout this year. And with that, I will turn it over to Jamie.

James M. Mock - *Moderna, Inc. - CFO*

Thanks, Arpa, and hello, everyone. This morning, I will cover our 2022 financial performance and provide a framework for our 2023 financial outlook.

Moving to our fourth quarter results, starting on Slide 29. Total product sales decreased by 30% year-over-year to $4.9 billion. The decrease in 2022 was mainly driven by lower sales volume compared to overall higher demand in the prior year. Cost of sales was 39% of product sales compared to 14% of product sales in 2021. The key driver of the increase in cost of sales as a percent of product sales was a catch-up royalty payment to the National Institute of Health, or NIH, of $400 million, representing 8% of product sales in the fourth quarter.

In December 2022, we entered into a non-exclusive patent license agreement with the National Institute of Allergy and Infectious Diseases and institute or center of the NIH to license certain patent rights concerning stabilizing prefusion coronavirus spike proteins and the resulting stabilized proteins for the use in COVID-19 vaccine products or 2P technology. Pursuant to the agreement, we have agreed to pay low single-digit royalties on future net sales of our COVID-19 vaccines.

Our cost of sales also includes a charge of $297 million for inventory write-downs related to excess and obsolete COVID-19 products, an expense for unutilized manufacturing capacity, and CMO wind-down costs and related charges of $376 million, and a loss on firm purchase commitments and related cancellation fees of $281 million. These charges other than royalties are driven by costs associated with surplus production capacity, overall lower demand and a shift to our most recent Omicron BA.4/5 targeting COVID-19 bivalent booster.

Research and development expenses were $1.2 billion, which increased by 87% versus prior year. The increase in R&D spend continues to be driven by our clinical trial expenses, particularly with our Phase III studies for RSV, seasonal flu and CMV. The increase in R&D was also driven by the acquisition of a Priority Review Voucher and an increase in personnel-related costs due to increased headcount.

Selling, general and administrative expenses were $375 million, also reflecting an increase of 87% year-over-year. The growth in spending was primarily driven by continued investments in personnel and outside services in support of our marketed products and company build-up.

The effective tax rate was 11% compared to 10% last year. After-tax net income decreased by 70% to $1.5 billion. Diluted earnings per share in Q4 decreased by 68% to $3.61.

Now turning to our full year 2022 financial results on Slide 30. Total product sales for the full year 2022 were $18.4 billion, an increase of 4% year-over-year. The growth was mainly attributable to customer mix and a higher average selling price in 2022 in certain markets. Cost of sales was 29% of product sales compared to 15% of product sales last year. The increase was driven by higher write-downs for excess and obsolete inventory related to our COVID-19 vaccines, unutilized manufacturing capacity and losses related to future purchase commitments for raw materials. The key drivers for these charges are similar to the drivers in Q4. Costs associated with surplus production capacity, overall lower demand for the year, in particular from low-income countries, and rapid product advance shift from our original vaccine to Omicron targeting COVID-19 bivalent boosters. The previously-mentioned catch-up royalty payment NIH of $400 million is also a driver of the increase year-over-year.

The effective tax rate was 13% compared to 8% last year. As a reminder, we had a net operating loss carryforward of $2.3 billion at the end of 2020, which resulted in a non-recurring benefit to the reported tax rate in 2021. After-tax net income of $8.4 billion decreased 31% versus prior year. The decrease of net income was primarily due to higher cost of sales, higher other operating expenses and a higher effective tax rate. Diluted EPS decreased 29% to $20.12.

Now turning to cash and cash deposits on Slide 31. We ended 2022 with cash and investments of $18.2 billion, compared to $17 billion at the end of the third quarter. The increase was driven by our commercial activity. Cash deposits for future product supply reduced from $3.8 billion at the end of the third quarter to $2.6 billion by the end of the year.

Now turning to Slide 32. I wanted to give an update on the progress we have made on our capital allocation priorities. Our top investment priority has been and will continue to be reinvesting in our base business across multiple areas.

Research and development spending increased 65% year-over-year from $2 billion in 2021 to $3.3 billion in 2022, and we are projecting an additional increase to approximately $4.5 billion in 2023. The clinical data from our PCV, RSV and flu trials were encouraging and further validates the potential of our mRNA technology. We are also investing in our digital capabilities, the commercial build-out of the organization as well as expanding our manufacturing footprint. We plan to significantly accelerate our capital expenditures in 2023 as we expand both our international and U.S. manufacturing footprint.

