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OVERVIEW:

Company Summary

REFINITIV

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PRESENTATION

Operator

Good day, and thank you for standing by. Welcome to the Moderna fourth quarter 2024 conference call. (Operator Instructions) Please be advised, today's conference is being recorded.

I would now like to hand the conference over to your speaker today, Lavina Talukdar. Please go ahead.

Lavina Talukdar - *Moderna Inc - Senior VP & Head of Investor Relations*

Thank you, Kevin. Good morning, everyone, and thank you for joining today's call to discuss Moderna's fourth quarter and full year 2024 financial results And business updates. 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 Stéphane Bancel, Chief Executive Officer; Jamey Mock, Chief Financial Officer; and Stephen Hoge, President.

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 twoof 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.

I will now turn the call over to Stephane.

Stephane Bancel - *Moderna Inc - Chief Executive Officer, Director*

Thank you, Lavina. Good morning or good afternoon, everyone. Thank you for joining us. I will start with a review of 2024. Jamey will present our financial results and outlook. Stephen will review our clinical programs. I will then come back and show our key priorities for 2025 before we take your questions.

In 2024, we recorded revenue of $3.2 billion. The team has looked how to generate cost savings of $2.6 billion or 27% down from 2023. We reported a loss of $3.6 billion.

While we have anticipated to end the year with $9 billion in cash, thanks to the team's work on OpEx, CapEx and also working capital, we ended the year with $9.5 billion of cash and investments at year-end.

In September 2024, we announced our focus on 10 high-value programs for which we expect financial approvals over the next three years, driving sales growth and diversification from our top line from COVID. This program includes the respiratory vaccine, next-gen COVID, combination of flu plus COVID, RSV 18 to 59 at five-week, flu. In late, CMV and Norovirus. In rare disease, PA and MMA. And oncology, INT for adjuvant melanoma. In addition to pulling sales growth, the prioritization of these programs will allow us to reduce our R&D expenses in this time frame.

From a pipeline standpoint, it was a year of strong progress. In 2024, we became a multiproduct company who we have power of . Along with buybacks, we now have two commercial products on the market.

We reported positive Phase III results in four of our program, and we filed for FDA approval on next-gen COVID, our combination of flu plus COVID and the RSV vaccine for RSV 18 to 59. And vaccine is currently in a Phase III efficacy trial.

We also reported additional progress across our programs for the Phase I/II from vaccine against Norovirus, EBV and BBB.

In oncology, we presented data at major medical meetings in 2024. For INT program, in June, we reported positive data in adjuvant melanoma for the Phase II trial. In addition, for checkpoint program vaccine, mRNA-4359, we presented positive Phase I data in September.

In [rare disease], we had positive early safety and clinical data from PA and MMA. With that, I will hand over to Jamey.

James Mock - *Moderna Inc - Chief Financial Officer*

Thanks, Stephane, and hello, everyone. Today, I will walk through our financial results for the fourth quarter and full year 2024, providing insights into the key drivers behind our performance. I'll also outline our 2025 financial framework as we continue to optimize our operations and position the company for long-term success.

Let's begin by reviewing our commercial performance on slide 8. For the fourth quarter of 2024, net product sales were $0.9 billion, with $0.2 billion in the United States and $0.7 billion outside the United States.

For the full year, net product sales were $3.1 billion, at the lower end of our revised guidance. US sales were $1.7 billion for the year, benefiting from a $0.2 million favorable adjustment related to a prior period return reserve reversal. Excluding this adjustment, sales volume saw a decline

compared to last year, primarily due to lower vaccination rates, lower market share and increased competition. However, we observed signs of stabilization and believe the COVID market will remain durable over time.

Outside the US, product sales were $1.4 billion, aligning with the midpoint of our guidance. This includes approximately $400 million from advanced purchase agreements that will not recur in 2025. The vast majority of our sales were from Spikevax.

While we launched our second product, mRESVIA, in the third quarter, sales were only $25 million for the full year. While early RSV sales were limited, we see long-term opportunity to expand our presence in this market, both in the US and internationally.

Moving on to slide 9. I will now walk through our financial results for the fourth quarter of 2024. Total revenue for the fourth quarter was $966 million, down 66% from the same period last year. As expected, sales were impacted by the earlier launch of our updated COVID vaccine in the US, with FDA approval granted three weeks earlier than the prior year.

This allowed us to meet demand sooner, shifting a portion of sales into the third quarter. International sales were also lower year-over-year, reflecting the ongoing phaseout of advanced purchase agreements.

Cost of sales for the quarter was $739 million, including $45 million in third-party royalties, $193 million in inventory write-downs and a noncash charge of $238 million from the termination of a contract manufacturing agreement. The contract termination is part of our continued effort to optimize our manufacturing footprint, following the strategic resizing initiative launched in 2023 to align with the transition to a seasonal endemic market.

While cost of sales declined by $190 million compared to the prior year, lower product sales volume drove cost of sales to 79% of product sales. Excluding the resizing charge, this would have been 53%.

R&D expenses in Q4 were $1.1 billion, reflecting a 20% year-over-year decline. The decrease was primarily driven by lower clinical development and manufacturing costs across our COVID, RSV, flu and combination vaccine programs. This was partially offset by increased investments in our Norovirus and INT programs. Additionally, last year's R&D expenses included $120 million upfront payment related to our collaboration with [Thematics], which did not recur this year.

