Q3 2021 Earnings Call

Company Participants

- Caroline Litchfield, Executive Vice President and Chief Financial Officer
- Dean Y. Li, Executive Vice President and President, Merck Research Laboratories
- Frank Clyburn, Executive Vice President and President, Human Health
- Peter Dannenbaum, Vice President, Investor Relations
- Robert M. Davis, Chief Executive Officer and President

Other Participants

- Andrew Baum, Citi
- Carter Gould, Barclays
- Chris Schott, J.P. Morgan
- Daina Graybosch, SVB Leerink
- Geoff Meacham, Bank of America Merrill Lynch
- Louise Chen, Cantor Fitzgerald
- Seamus Fernandez, Guggenheim
- Steve Scala, Cowen and Company
- Tim Anderson, Wolfe Research
- Umer Raffat, Evercore ISI

Presentation

Operator

Good morning. My name is Grace Lacquer and I'll be your conference operator today. At this time, I would like to welcome everyone to the Merck & Co Q3 Sales and Earnings Conference Call. All lines have been placed on mute to prevent any background noise. After the speakers' remarks, there will be a question-and-answer session. (Operator Instructions).

Thank you. I would now like to turn the call over to Peter Dannenbaum, Vice President of Investor Relations. Sir?

Peter Dannenbaum {BIO 20569031 <GO>}

Thank you, Grace, and good morning. Welcome to Merck's third quarter 2021 conference call. Speaking on today's call will be Rob Davis, our Chief Executive Officer; Frank Clyburn, President of Human Health; Caroline Litchfield, Chief Financial Officer; and Dr.Dean Li, President of Merck Research Labs.

Before we get started, I'd like to point out a few items. You will see that we have items in our GAAP results such as acquisition-related charges, restructuring costs, and certain other items. You should note that we have excluded these from our non-GAAP results and provided a reconciliation in our press release. I would like to remind you that some of the statements that we make today may be considered forward-looking statements within the meaning of the Safe Harbor provision of the U.S. Private Securities Litigation Reform Act of 1995. Such statements are made based on the current beliefs of Merck's management and are subject to significant risks and uncertainties.

If our underlying assumptions prove inaccurate or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements. Our SEC filings including item 1A and the 2020 10K, identify certain risk factors and cautionary statements that could cause the company's actual results to differ materially from those projected in any of our forward-looking statements made this morning. Merck undertakes no obligation to publicly update any forward-looking statements.

During today's call, a slide presentation will accompany our speakers' prepared remarks. The presentation of today's earnings release as well as our SEC filings are all posted to the Investor Relations section of Merck's website.

With that, I'd like to turn the call over to Rob.

Robert M. Davis {BIO 6955931 <GO>}

Thanks, Peter. Good morning, everyone and thank you for joining today's call.

I'm very pleased to report significant progress across our key growth and strategic priorities in Merck's first four quarter as a more agile and focused science-driven company. We have strong momentum in our business. We've achieved notable clinical milestones, acted on a significant business development opportunity consistent with our strategy and executed commercially to drive strong performance this quarter. We're also working with diligence and urgency which is reflected in the speed with which we were able to bring forward our investigational COVID-19 antiviral molnupiravir, and to rapidly file for Emergency Use Authorization with the FDA.

It's an exciting time at Merck, and we are determined to build on our recent successes as we pursue our mission to deliver innovation that save and improve lives and as we seek to create long-term value for both our patients and our shareholders.

Dean will speak to the significant pipeline advancements we are making, in a minute. But I first want to congratulate him and our research colleagues, as well as our partners at Ridgeback Biotherapeutics on the meaningful clinical results we recently reported regarding the development of molnupiravir.

From the onset of the pandemic, Merck has sought out opportunities to apply its scientific expertise in the global fight against COVID-19, and we are very pleased to now be in a position to make a meaningful difference.

As you are aware, at a planned interim analysis of our Phase 3 trial in at-risk, non-hospitalized adult patients with mild-to-moderate COVID-19, molnupiravir reduced the risk of hospitalization or death by approximately 50%, compared with placebo. Based on these results and in consultation with the FDA, we stopped our trial early. We are now working with the FDA as the agency reduced our EUA application and we look forward to next month's advisory committee discussion.