Our second investment priority is to seek attractive external investments and collaboration opportunities that will enable and complement our platform. We've recently announced several new transactions, and I'm happy to report that we have successfully closed our acquisition of OriCiro Genomics in the first quarter of 2023. OriCiro is a great example of the companies we are evaluating to enable our mRNA platform. It will create substantial value from both the speed and cost viewpoint and impact our pre-clinical, clinical and commercial pipeline for years to come.

Our collaboration with LifeEdit, which we announced yesterday, is another example for an attractive external investment opportunity. We believe the combination of Moderna's mRNA platform with LifeEdit's proprietary gene editing technologies, including base editing capabilities, has the opportunity to advance potentially life transformative or curative therapies for some of the most challenging genetic diseases.

We are in multiple active discussions regarding additional external collaboration opportunities, and we will be disciplined in our approach.

After evaluating internal and external investment opportunities, we then assess additional uses of cash. In 2022, we repurchased 23 million shares for $3.3 billion at an average price of $143 per share. And we have $2.8 billion of share repurchase authorization remaining.

Now, let's turn to our 2023 financial framework on Slide 33. As Arpa mentioned earlier, we currently have COVID vaccine sales of $5 billion contracted for delivery in 2023. Also, we are actively working on preparing for the private market and government contracts in the U.S. and additional contracts for Europe, Japan and other key markets.

To help you with your modeling purposes, we expect first half '23 sales to be approximately $2 billion. Our total cost of sales includes the cost of goods manufactured, third-party royalties, as well as logistics and warehousing costs. We expect full year 2023 reported cost of sales to be 35% to 40% of sales. This includes royalties of approximately 5% of sales, which are payable to UPenn and CellScript for modified chemistry licenses, and to NIAID and NIH for the 2P license that I mentioned earlier. The increase in cost of sales as a percent of product sales compared to 2022 is primarily driven by presentation mix change as we move from a pandemic to endemic setting, with single-dose application significantly increasing in volume.

Longer term, as the endemic market normalizes and we add additional respiratory and other products, we expect our cost of sales as a percent of sales will significantly decrease in the rates we're experiencing in 2023.

For R&D and SG&A, we expect full year expenses to be approximately $6 billion, with approximately $4.5 billion in R&D. The increase is driven by our maturing development portfolio and the global scale up of our company. We expect a negligible provision for income tax in 2023. And finally, we expect capital expenditures of approximately $1 billion. The increase is primarily due to investments in expanding our manufacturing footprint.

This concludes my remarks concerning our financial performance, and I will turn the call back over to Stephane.

Stephane Bancel - *Moderna, Inc. - CEO & Director*

Thank you, Jamie, Arpa and Stephen. Let me now share some thoughts about where we're heading.

I'm really excited to see our mRNA platform and the investments we have made in science over the last 11 years lead to such a promising pipeline. We anticipate a number of important developments.

Let me start with our first franchise, respiratory vaccines. In COVID boosters, we are working for the switch to U.S. commercial market, and we anticipate being able to quickly meet the full 2023 market needs for updated vaccines after VRBPAC and the FDA make this transaction in the spring of 2023. We plan to submit RSV vaccine for regulatory approval in the first half of 2023, and as you heard from Arpa, we'll be ready to launch the RSV vaccine in late '23 or early '24.

In flu vaccine, for Northern Hemisphere, mRNA-1010 Phase III trial, the Data and Safety Monitoring Board is expected to complete its interim efficacy analysis in the first quarter of 2023. Our second franchise Latent virus vaccine. It's progressing very well with a broad spectrum of programs. In our large CMV Phase III study, we look to complete the enrollment. For EBV, HIV and VZV programs, our next milestone will be Phase I data.

Turning to Slide 37, let me review the milestone for mRNA therapeutics programs. For personalized cancer treatment, we expect to start our Phase III study in partnership with Merck in adjuvant melanoma, and we expect to rapidly expand to additional tumor types, including non-small cell lung cancer. Full Phase II data will be presented at an upcoming oncology meeting and published in a top quality medical job.

In PA, we plan to select those and begin the expansion arm of our Phase I/II study.

MMA, we will have Phase I/II data. The next milestone for heart failure for Relaxin will be Phase I data in patients. In Inhaled therapeutics, our partner Vertex expects to complete its single ascending dose study and initiate a multiple ascending dose study.