SG&A expenses for the fourth quarter were $351 million, down 25% year-over-year. The decrease was primarily driven by reductions in purchased services and external consultants as we continue to focus on cost management and operational efficiencies.

We recognized an income tax benefit of $64 million in the fourth quarter. Similar to the prior year, the benefit was not material, due to the global valuation allowance maintained against most of our deferred tax assets. Net loss for the quarter was $1.1 billion compared to net income of $217 million in Q4 2023.

Loss per share was $2.91 compared to earnings per share of $0.55 in the prior period. We ended the quarter with cash, cash equivalents and investments totaling $9.5 billion, up from $9.2 billion at the end of the third quarter. The increase was primarily due to accounts receivable collections.

Now let's turn to our full year 2024 financial results on slide 10. Total revenue for the year was $3.2 billion, a 53% decline from 2023, primarily driven by lower product sales, which I discussed on the prior page. Other revenue contributed $127 million for the year, reflecting grant revenue, collaboration, licensing and royalty revenue.

Cost of sales for the full year 2024 was $1.5 billion or 47% of net product sales. Excluding the $0.2 billion noncash resizing charge, this would have been 39% and below our previous guidance of 40% to 45%. This represents a $3.2 billion decrease from 2023 due to lower manufacturing resizing charges as well as lower inventory write-downs and reduced unutilized manufacturing capacity costs, all of which reflect improved efficiency.

R&D expenses for the year were $4.5 billion, down 6% from 2023. The decrease was largely due to lower clinical trial and manufacturing costs as well as fewer upfront payments for collaboration agreements. We did, however, purchase two priority review vouchers during the year, which offset some of those savings.

For the full year, SG&A expenses totaled $1.2 billion, a 24% decrease compared to 2023. The decrease reflects disciplined cost management across the organization. We have continued to build capabilities and build -- bring more functions in-house, allowing us to reduce reliance on external consultants while improving operational efficiency. Additionally, these savings were exported by better leveraging digital technology and artificial intelligence to streamline operations.

We reported an income tax benefit of $46 million for the full year compared to an income tax expense of $772 million in 2023. The shift is mainly due to the global valuation allowance we established last year on most of our deferred tax assets, which continues to impact our tax position. Net loss for the year was $3.6 billion compared to $4.7 billion in 2023, with a loss per share of $9.28 compared to $12.33 in the prior period.

Moving to slide 11. We want to highlight the significant reduction in our operating expenses in 2024. On a GAAP basis, cost declined $3.9 billion, from $11.1 billion to $7.2 billion. Excluding resizing charges of $1.6 billion and $0.2 billion for 2023 and 2024, respectively, we reduced operating expenses by $2.6 billion compared to 2023, driven by manufacturing footprint resizing, pricing renegotiations, R&D prioritization, volume reductions and a greater use of digital tools to improve efficiency. Additionally, both 2023 and 2024 operating expenses included noncash costs of $0.9 billion and $0.6 billion, respectively, related to stock-based compensation and depreciation and amortization.

If we would exclude the manufacturing footprint resizing charges, stock-based compensation and depreciation, our defined cash costs were $8.9 billion in 2023 and $6.3 billion in 2024, representing a year-over-year decline of $2.6 billion. To avoid double counting, please note that in 2023, there was approximately $300 million of depreciation and amortization included in the $1.6 billion of resizing charges.

We are committed to drive additional cost efficiencies in 2025 and beyond by prioritizing investments to support the 10 product launches over the next three years. Our 2025 GAAP expenses are projected at $6.4 billion in 2025, which includes $0.9 billion of noncash charges from stock-based compensation, depreciation and amortization.

Excluding those items, we project a cash cost of $5.5 billion. This represents an approximately $1 billion year-over-year reduction from our prior 2024 projection of $6.5 million. We are also planning for an additional $0.5 billion of expense reduction in 2026 as we continue to drive efficiencies across all areas of the business.

Now let's turn to our financial framework for 2025. We expect total revenue in 2025 to be in the range of $1.5 billion to $2.5 billion, with first half sales of approximately $0.2 billion, reflecting the seasonality of our respiratory vaccine business.

As discussed with investors in January, our wider guidance reflects the uncertainties in vaccination rates, the competitive market environment, the size of the RSV market and timing of licensure of our factories and product approvals in Australia, Canada and the UK.

As a reminder, we filed three products to the FDA in 2024, and we are not including any new product revenue in our guidance range. Also, we expect the revenue and R&D expense from our recently announced pandemic influenza program to be relatively immaterial in 2025, and is embedded in our guidance.

Positive [sales] is projected to be approximately $1.2 billion, reflecting continued improvements in manufacturing efficiency and lower expected inventory write-offs offset by increased costs associated with the go-live of our new manufacturing sites in Australia, Canada and the UK.

R&D expenses are anticipated to be approximately $4.1 billion as we continue to invest in our late-stage pipeline, while maintaining financial discipline. SG&A expenses are expected to be approximately $1.1 billion, reflecting a continued focus on efficiency while supporting our commercial execution. We expect taxes to be negligible in 2025.

Capital expenditures are projected to be approximately $0.4 billion. This increase from our prior guidance of $0.3 billion is primarily due to the timing of spend between 2024 and 2025. 2024 actual capital expenditures was approximately $150 million below our prior guidance. Some of that reduction was attributable to prioritization changes, but the majority of the impact was timing of spend between 2024 and 2025. We expect to end 2025 with approximately $6 billion in cash and investments.