I'm pleased with the progress we're making to enter supply and purchase commitments with numerous governments and healthcare systems around the world and with the success of our effort to rapidly build supply. I'm also proud that we will be positioned to provide access to patients around the world through voluntary license agreements, tiered pricing based on country affordability and to our agreement with the Medicines Patent Pool.

We've also taken a meaningful step towards augmenting our pipeline to business development, a key strategic priority. We announced acquisition of Acceleron is a perfect example of our effort to identify in bringing the strongest external science to supplement our own work. Acceleron's lead product candidate, sotatercept, has the potential to become foundational as an add-on therapy in the treatment of pulmonary arterial hypertension, where there is a strong need for new agent that can potentially address the underlying illness and not just the symptoms of this grievous disease.

We look forward to the completion of our tender offer in the near future and to receiving the necessary regulatory approvals that will permit us to close the transaction with its multi-billion dollar peak sales potential and commercial exclusivity well into the next decade. Sotatercept can contribute meaningful revenue growth in the KEYTRUDA LOE period, an important attribute of this and potential future targets. Dean and I will continue to work with our team to identify additional scientifically compelling business development opportunities, we'll also continue to pursue our robust and growing internal pipeline.

Our business performed exceptionally well this quarter and the team continues to display superior and focused execution. We achieved very strong commercial and financial results with meaningful growth across our oncology, vaccines and animal health businesses, and even greater growth in earnings. As expected, GARDASIL sales were particularly robust as we benefited from a sharp improvement in manufacturing output and availability of more doses to help address ongoing strong underlying demand.

We are confident that the momentum we are seeing will continue through the end of the year, setting us up for continued growth over the next several years. We remain focused on our efforts to transform the way we work by evolving our operating

model to be leaner, nimbler and more digitally enabled. My leadership team is fully aligned behind the need for Merck to work with more speed, urgency and agility across all aspects of our business. We must stay ahead of the evolving external environment to ensure we are able to make the significant investments required to deliver future innovations that will address unmet medical needs across the globe. In doing so, we aim to deliver important medicines and vaccines to patients, while continuing to drive long-term sustainable growth and value creation for all of our stakeholders.

Finally, I want to highlight the recent publication of Merck's environmental, social and governance progress report. This year's report highlights important updates on metrics and goals around our four ESG priority areas which include, access to help our employees including their health and safety as well as engagement and diversity; environmental sustainability, and ethics and values. These ESG efforts are grounded in the core values that have always guided our mission and support our business strategy. We look forward to providing ongoing updates on these important efforts.

With that, I will pass it to Frank to review the details behind our Human Health performance.

Frank Clyburn {BIO 20654315 <GO>}

Thanks, Rob. Good morning. As Rob highlighted, the momentum in our Human Health business continued in the third quarter, and we achieved 17% growth excluding the impact of foreign exchange. We have continued to invest with urgency and patient activation programs that improve patient awareness and encourage more normal levels of physician office visits, oncology screenings and vaccinations rates. These actions, well ended benefiting patient health, also meaningfully benefited our largely physician-administered portfolio in the quarter.

In United States, we are encouraged that wellness visits and surgical procedures remain at mostly normal levels. In oncology, while screening rates and diagnosis continue to improve, they are unfortunately still below pre-COVID levels, and this is impacting new patient starts. Outside of the United States, our business performance remain strong, despite lingering impacts from the pandemic in certain markets.

Now turning to the third quarter performance of our key brands. My comments will be on an ex exchange basis. In oncology, KEYTRUDA sales grew 21% to $4.5 billion, reflecting continued robust global demand. In the United States, KEYTRUDA continues to demonstrate durable momentum across all key tumors, including growth for our recent launches such as KEYNOTE-522 and neoadjuvant -- adjuvant triple-negative breast cancer. KEYTRUDA is continuing to extend its very strong overall IO class leadership, improving new and total patient market share.