To continue to build the best version of Moderna, we have established 7 priorities for 2023. Priority number one, execute the operational and sales plan for COVID booster for fall of '23. Priority #2, build an unrivaled seasonal respiratory vaccine franchise. Priority #three, execute a bold campaign of cancer vaccine studies. Priority #4, advance rare metabolic disease programs. Priority #5, drive rapid advancement and growth of our latent vaccine portfolio. Priority #6, deliver the next-generation pipeline and platform. As we said before, this is just the beginning. And Priority #7, build a culture of perpetual learning and strengthen our processes and digital system as we want to scale the company to another level.

On Slide 39, some key dates for 2023 Moderna Investor Days. April 11 will be our Annual Vaccine Day. September 13 will be Annual R&D Day, where we'll present development pipeline key updates. And December 7 will be our second ESG Day.

Now that we have delivered on the promise of mRNA science with our first product launched, our mission has evolved. Our mission is to deliver the greatest possible impact to people through mRNA medicine. We are passionate about our ability to have a profound impact on humanity. We believe we have the technology to eliminate or greatly reduce human suffering caused by respiratory viruses, latent viruses, many cancers, (inaudible) diseases and the growing list of other diseases. We believe we can have an impact on these treatments with our therapeutic first and then with our clean editing programs. This is just the beginning. With that, the team and I are happy to now take your questions. Operator.

QUESTIONS AND ANSWERS

Operator

(Operator Instructions) First question comes from Salveen Richter with Goldman Sachs.

Salveen Jaswal Richter - *Goldman Sachs Group, Inc., Research Division - VP*

Could you speak to the regulatory strategy for flu, given the miss on the B strains for immunogenicity and if you're confident into the interim efficacy analysis given the dominating prevalence of A strains here.

Stephen Hoge - *Moderna, Inc. - President*

I'll take that. Look, I think the honest answer is we're still have incomplete information to provide guidance on the regulatory strategy. At this point, we are looking to the efficacy results from the P302 study that I described, which will guide us on that filing strategy. It's important to note that efficacy, ultimate demonstration of non-inferior efficacy against an approved vaccine was always going to be required for full approval, and that the only thing that you could do with immunogenicity would be an accelerated approval path with an obligation to subsequently demonstrate efficacy.

And so right now, we are actually very encouraged that the data that we've seen from our immunogenicity and safety study, which is running the Southern Hemisphere, P301, shows superiority on 3 out of 4 endpoints for the influenza A strains, which drive the overwhelming majority of disease, and the population of interest here are older adults, and account for over 99% of the cases in our efficacy study. And so that first interim efficacy analysis that we're conducting now in P302 will involve over 200 cases, 99% of them are influenza A, and it will be our first chance to really see the performance of the vaccine in terms of prevention of influenza-like illness from Flu A.

That is the first interim analysis. And so it's quite possible, as you would expect in any efficacy study, and we've all got some experience now with these respiratory efficacy studies, that we may end up -- need to go to a second subsequent interim analysis and accrue even more cases to demonstrate either non-inferiority or superiority in that study. And so what we'll do is we will wait for the results from the DSMB, the independent DSMB, and guidance from that. Based on those results, obviously, if we do see efficacy, that is the gold standard for proceeding with regulatory filing and full approval. If we do not yet meet that threshold, then we'll be looking forward to subsequent interim analyses in that study.

Operator

Our next question comes from Gena Wang with Barclays.

Huidong Wang - *Barclays Bank PLC, Research Division - Research Analyst*

Just quickly follow Salveen's question. Do you need to show superiority in order to receive approval regarding the efficacy study? And then quickly on the revenue. Did I hear correctly the existing contract of $5 billion mainly will be in the second half '23? If that's the case, is it fair to say that total COVID revenue in 2023 should be around $7 billion?

And then regarding the $2 billion in the first half '23, how much will be from the U.S. market, i.e., out of estimated 100 million doses in the U.S., what could be your market share?

Stephen Hoge - *Moderna, Inc. - President*

I'll take the first question. So first on superiority. You do not need to demonstrate superiority to get a flu vaccine approved. That's well precedented. Non-inferior efficacy is the threshold. Our goal, though, over time is absolutely to develop a superior influenza vaccine. And so if we don't see it with the first-generation product, which is mRNA-1010, I would note that we have 4 other programs -- flu programs in development, different stages of clinical trials, that are looking to do even better than perhaps flu mRNA-1010. And our goal over time would be to demonstrate that we have a superior influenza vaccine. But it is not actually required for approval non-inferiority should suffice.