In summary, 2024 was a year of financial discipline, and we are well positioned as we enter 2025. We remain committed to managing costs, optimizing our operations and investing in our future growth. With that, I will now turn the call over to Stephen.

Stephen Hoge - *Moderna Inc - President*

Thank you, Jamey, and good morning or good afternoon, everyone. Slide 15 shows the prioritized programs we highlighted at our R&D Day in September. As Stephane mentioned earlier, we are focused on pursuing these 10 approvals over the next three years to drive growth. We've now filed for approval for three respiratory vaccines, our next-gen COVID vaccine, our RSV vaccine for high-risk adults ages 18 to 59 and our flu COVID combination vaccine for people aged 50 and older. Most of the other seven prioritized programs are in pivotal studies, and the remainder are expected to begin their pivotal studies in the near future.

Slide 16 highlights the most recent updates from our late-stage portfolio. As a reminder, in September, we presented positive efficacy and immunogenicity data from our next-gen COVID vaccine mRNA-1283. We have since filed for approval in multiple jurisdictions, and have a PDUFA date of May 31, in the United States.

Also in September, we shared positive Phase III data for our RSV vaccine in high-risk adults ages 18 to 59. This vaccine has also been filed for approval in multiple countries, with a PDUFA date of June 12 in the United States.

For our combination flu COVID vaccine, we previously shared positive Phase III immunogenicity and safety data. And on the basis of that data, we filed for approval at the end of last year in the United States and other countries. We have previously demonstrated efficacy for the COVID component of the vaccine, demonstration of efficacy for the flu component may ultimately be required for approval.

To that end, our stand-alone flu vaccine, mRNA-1010, is currently in a Phase III efficacy study that is accruing cases rapidly. Based on the current pace of case accrual, we are optimistic that we will be able to conduct the first analysis of efficacy for our flu vaccine at the end of the currency.

Now turning to our nonrespiratory portfolio. Starting with our latent and other virus vaccines. For our CMV vaccine, we announced last month that the Data and Safety Monitoring Board informed us that the early efficacy criteria was not met, and recommended that the study continue to its final analysis. We remain blinded to the study and continue to expect the results for the final analysis later this year.

Our Norovirus vaccine Phase III study is fully enrolled in the Northern Hemisphere, and we are preparing to enroll participants for the upcoming Southern Hemisphere season. The trial is currently on FDA clinical hold in the US, following a single case of syndrome, which remains under investigation. Given that enrollment had already completed for this season, we do not currently expect any impact on time lines, while we complete the investigation and update trial documents with this information.

In oncology, we and our partner, Merck, have multiple late-stage studies underway evaluating INT or mRNA-4157 in combination with KEYTRUDA. The first of which, adjuvant melanoma, is part of our 10 prioritized program. The Phase III for this is now fully enrolled.

Two additional Phase III studies are underway in non-small cell lung cancer, and there are tworandomized Phase II trials ongoing in high-risk muscle-invasive bladder cancer and adjuvant renal cell carcinoma.

In rare diseases, propionic acidemia, or PA, is in its registrational study, and methylmalonic acidemia, or MMA, we have -- with MMA, we have agreed with FDA on our pivotal study design and expect to start that study in 2025.

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

Stephane Bancel - *Moderna Inc - Chief Executive Officer, Director*

Thank you, Stephen and Jamey. For 2025, we have three priorities. Priority one is to sales of approved products. Priority two is to focus on our late-stage pipeline, where we believe we have up to 10 product approvals over the next three years, which will drive sales growth and diversification. Priority three is to deliver cost efficiency across the business. Let me take you through each of these.

Our first priority is to review those backs and our vaccines. Importantly, we enter 2025 with two approved products, which gives us a better competitive positioning that when we enter 2024. We have full contracting in the US We expect to better compete in the respiratory vaccine market. In addition, upcoming MREL approvals outside the US should also add to sales in 2025.

Priority two, we are focused on delivering up to 10 products approval over the next three hree years, which we believe will drive sales growth. Together, these 10 expected products target the total addressable market of over $30 billion.

Priority three, there is a cost efficiency across the business. We've demonstrated our commitment to cost savings by the $2.6 billion cost reduction we made in 2024. We will continue to focus on improving efficiency costs across the entire company across manufacturing, across and across SG&A in 2025, but also in 2026.

For our efficiency program, we're reducing cash costs to an estimated $5.5 billion in 2025 and $5 billion in 2026. This brings our total cash cost reduction to well over [$1 billion] over these two years from a $6.3 billion in 2024.

We will continue to address our cost structure to ensure we breakeven on a cash cost basis no later than 2028. In the -- to be very clear. If needed, we will reduce our cost structure further than the [$5 billion] cash cost level if our sales objectives are not met.

For products, we expect important milestones. We filed three years of move forward to having the final reason to our Phase III study in 2025, vaccine Phase III studies and the timing of data that will be subject to we will also be subject with -- For PA, we're already data from our retraction study, and we expect to start researching study -- this year.

We will continue to focus on the possible impact to people . Our offering of products and pipeline are promising work, [two] approved products and fixed base for pivotal studies ongoing. So our money platform is working. We've demonstrated progress in our cost reduction program. We have shown that we have a financial discipline to achieve our goals and fulfill our mission.

With this, operator, we'll be happy to take questions.