I'll turn it over to Arpa, I think, for the other questions?

Arpa Garay - *Moderna, Inc. - Chief Commercial Officer*

Sure. Yes, I can take the second question. In terms of the total sales, we are anticipating about $2 billion of the $5 billion in the first half of the year, and none of that $2 billion is coming from the U.S. market. The remaining advance purchase agreements that we have of $3 billion will be coming in the second half of this year. Now, that $5 billion is just the total that we have from advanced purchase agreements as well as deferrals from 2022. We do anticipate additional sales from the U.S., Japan, EU and other markets, and we believe the majority of these sales will be in the second half of 2023.

Huidong Wang - *Barclays Bank PLC, Research Division - Research Analyst*

And then your market share regarding the U.S. market?

Arpa Garay - *Moderna, Inc. - Chief Commercial Officer*

We continue to believe in the strong, differentiated profile of our products. We do not have any updates on market share projections as we are currently in discussions with customers right now for fall 2023 contracting.

Operator

Next question comes from Matthew Harrison with Morgan Stanley.

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

Great. I was hoping to ask about the regulatory strategy for PCV, and specifically, how you're thinking about the potential for filing off the Phase II data set, as well as how you're thinking about the time lines for enrollment in the Phase III program and how that may impact the time line for potentially filing off the Phase II data set?

Stephen Hoge - *Moderna, Inc. - President*

Great. So we're obviously really pleased yesterday to announce that we received FDA breakthrough designation therapy for the PCV program. And what that allows us to do is very rapidly accelerate our conversations with the FDA and other regulators on the path forward for filing 4157. As you noted, the Phase IIb study that we've run is a randomized study compared against, really, the standard of care which is KEYTRUDA alone, and has already shown a quite significant benefit at 41% reduction of the rate of recurrence and -- or death. And that study is ongoing, and so we're continuing to follow over time and conduct additional interim analyses. And it's possible that those -- in fact, we would hope that those data mature and continue to get stronger and stronger. And so it is entirely possible that in our discussions under breakthrough with the FDA and others that we will come up with a path forward for beginning the filing process based on that Phase II and potentially proceeding with an accelerated approval.

Now as you know, in this country, and I think it's where your question is coming from, as well globally, if there is a path forward there, we haven't yet engaged with the FDA on because the breakthrough happened yesterday. But if there is a path forward there, it would require us to rapidly enroll a confirmatory Phase III study. And in fact, there's more and more attention on perhaps requiring that those Phase III studies be enrolled prior to an accelerated approval.

And so for that reason, ourselves and Merck are working really quickly now to try and stand up that confirmatory Phase III melanoma study and enroll as fast as possible. Now, we're not ready yet to guide on how quickly that will be, but we are fully aware of the fact that in fact, if there is a path forward for accelerated approval, the enrollment of that Phase III may begetting, and therefore, we want to have it enrolled as quickly as possible.

So at this point, we've just received the breakthrough designation, we're engaging with regulators, and we're going to try and develop that path forward. But it is theoretically possible that there is an accelerated approval path and that we would need to enroll that Phase III study based on recent regulatory guidance, more generally to the industry. And working hard to make sure that we can do that as fast as possible here, while continuing to conduct the additional interim analyses and see the maturity of this data continue to proceed, and hopefully, the strength of the benefit provided by the combination to be further validated.

Operator

Next question comes from Edward Tenthoff with Piper Sandler.

Edward Andrew Tenthoff - *Piper Sandler & Co., Research Division - MD & Senior Research Analyst*

Great. And thanks for all the detail on the call today. My question, I had to go back to flu form and just with respect to the follow-on candidates, including I think the one that's pentavalent hemagglutinin and then fixed hemagglutinin and then also into the neuraminidase, the candidates at that neuraminidase, what should be our expectation both in times of timing for data here? And how do you ultimately see your seasonal flu product offering kind of evolving?

Stephen Hoge - *Moderna, Inc. - President*

So let me start with the most advanced program, obviously, is our 1010 program, which we've talked about. And we have done an update to that vaccine that we think will increase the B immunogenicity for those populations for whom that matters, and we expect to advance that in clinical study quite quickly.

That, in combination with the efficacy data that we were just talking about with P302, probably is the most important information for guiding our next step on the second-generation products. Our multiple -- sorry, penta and hexavalent vaccines as well as the 1020, 1030 programs, which include neuraminidase, as you said, are all in various Phase I studies. And as we've shown repeatedly hopefully over the last couple of years, we can proceed very quickly in the subsequent Phase III in pivotal studies once we select 1 of those candidates to move forward. But the really important gating information is understanding how is our first generation product performing in terms of efficacy as a first mRNA flu vaccine. And so we are waiting for that information before proceeding forward.

But we do expect that at least one, if not multiple, of these second-generation products would move into subsequent pivotal studies, Phase III studies. And in those cases, because we would be looking to demonstrate some form of superiority either against a broader range of influenza strains or better protection against influenza-like illness because we've included additional antigens, we would expect those studies to include both immunogenicity and safety and efficacy end points as we move forward. And so we'll make a selection on which ones we might move forward based on the ongoing interim analysis of efficacy from our 1010 program.

We don't have another way to update at this point on which one we'll move forward.

Operator

Next question comes from Michael Yee with Jefferies.

Michael Jonathan Yee - *Jefferies LLC, Research Division - Equity Analyst*

A couple follow-up on the flu vaccines and also a PCV question for Stephen. I guess -- could you clarify -- do you have a hypothesis around why the B-strains were not non-inferior and what the ramifications are for that? Either for this flu vaccine, but also for the infection study, and what that would mean for combinations? So first of all, just to clarify what's going on there with the B-strain, the ramifications for flu vaccine.

And then my second question is on PCV. Obviously, we're excited about the adjuvant data. There is also a competitor reading out in metastatic melanoma this summer so I wanted to understand how we should compare and contrast that? And if you could walk us through how to think about metastatic and what competitors might show?

Stephen Hoge - *Moderna, Inc. - President*

So first on the flu, on the B. We're still looking into the data, and we're going to develop a more complete picture of what we think happened in the influenza B immunogenicity study.

I would note a couple of things that are important. The first is these are active comparator studies. And so when you look at non-inferiority on 0 conversion or titers, it's important to note that we're going against the standard-dose influenza vaccine active comparator. And between the Phase II study and the Phase III Southern Hemisphere study, there were changes in the composition of those active comparators and the comparator used, and so that can drive some difference.

The second thing I would note is that they were different populations, and so we went from a Northern Hemisphere to a Southern Hemisphere. And obviously, that can drive some differences in background history of influenza illnesses.

But the third and perhaps maybe most relevant is we did expect that the influenza B neutralizing titers were lower. As you remember, we shared with the Phase II data about a year ago. We did have lower neutralizing HAI titers for the influenza B strains. And for our older adult influenza vaccine, we thought that was acceptable because at the end of the day, our goal was only to achieve non-inferiority, not to demonstrate superiority. Whereas for the influenza A strains, we really wanted to maximize those neutralizing titers and potential for benefit because influenza A really is what drives illness in older adults, which is our first generation...

So we did focus heavily on the influenza A. We were aiming at non-inferiority on the influenza B. And as you said, we did not make non-inferiority on those, and we'll continue to pull apart the reasons as to why. But we have already identified an update that would allow us to improve immunogenicity against the Bs to the extent that is important going forward, not just in younger populations but perhaps from an overall regulatory perspective.

And so we've made that update, we're actually going to be evaluating that in the clinical study very shortly here. And we expect that we'll be able to address that lower immunogenicity that we saw on the Bs quite quickly.

But as I said a moment ago, what really matters is efficacy and efficacy against influenza disease. And in this case, we really do see that as influenza A related for our first-generation product. But we will obviously be updating influenza B-strain for other subsequent generation of products. And it's important to note that that's really important as you get into pediatric populations where influenza B is a burden of disease, particularly in the young.

Now on the question of PCV, we're pretty encouraged by the adjuvant melanoma data. We do have some early metastatic data, as you'll note from our prior Phase I studies. And in the Phase II, there was some Stage IV disease as well in that study. We did not conduct it only in first-line metastatic, and so we're actually looking forward to understanding the performance of a competitive product in that space because it may actually identify an opportunity for us to move into earlier stages of treatment.