QUESTIONS AND ANSWERS

Operator

(Operator Instructions) Ellie Merle, UBS.

Eliana Merle - *UBS Investment Bank - Analyst*

Can you help us understand the breakdown of the R&D spend across your program? So if you needed to or wanted to reduce R&D spend further, how much flexibility is there on the expense structure there for, say, further cuts in the 2026 time frame?

And then just a second question. On the clinical hold on Norovirus, can you give any more detail around sort of this, why one case of GBS prompted the clinical hold? And yes, adding more color surrounding the situation there would be helpful.

James Mock - *Moderna Inc - Chief Financial Officer*

Yes. Thanks, Ellie, for the questions. Maybe I'll address the first one on R&D. So we still think there's a lot of room to be reduced and a lot of flexibility. So as a reminder, we're guiding $4.1 billion for 2025. And in R&D Day, we said we would take it down by $1.1 billion from the $4.8 billion level by 2027. So that suggests a number of about $3.6 billion, $3.7 billion.

To answer your question on what we're spending on, that's still back primarily over 50% of our trial spend, and therefore, overhead is related to respiratory trials, which, as you know, we expect to roll off over this year and the following year.

And then the only other Phase III trials that we started are in latent disease, in oncology for Norovirus, and CMV and INT, and we expect those to be reduced over the coming years as well. So we expect that there will be some flexibility beyond the $3.6 billion that we've already indicated. But right now, we're still monitoring the sales line, but that is an area that we could continue to reduce if need be.

Stephen Hoge - *Moderna Inc - President*

And thank you for the second question. I'll take it. So just a little bit of context, as you alluded to, GBS does happen, obviously, in the background population. It's usually seen in older adults, about one to two per 100,000 participants per year or people per year. And given we've enrolled well over 250,000 participants in studies over the last couple of years, it wouldn't be surprising to see cases in our clinical trials, as you suggested. And although that hasn't been associated as a risk factor with our approved vaccines, this is something that does happen.

As it relates to this case, when we identified it, we proactively decided to pause our activities and update our study documents because we prioritize the patient safety and obviously, transparency, first and foremost. And we wanted to make sure that all that information was shared as soon as the case merged. We submitted those for review with regulators globally, and the FDA has placed us on a clinical hold while they review that information in those documents.

Perhaps most importantly for study conduct, because we had enrolled and dosed everybody prior to the emergence of this case in the current season study, we really don't expect there to be any impact on the conduct of the study or its time line for readout on efficacy, which will ultimately be case driven.

So from our side, this is just about being prudent and transparent and making sure that we're prioritizing patient safety.

Operator

Gena Wang, Barclays.

Huidong Wang - *Barclays Bank - Analyst*

Maybe just follow up on Norovirus. What would it take for the FDA to remove the clinical hold? What kind of outcome that we deem to be okay? And then really another question regarding the CMV, now we should see more events accrued? Will it still happen in the first half '25? Should we see the final readout?

Stephen Hoge - *Moderna Inc - President*

Gena, you broke for just a second. Could you repeat the CMV portion of the question?

Huidong Wang - *Barclays Bank - Analyst*

Sure. CMV, since now we've seen additional months of events accruing, should we still be able to see the final readout in the first half '25?

Stephen Hoge - *Moderna Inc - President*

Thank you. So I think -- let me deal with that first. So yes, we continue to accrue cases in the CMV trial. As I said, we remain blinded to the interim analysis. We still do expect that result in 2025. I don't know that we've got into the specific timing, but we still do expect the result in '25.

As it relates to Norovirus, clinical hold, obviously, I think the FDA needs the time to review the materials we've submitted. They may come back with some questions. If they do, we'll answer those. But as has been suggested even in the question, a case of GBS is not necessarily unexpected.

And because we've updated the documents, we really do expect there to be minimal impact on trial conduct at this point But it will be ultimately up to the agency, what they need to see before we move forward with further enrollment.

Operator

Michael Yee, Jefferies.

Michael Yee - *Jefferies - Analyst*

We had two timing questions for you guys. First, on the INT cancer vaccine, which, of course, is a really exciting product. I think previously, if you've done some math on the Phase II, it's certainly possible on the event rates that were seen in Phase II that the data could come by end of year or first half of '26 and the company has not totally dissuaded us or others from that type of timing.

Do you generally agree with that timing? And can you shed some light on how to think about the powering for the INT cancer vaccine primary end point? And then similarly, with the Norovirus, I think you mentioned that you're enrolling the Southern Hemisphere but completed the Northern.

Do you need both to hit the primary or to hit the event rate and just help us understand the timing of that despite the fact that it's on hold, the Northern which already completed enrollment.

Stephen Hoge - *Moderna Inc - President*

Thanks for your questions. So first on INT, there are some differences between the study population between the Phase II and the Phase III. And so we will want to be guided by the actual event accrual, a case accrual rate, the relapse rate in the Phase III study before we feel confident that we could offer a timing on that.

And so as we have started to accrue cases, the study, as you know, is fully enrolled. So there are to be events that start to happen. We'll have a better sense of that. Certainly, 2026 seems possible, plausible. But whether or not it could be on the early side of that or the late side of that, we just don't know at this point, it is event driven. And so more as we have information in the future.

On the question of Norovirus, so we have -- we fully enrolled and fully dosed the Northern Hemisphere study, which is the majority of the study. But given epidemiology, we also wanted to enroll some participants in Southern Hemisphere geographies.