Now for now, our approach has been to focus on places where checkpoint including KEYTRUDA, our standard of care and have demonstrated a really strong signal, which is why you see us expanding from adjuvant melanoma into adjuvant non-small cell, and ultimately, will go first into other adjuvant indications where we really think there's the most immediate biologic benefit or biologic rationale for potential benefit that we'll be looking to demonstrate.

But obviously, as others start to move into the space. If they show benefits in other lines of therapy, we will absolutely want to proceed very quickly in those directions as well. So we're looking forward to those results, and we'll obviously launching them as everyone else will.

Operator

Next question comes from Tyler Van Buren with Cowen.

Tyler Martin Van Buren - *Cowen and Company, LLC, Research Division - MD & Senior Equity Research Analyst*

For RSV, a few years from now, do you expect it to be a 2, 3 or perhaps a 4-player market when including J&J? And how do you believe that the tolerability profile compares to others based upon the full data presented this morning?

Stephen Hoge - *Moderna, Inc. - President*

Sure. I can maybe -- I'll take the first portion of that question. At this point, there are obviously 3 companies that have read out their Phase III pivotal efficacy studies and are proceeding right now to filing. I think -- I don't have a specific view on J&J, maybe Arpa can offer perspectives on that, but it is an adenoviral vector program, and otherwise still unclear about the regulatory path forward.

Now on the question of reactogenicity and tolerability profile. As we presented today or as our collaborator presented today at RSVVW, we do see, we think, a favorable tolerability profile. Grade 3 adverse reactions, whether local or systemic, were all below 2% for any of the individual symptoms. And actually compared relatively favorably with a placebo in that arm, often maybe 1.5x as frequent as what we're seeing in placebo, which we think is a compelling overall reactogenicity profile.

We then think the other parts of the benefit of the product are obviously efficacy. We're incredibly pleased. If you look at the most common definition of cases, so RSV lower respiratory tract disease involving 2 symptoms, which has been relatively consistent across the different products. We have

seen very high efficacy 83%, which we really think is among the best. And as we presented today, that efficacy actually holds up beautifully as you look at older populations, those over the age of 70, as well as those with high-risk comorbidities. Those would drive the majority of the expense associated with caring for patients, older adults with respiratory disease from RSV.

So overall, it's very difficult, obviously, to do cross-trial comparisons. And ultimately, it will fall for public health officials to make those decisions, but we are really encouraged by both the efficacy and tolerability profile of 1345, and look forward to filing and ultimately to the commercialization of that product. Arpa, would you like to add anything in terms of your perception of the market going forward?

Arpa Garay - *Moderna, Inc. - Chief Commercial Officer*

Sure. So I would say we do anticipate it being at least the 3-player market with Moderna, Pfizer and GSK. There is a possibility of a 4-player market if J&J has a regulatory path forward with their adenovector virus vaccine. Nothing more to add there.

Operator

Our next question comes from Jessica Fye with JPMorgan.

Jessica Macomber Fye - *JPMorgan Chase & Co, Research Division - Analyst*

Following up on flu or mRNA-1010, just to be very clear. If you hit on non-inferiority in the efficacy Northern Hemisphere study, do you think that mRNA-1010 would be approvable in spite of missing on non-inferiority on the B strains? And related to that, would you envision the approval only being for older adults?

And on RSV, can you comment on the expectation for dosing frequency for your RSV vaccine? And how do you think about the value and potential pricing of that vaccine, maybe benchmarking off other vaccines for that age group?

Stephen Hoge - *Moderna, Inc. - President*

So let me take the flu stuff first. So again, the full approval gold standard is a head-to-head efficacy study. And so if we demonstrate non-inferior efficacy against an approved vaccine in the population which we're studying in which in this case in P302 is 50-plus adults. We do believe that could form the basis of an approval. At the end of the day, immunogenicity results, in particular, are only surrogates for efficacy, and ultimately, efficacy is the gold standard. That's what's required for traditional approval, and that's why we're running the P302 study.

So it will depend upon how our conversation with regulators around that data package, but it is certainly plausible. And in fact, one might say likely that if we meet efficacy in the efficacy study that, that would be sufficient to move forward for a full approval. It doesn't mean that there may not be questions about demonstrating non-inferior immunogenicity with influenza B strains or other things in subsequent studies, but we do believe there's a possibility there. But at the end of the day, it will be dependent upon data and discussions with regulators, including the FDA. And so we'll wait till we have that data and have those conversations, but I think it's certainly a possibility.

Now as it relates to age for approval, we're currently studying mRNA-1010 only in older adults. And so as I said, the P301 was in 18-plus, P302 is in 50-plus, and that's really where we see the broadest recommendations for seasonal influenza vaccines and where we have been most focused initially on building out our respiratory portfolio. We will evaluate our influenza vaccine, in fact, many of our store vaccines in younger populations over time. But we'll have to do age deescalation, dose finding and then bridge down from an immunogenicity perspective, very much like what we did with COVID. And so our initial filings for approval, if they proceed based on data, would be in adults and older adults principally. And then eventually, we would follow on with pediatric populations.

And as I said a moment ago in response to Michael's question, that may involve using updated B antigens to increase immunogenicity in that population. But again, that's subsequent studies that we would do in children.

Could you remind me of the second question?

Jessica Macomber Fye - *JPMorgan Chase & Co, Research Division - Analyst*

For RSV, what are you thinking for dosing frequency? And how do you think about value and potential pricing of that vaccine, maybe benchmarking off of other vaccines for that age group?

Stephen Hoge - *Moderna, Inc. - President*

Sure. So I'll let Arpa take the second part of that question.

First on frequency. It is not yet clear on how frequently people will need an RSV vaccine. It's a seasonal virus, a seasonal epidemic of disease that shows up. Most of us have been exposed to RSV all over a dozen times over the course of our life. And what really happens from a biology perspective is as we get older, our ability to maintain high neutralizing titers to protect us goes down, and what we have is breakthrough disease and ultimately, a disease leads to substantial cost and morbidity and even some mortality in older adults.

We do not -- we have not yet had approved vaccines, and so what we don't yet know is what's the frequency of vaccination. Is it going to be seasonal every year, or is it going to be less than seasonal every couple or few years? But what's pretty clear, based -- from my perspective, based on the epidemiology of RSV infection, is that we do see RSV fairly regularly as adults, and unfortunately, over time, it breaks through more frequently, and so there probably will need to be repeated boosting to protect against RSV.

At the end of the day, the initial recommendations will come from ACIP as well as from regulators around that frequency, and we will have to defer to them on how they want to administer and roll out the RSV vaccines. Whether they want to follow a flu model, which would be annual to make sure that we get the broadest amount of protection, or that they want to initially roll out RSV vaccines and then follow over time for the durability of that efficacy. At this point, none of us, none of the 3 products that have read out in Phase III, have a clear answer on the durability of that efficacy, although we would expect it to wane as it does against natural RSV infection over time in older adults.

Arpa, do you want to take the next part of the session?

Arpa Garay - *Moderna, Inc. - Chief Commercial Officer*

Sure, yes. I can take the question on pricing. So overall, from a pricing philosophy perspective, Moderna is committed to pricing that reflects the value of our vaccines in terms of what they deliver to patients, to societies and the healthcare systems, while also ensuring full access for patients regardless of their ability to pay. So with that broader principle around pricing, we will be looking at the full recommendations that come out of ACIP as we get the filing and the ACIP recommendations to look at what the full value that could be provided back is based on things, as Stephen mentioned, around dosing frequency. And the pricing will be based on both value and access.

I'm not able to share any additional details on what sort of range that pricing might fall into, but it will be consistent with our overall pricing philosophy.

Operator

Our next question comes from Ellie Merle with UBS.

Eliana Rachel Merle - *UBS Investment Bank, Research Division - Analyst*

Just another on flu, just -- any more details on the titer level specific that you saw or when we'll get more details on the titer levels? And then how should we think about the importance of having titers above that 40 benchmark versus demonstrating non-inferiority. Like I guess, what is the comparator vaccine titers in your Phase III say did very well and were well above 40? How should we think about the implications then, say, you're at 30 or near 40, what that would mean from a regulatory standpoint as well as a commercial standpoint in interpreting the immunogenicity idea?

Stephen Hoge - *Moderna, Inc. - President*

All very good questions, and I think the short answer is we're looking into that data right now, and we will provide an update. I'm not exactly sure when we will have that, but we do have the Vaccines Day investor meeting coming up in April of the spring, and then obviously, we'll be looking to publish that data and share it as it comes in and is it available.