At the end of the day, we will also be case driven, so you ultimately need cases of Norovirus towards that efficacy endpoint because the majority -- the sizable majority study is completely enrolled now. That's Northern Hemisphere is completely enrolled, which is the majority of the participants we intended. It's possible that we won't need Southern Hemisphere participants. But we do intend to enroll Southern Hemispheres if we want broader epidemiology towards that final endpoint.

So again, we don't know when that will happen. We do currently hope that we're sufficiently powered in this season to see efficacy, but if more participants are needed, then of course, we will enroll them to accrue more cases towards that efficacy endpoint.

Operator

Salveen Richter, Goldman Sachs.

Salveen Richter - *Goldman Sachs Group, Inc. - Analyst*

Could you help us understand what the clinical bar is for the Norovirus program? And then on the INT portfolio, will we get any data or just enrollment updates for the programs beyond melanoma?

Stephen Hoge - *Moderna Inc - President*

So the -- on the clinical bar for Norovirus, obviously, there are other vaccines out there for gastrointestinal infections, and others, where we will want to show a meaningful decrease in the rate of moderate to severe gastrointestinal symptoms. Those are really where the burden of disease happens, particularly in higher risk populations like older adults or the immuno-compromised.

We'll look at a pretty broad range of endpoints as secondary and exploratory influence as well, things like hospitalization, utilization of health care services. We have not disclosed our target product profile for that yet or the powering assumptions we have in those interim analyses. And so I won't do that here. We will, perhaps, in the future, provide an update on that, but we will be looking for a meaningful reduction in the rate of moderate to severe acute gastroenteritis.

As for INT, obviously, we're all looking forward to the melanoma adjuvant melanoma Phase III readout. As you know, and as I mentioned, there are additional Phase IIIs as well as tworandomized Phase IIs, including bladder cancer and renal cell carcinoma, which, depending on the rate of accrual of events, could have read outs that we would be updating on as well in the coming years.

Operator

Terence Flynn, Morgan Stanley.

Terence Flynn - *Morgan Stanley - Analyst*

Maybe a two-part for me. Just wondering if you can confirm if you still have not seen any cases of GBS with your RSV vaccine? And then I know you filed for approval for the COVID flu combo vaccine, and it sounds like now you're waiting for some vaccine efficacy data. Can you tell us anything more there about what the bar is? Is it only on the flu side? Or do you need vaccine efficacy for both COVID as well and kind of what level of protection you need to see?

Stephen Hoge - *Moderna Inc - President*

Flynn, thanks for both questions. So first, I can confirm that GBS has not yet or has not been identified as a risk factor for our RSV vaccine or our COVID vaccine today. And so obviously, we'll continue to track that closely, but that's encouraging.

On the combo study, so we have demonstrated efficacy for the COVID component. As you may remember, mRNA-1283 had a successful efficacy study in -- that we announced last year. And that is the COVID component of the combination vaccine so to satisfy that requirement.

As for the flu vaccine, we have had multiple Phase III readouts in our flu vaccine as well as for the combo vaccine demonstrating non-inferior or superior immunogenicity and a good safety profile for those . But we have not yet demonstrated efficacy for the flu component of that vaccine.

That trial, as I mentioned, is actually ongoing right now. And given that it is a robust flu season in the Northern Hemisphere, as many folks know, and given the case accrual rate we see there, we do expect that we'll -- we're actually quite optimistic we'll be able to kind of the first interim analysis of efficacy at the end of this current season. And so that would then be the demonstration of efficacy for the flu component of the combo vaccine.

Operator

Tyler Van Buren, TD Cowen.

Tyler Van Buren - *TD Cowen - Analyst*

Regarding Thank for taking question. CMV, just to confirm, even though the criteria on for early efficacy was not met at the interim, is it still possible that higher vaccine efficacy threshold from the first interim could still be reached from the final analysis due to a wide confidence interval with fewer patients at the time of the CMV review? Or do you think that's less likely?

Stephen Hoge - *Moderna Inc - President*

Thanks for the question. So what we -- if you look at the tower that we had at that first interim analysis, it actually was intended as an early look, but not sufficiently powered that you would have high compound if it was in between efficacy. And for that reason, it is still very much possible that at the final analysis with many more cases, the confidence interval is narrow and what we see as a point estimate for efficacy that is favorable from our perspective, meets or exceeds our expectations for the target .

The most important thing to say, though, is that we remain completely blind to this. All we know is that the confidence interval did not exclude the lower bound target. And given the powering of the study that -- for that interim analysis, does not necessarily surprising, stopping for early efficacy early criteria and would have been an upside scenario in our view.

So we remain blinded. We will accrue the full number of cases. We continue doing this in that study, and then we'll look to that final announces, which is actually the fully powered analysis for assessing against our target product profile.

Operator

Luca Issi, RBC Capital.

Luca Issi - *RBC Capital Markets - Analyst*

Great. Maybe, Stephane, big picture. We all know that you have worked very closely with the Trump administration during the pandemic. But have you talked to either the President, RFK or any of the representative this time around? If so, what has been the message that you have been hearing from them? I think any color there would be much appreciated.

And then maybe second, Stephen, on Norovirus, can you just talk about the timing of the GBS case? Is that something that occurs soon after the individuals receive the vaccine or maybe many months after that? I'm just trying to understand the correlation versus causation here. So again, any color, much appreciated.

Stephane Bancel - *Moderna Inc - Chief Executive Officer, Director*

Thank you for the question. So as we work productively with the Trump administration in the President Trump's first mandate, and we look forward to working with a new team as they get confirmed by the Senate and the different members. Vaccine are variable and piece of keeping people healthy, and we look forward to having those discussions as people get confirmed. Stephen?

Stephen Hoge - *Moderna Inc - President*

Yes. And on the Norovirus case, as you probably will note, we've enrolled about 20,000 participants in that study in just the last couple of months. It's all been relatively rapid enrollment for the current Norovirus season. For that reason, you can imagine that it's relatively proximal, which is why we're being cautious and communicating around it, first and foremost, with participants, investigators and regulators just so they have that information.

Now to the point of correlation versus causation, it's important to note that in this case, these extremely rare events that do happen, it's very hard of -- to finally determine cause or relationship. And so other than reporting it that it happened around this time and investigating it, thoroughly communicating around it, we may never have an interview on that.

But yes, respect for the confidentiality for that participant and more generally, I don't think I would offer any more information other than we continue to investigate it and see if what the potential causes would be.

Operator

Cory Kasimov, Evercore ISI.

Cory Kasimov - *Evercore ISI - Analyst*

This is [Adi] on for Cory. I wanted to ask on what possible changes have you seen in the past month that has caused the bump to expense guidance already?

James Mock - *Moderna Inc - Chief Financial Officer*

To expense guidance, Adi?

Cory Kasimov - *Evercore ISI - Analyst*

The increase in R&D and SG&A spend?

James Mock - *Moderna Inc - Chief Financial Officer*

I think -- so I don't know if it's a bit confusing. So we've been basically talking about twodifferent sets of numbers, neither have changed. One is our GAAP cost, Adi, and one, which includes stock-based compensation and depreciation and amortization. So maybe that's what you're referring to versus what we define as cash costs, which excludes those twonumbers, which have not changed.

And as a reminder, those numbers were close to $9 billion in 2023. We had $6.3 billion in 2024. We're guiding to $5.5 billion in 2025 and $5 billion in 2026. So perhaps you're looking at the GAAP inclusion, but I -- we have not changed any estimates from our cost.

Cory Kasimov - *Evercore ISI - Analyst*

Got it. And I have just one more follow-up. If you can provide any more color on the language of the PA program, the PR at GPM and today's PR suggests potential decrease in MDE sequencing. I wanted just some additional color on it.

Stephen Hoge - *Moderna Inc - President*

Yes. So -- as we had previously disclosed, from our ongoing clinical trial there, we have seen a significant -- a substantial decrease in the rates of metabolic decompensation events in that propionic acidemia PA study. And we believe and ultimately have agreed with regulators that, that is the endpoint that we will assess for the pivotal part of that study.

We've moved forward into that pivotal phase, so what we'll be looking at is the rate of metabolic compensations or MDE, for participants prior to being on drug versus once they start treatment with that medicine. That rate and the reduction in it will ultimately be -- we believe the pivotal endpoint that would support registration for the drug for PA. And so as we move forward with new participants, as well as some older -- other participants who are already on the study, we'll be looking at that comparison on reduction in the rates of MDE.

Operator

Courtney Breen, Bernstein.

Courtney Breen - *Sanford C. Bernstein & Co. - Analyst*

I wanted to kind of pivot a little bit to some of the costs as well and specifically the inventory write-downs. I think they continue to be an issue for kind of seasonal vaccines. We have to produce in advance and then see the season play out. I would love to understand a little bit more about what the future looks like in this space?

You're going to continue to be in a seasonal market kind of both with COVID, now with flu and with RSV. And so as we think about kind of projecting and manufacturing appropriately to minimize those write-downs but maximize the opportunity, what does good look like, number one, kind of what goal in terms of limited inventory write-downs? And number two, kind of what are the things that you're changing to kind of continue to improve your ability to make to the?

James Mock - *Moderna Inc - Chief Financial Officer*

Yes. Thanks for the question, Courtney. It's a great one. So as you know, and maybe just to step back, in 2023, I forget what the numbers are, but we've reduced this dramatically already. But nonetheless, we did have $500 million of inventory write-downs in 2024 and about $100 million of unutilized manufacturing capacity. And so that $600 million on $3 billion of sales, that is obviously not what good looks like yet.

What I will say is much of this is related to our raw materials where we take an inventory reserve based on future demand. And if you look at our inventory levels now, Courtney, we are under $300 million. I think, $270 million. So the go forward should look much better as we project moving forward on the raw material side.

On the excess capacity side, you're right. We still have a fair amount of either write-offs of good product that we produce because we produced last year, for example, we assumed $4 billion in sales, and we came in at $3 billion, so we obviously overproduced. And we are still going to produce to the higher end of our guidance range of $1.5 billion to $2.5 billion, which is why you see a cost of sales in the neighborhood of 50%.

But as we get better, what we're working on is matching what does that future demand look like and what is the supply that we should account for? And as an example, as we've continued to adjust for that, that's the example of the termination of a contract manufacturing agreement that we had in the fourth quarter.

So we continue to be proactive about what is that future demand, what is the capacity we require, and you should see that come down. And certainly, $600 million on $3 billion is not what we expect. We want that to be less than 10%, let's say, over time, but I'm not saying that, that will happen in the year 2025, but it will get better also because our inventory balance is down dramatically.