You've highlighted 1 of the key challenges in active comparator studies in particular, which is that you can see high titers but actually because you're looking at a ratio, say for whatever reason, your active comparator does really well against one of the strains, that can impact your ability to tease non-inferiority statistically. And at the end of the day, the challenge is even more complicated as you look at older adults where, for instance, the influenza B strains are not a big driver of efficacy or disease, and so we will look at all of that as well regulators.

I would note that it is well precedented. In fact, many of the currently approved influenza vaccines have, in the past, missed on non-inferiority for -- and influenza B-strain end points here over there and still haven't received full approval or accelerated approvals. And the reason for that is, as we've said sort of throughout, that at the end of the day, influenza B is not a primary driver of concern and it is known to be among the different strains of influenza in the virus -- in the vaccines of lower import for disease in older adults. In fact, 1 of the 4 strains, there have been active debates about the B/Yamagata strain as to whether or not it's gone extinct, and even should be removed from quadrivalent vaccines in many of the recent WHO and other debates.

And so influenza B is a well-trodden path for many of these vaccines as well as now for mRNA-1010, where there is differential performance, and ultimately, there is precedent for moving forward where you do not technically need non-inferiority on immunogenicity or seroconversion endpoints and still moving forward because of the lower concern about that disease in older adults.

So we will look at that data. We will develop our strategy. We will obviously engage with regulators with that data, and ultimately determine a path forward. The most important thing for us, though, in the near term is continuing with the efficacy study trying to establish whether or not we have non-inferior or even superior efficacy for mRNA-1010 in its current form against influenza A, which is really where we think payers and public health officials will have the most attention because it is prevention of that disease, not the immunogenicity endpoint, prevention of influenza-like illness, hospitalizations, that is the primary objective of the vaccine and that's where we're focusing our attention right now.

Operator

Our next question comes from Joseph Stringer with Needham.

Joseph Robert Stringer - *Needham & Company, LLC, Research Division - Senior Analyst*

Two from us, the first one on 4157 KEYTRUDA combo program. Just curious, if you could give us a little bit more color on how we should think about the cadence of the additional trial starts? Is it something that will be a more stepwise and measured approach, or should we expect sort of a full force kind of multiple trial starts approach?

And then secondly, on rare disease, outside of your M&A, GSD and PA programs, what is the next rare disease program that we can expect to enter the clinic?

Stephen Hoge - *Moderna, Inc. - President*

So on 4157, I think I'll just reiterate our prior guidance, I don't want to expand it, to say that we are trying to move into those pivotal studies, Phase III confirmatory Stage IV melanoma and non-small cell lung cancer, both adjuvant settings, this year. And we -- you can look at the history of Merck and their ability to execute those studies, enroll quite quickly and now working together with us, we hope to be able to at least do that well. And we will look to enroll those at least as quickly as other confirmatory Phase III studies and similar populations have been run generally. But I don't think we're going to provide more specific guidance on enrollment time horizon except to say we want to go as fast as possible.

I will also clarify, too, that from an accelerated approval perspective, if that pathway were to become available based on the current Phase II data, which again is subject to future conversations with regulators, that we would want to have started those confirmatory studies. We wouldn't have needed to complete enrollment, but definitely, we want to be demonstrating that we're moving forward in those confirmatory studies as quickly as possible. And so we have double impetus. We're moving fast in enrolling them in the near term.

Now in the rare disease space, programs moving out of pre-clinical and clinical. The first I would say is we do have a clinical program for MMA, which you referenced, but that MMA program is another place where we expect to see additional data following on, hopefully, the continued strong performance of the propionic acidemia PA program. And then the pre-clinical development space, we have programs against OTC and PKU, so proteinuria and a urea cycle disorder OTC, and those are both programs that we would hope to move into clinical testing in short order. We haven't specifically guided on the timing of that yet.

Operator

Ladies and gentlemen, this does conclude the question-and-answer portion of today's call. I'd like to turn the call back over to Stephane for any closing remarks.

Stephane Bancel - *Moderna, Inc. - CEO & Director*

Thank you very much, everybody, for joining us and for the many thoughtful questions. We look forward to hosting you for Vaccine Day on April 11. It will be live in Boston, for those of you who can join us, and also, of course, virtual. Have a great day. Thank you.

Operator

Ladies and gentlemen, this does conclude today's presentation. You may now disconnect, and have a wonderful day.