Operator

Edward Tenthoff, Piper Sandler.

Edward Tenthoff - *Piper Sandler & Co. - Analyst*

Most my questions have been answered. But I think I saw some news maybe on the [Vertex CF] program. And I was wondering if you could just kind of give us an update on what's going on there with that rare disease program?

Stephen Hoge - *Moderna Inc - President*

Yes. So thank you for the question, Ed. So we continue with our partner, [Vertex], who is conducting that clinical trial. So the sponsor study have the most information on it. But we continue to have the path of -- we've completed the single ascending dose portion of that trial and are now in the multiple ascending dose portion of that trial.

That is, patients receiving treatment regularly to ultimately measure whether or not we're having an effect on respiratory measures and hopefully, overall, addressing the burden of CF in those patients that can't take the small molecule correctors. We do expect a readout from that multiple ascending dose trial. I think Vertex previously guided that we expect that this year, and we will look for them to provide further updates on that timing, if they happen.

Operator

Jessica Fye, JPMorgan.

Jessica Fye - *JPMorgan Chase & Co - Analyst*

I have a few follow-ups for Stephen, just from prior questions I was hoping to clarify the response on. On Norovirus, how confident are you that the trial will not go on some equivalent of clinical hold in the Southern Hemisphere? Have other global regulators confirmed they do not need a pause to review the information? Or is there a chance of stoppage there?

For CMV, just following up on Gena's question. I think in the past, you had said the final CMV analysis could come near months after the interim, which we heard about in January. So should we still think of that as the first half of '25? Or can you clarify the prior answer?

And then on the 1083 COVID flu filing, I think the press release states that approval may require a vaccine efficacy data from the Phase III flu trial. Why is that a point of uncertainty that the FDA may require? Has it been up and clear with you in your pre-submission meeting?

And then lastly for Jamey. Can you recap what variables in the COVID vaccine and RSV markets would land you at the low end or the high end of your '25 guidance, like price vaccination rates, market share or stuff like that?

Stephen Hoge - *Moderna Inc - President*

So a lot there for me, so I'll go first and then kick you to Jamey. So first, on the Northern -- the Norovirus study. As we said, we will look to enroll a second season in the Southern Hemisphere. At present, we do not expect any delays in doing that, given that we have enrolled over 20,000 participants in that study already in Northern Hemisphere, if there were any delays, we're not sure that it would have an impact to study time line. But at this point, we're as confident as we can be that there won't be any in the Southern Hemisphere.

As it relates to CMV, on case accrual. The second half, we have previously said that case accrual was moving relatively quickly. It continues to accrue steadily in the study. Ultimately, it's an event-driven analysis, so we can't necessarily predict the time line, but we previously indicated that we expected it perhaps mid-2025. We're not changing that here. We continue to believe if that's possible. And ultimately, again, it will depend upon the rate of case accruals, which we don't control.

As to 1083, and so for the flu COVID product, when we submitted the package as part of our initial exchange with regulators, we are identifying review questions that they have or issues. And as we said in our press release, in some cases, the proximity of the flu efficacy readout really does loom large on the overall review for the combination product. And we will be -- we do expect that, that may be necessary in some cases now that, that flu readout is expected shortly.

As it relates to individual conversations with individual regulators, I'll say, we're working through their review questions in that submission, and I won't otherwise comment on the specific back and forth.

And with that, I guess, I'll turn it over to you, Jamey.

James Mock - *Moderna Inc - Chief Financial Officer*

Okay. Thanks. So thanks, Jess. Yes. So as a reminder, on the high end, the $2.5 billion, if you exclude the unusual we saw in 2024, we called that essentially flat. So in my prepared remarks, the US came in at $1.7 billion. It had a $200 million return reversal adjustment from the prior year, which would take that to about a $1.5 billion number. And then outside the United States, we were at $1.4 billion, and we said that there was about $400 million of advanced purchase agreements that the demand level we do not anticipate repeating.

So the high end is essentially flat, Jess. So you can anticipate both inside the US and outside the US, similar market share, vaccination rates. We do have a little bit of uptick in RSV in the high end, but it's all together rather minimal in general.

On the low end, it basically assumes no increase in RSV. In the US, you would have to expect it to go down substantially. So you'd have to expect it to go down 5% to 10% from a market share perspective. Vaccination rates would have to go down again 7% to 10%. Both of those things would have to happen to go down, let's say, $0.5 million.

And then really the biggest factor outside the United States are the [licenser] timing of our plants in the UK., Canada and Australia. So should those be licensed and registered on time, we will be on the upper end, but if they are delayed, we've factored that into the lower end of our guidance.

Operator

Simon Baker, Redburn.

Simon Baker - *Redburn (Europe) Limited - Analyst*

There's also a clarification, Jamey. You mentioned the spend on respiratory trials being 50%. Was that 50% of your total trial spend or 50% of your R&D spend?

And then just another question on the flu COVID combo following off from Jessica's question. I'm just interested in what the mechanism is and the timing at which point the regulators could ask for an extra data. Is this something that could come at any time? If it happens sooner rather than later, do you think it would have an impact on the approval time line? And is there any risk in the US that the initial filing gets a complete response and then you have to refile with that COVID data. Any color on the machinations, that would be very handy.

James Mock - *Moderna Inc - Chief Financial Officer*

Yes. Thanks, Simon. On the first one, I was referencing 50% of the trial expense, which is what we break down in our 10-K. There are other line items that hit R&D in terms of the overhead that supports it, people, the sites, et cetera, or manufacturing facilities as well as research, but the 50% that I was referencing is really trial related, but you could imagine many of those other costs are also related, therefore, to the respiratory trials as well.

Stephen Hoge - *Moderna Inc - President*

Yes. Thank you. And so for the clarifying question, again, we have filed in multiple geographies, and I won't comment on individual regulatory exchanges. But generally speaking, we -- as a part of the initial round of questions and feedback that we're receiving, there are instances where we think we will be dependent upon that efficacy data from the 1010 study, which we do expect in the coming months, the current season to be available.

The timing of that readout and the impact on the review process for regulators is not something I can predict at this point, but we're in active discussion with regulators about it. Certainly, it is possible that if that is substantially delayed or if it is not a favorable efficacy readout, that it could, for sure, delay or impact the time line of approval for the combination product.

If we are able to complete that submission, get that data to regulators and they're able to conduct their review, it's possible that we continue with that review without substantial delays. Ultimately, we don't know at this point because it will depend upon those submissions and discussions with the regulators that we're having right now. But we did want to flag that we do think, based on some of the initial conversations that we may be dependent upon that data ultimately for approval with some in some geographies.

Operator

Myles Minter, William Blair.

Myles Minter - *William Blair & Company L.L.C. - Analyst*

Just one on potential ACIP recommendation review for RSV vaccines. Do you expect that hearing to be in February or the June meeting? And is there anything built into the top end of that $2.5 billion revenue guidance for mRESVIA that would require a widening of that recommendation that it currently stands?

Stephen Hoge - *Moderna Inc - President*

So I'll take the first question on timing. We are obviously working closely with public health officials on the widening we filed for approval for the 18 to 59 high-risk population. At this point, we are not yet approved. And so from a broader sort of engagement with ACIP perspective, we'll wait for approval before we do that too broadly.

We do expect that the benefit risk is favorable for RSV vaccines, including mRESVIA. And so we do look forward to expansion of the recommendation to cover high-risk populations, both the 50 to 59, which have previously been discussed, but ultimately, hopefully 18-plus high-risk populations.

And Jamey, I don't know if you take --

James Mock - *Moderna Inc - Chief Financial Officer*

Yes. Sure. Yes. So Myles, as I mentioned in Jess' question, we have a little bit of growth in RSV. But I also mentioned that we have nothing related to new product approvals in our guidance for 2025. So that doesn't include the next-gen COVID vaccine or what Stephen just talked about, about the expanded indication related to RSV or anything from a combination approval should it happen.

Operator

Tim Anderson, Bank of America.

Timothy Anderson - *BofA Securities - Analyst*

So if I could just go back to that very last point, on your 2022 revenue guidance, you're not including any new products. Makes sense for RSV because that would be tiny. Makes sense for the combo product because of the reasons that you outlined. But why wouldn't the next-gen COVID product be included in guidance at this point, given that the PDUFA date is not very far away, end of May.

It's well-characterized paradigm having COVID vaccines out there. I'm just wondering if that lack of inclusion guidance anticipates some uncertainty about approval, given the new administration coming in and this common thread of kind of an anti-COVID stance across lots of people from the Trump administration.

And then second question, on Norovirus. If you're fully enrolled, what does FDA gain by putting the program on clinical hold? Is that just a forced disclosure of that adverse event to the clinical and patient community? Or is there some other reason why they would do this?

James Mock - *Moderna Inc - Chief Financial Officer*

Yes, Tim, thanks for the question. Maybe I'll take the first one. So I don't think there's much to read into here. I think we've learned our lesson coming into 2024 in terms of guiding with a product that is yet to be approved.

So moving forward, we have eliminated any products. Of course, there could be upside. But I think we approach our guidance understanding that there is variability and therefore, we will not put the any revenue related to the next-gen COVID or any of the other twoproducts as well. And again, I don't think there's anything else to read into as a result of that.

Stephen Hoge - *Moderna Inc - President*

Yes. So on the question of Norovirus. So importantly, we have already proactively communicated around this to all the investigators and IRBs and regulators around the world. So that communications happened. And actually, we've updated all the documents that would be necessary to sort of broadly identify this.

So the purpose for the clinical hold, ultimately, have -- anticipate or asked the FDA that question. I mean, at this point, they're appropriately, and we think prudently and conservatively, reviewing the documents and making sure that all their questions are answered around this. It does not impact from our perspective right now in the Northern Hemisphere of study conduct.

And so we'll look forward to engaging with them answering those questions, hopefully completing that review, removing that hole. But as we said, we will not then reinitiate any enrollment because we now have 20,000 participants in the Northern Hemisphere, which is more than we feel like we need. And so we'll just answer those questions and look for. But I really couldn't offer any other insight around it, but it certainly isn't around transparency communication because that will happen proactively. We did that before -- as we submitted all the information to them and others.

Operator

Ladies and gentlemen, this does conclude the Q&A portion of today's conference. I'd like to turn the call back to Stephane for any closing remarks.

Stephane Bancel - *Moderna Inc - Chief Executive Officer, Director*

Thank you very much, everybody, for joining us and for your good questions. Have a great day, and we look forward to speaking to some of you in the next hours and in the next days. Bye.

Operator

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