KEYTRUDA continues to maintain its leadership position in lung cancer, capturing 8 out of 10 eligible new patients despite continued competition. Outside of lung, key tumors contributing to growth include renal cell carcinoma, triple-negative breast,

MSI-high, esophageal and head and neck. We're also excited by the recent approval and upcoming launch of KEYNOTE-826, which is the first anti-PD-1 combination approved as a first-line treatment of cervical cancer.

Outside of the United States, KEYTRUDA growth continues to be driven by lung cancer indications and the ongoing launches in head and neck in renal cell carcinoma. We are continuing to see the opportunity to expand our reach into earlier lines of therapy materialize. We are very excited about the potential upcoming adjuvant launches of KEYNOTE-564 in renal cell carcinoma and KEYNOTE-716 in melanoma. In fact, in United States, we expect over half of KEYTRUDA's growth to come from indications in early-stage treatment settings through 2025, and to represent roughly 30% of total KEYTRUDA sales by that time.

Lynparza sales grew 25% and remains the leading PARP inhibitor. Growth was driven by our breast cancer indication and continued uptake of the most recent indications, including ovarian prostate and we look forward to the potential launch next year in a broader prostate population based on the PROpel trial.

Lenvima sales grew 30%. In the United States, growth was driven by renal cell carcinoma and endometrial cancer. We've seen very encouraging early trends from the launch of KEYNOTE-581 in first-line renal cell carcinoma. Outside the United States, growth is reflective of increased demand following NRDL listing in China, in March of this year.

We're also excited by the recent approval of WELIREG for patients with certain VHLassociated tumors. We received very positive feedback from scientific leaders, providers and patients about the benefits of WELIREG, which is off to a promising start and we are hopeful to extend the reach of WELIREG to broader RCC indications in the future.

Our vaccines portfolio continued to deliver strong growth from GARDASIL, which grew 63% to $2 billion and has grown 35% year-to-date. In the United States, the increase in year-over-year growth was primarily driven by the timing of CDC purchases, which helped us overcome a below-normal back-to-school season. Underlying demand for GARDASIL remain strong and we are seeing some benefits from recovery of misdoses due to the pandemic.

Outside the United States, growth was largely driven by strong underlying demand in China, as well as increased supply and our ability to reallocate doses. In our hospital acute care portfolio, BRIDION sales grew 15%, driven by our ability to capture increased market share within the growing neuromuscular blockade reversal class.

Turning to our outlook. The robust underlying demand for our products paired with our continued excellent commercial execution, gives us confidence in the outlook for our business. Merck has shown increased urgency and agility across our organization, that has resulted in improvements that will enable meaningful future

growth. On GARDASIL, we continue to expect robust ex-US demand and increase supply to drive fourth quarter performance. We expect to see more normal seasonality for GARDASIL with the third quarter reflecting the highest in sales.

Our teams have been working to ensure we have the right processes in place to appropriately allocate doses to areas of increased demand, particularly as COVID variants continue to impact certain geographies. These dynamics will drive very strong year-over-year growth for GARDASIL in the fourth quarter driven by ex-U.S. markets such as China. Given global HPV vaccination levels remain low, we continue to believe long-term growth opportunity for GARDASIL remain significant.

In oncology, we are encouraged by our strong performance throughout the pandemic, with new launches more than offsetting the headwind scene from reduced new patient starts. We remain confident in the underlying demand for a broad and innovative portfolio, including KEYTRUDA, Lynparza and Lenvima, and we expect to drive sustained growth across key tumor types and in earlier stages of disease.

Next, let me provide a few comments on the outlook for molnupiravir. As Rob mentioned, we are very excited about the potential to offer the first oral treatment option to at-risk adults, with mild-to-moderate COVID-19 in an effort to help combat the pandemic.

Merck is committed to providing widespread access to molnupiravir globally and is implementing a tiered pricing approach based on World Bank country income criteria. We have announced a number of supply and purchase commitments to-date and we continue to have discussions on similar agreements with customers around the world.

We are also encouraged by the recent unanimous vote by the advisory committee on immunization practices. Upon adoption, as a final recommendation by the CDC, this sequence would offer patients the broadest coverage with a strong immune response against serotypes responsible for about two-thirds of invasive pneumococcal cases in adults. As we think about our pneumococcal portfolio more broadly, we're excited about the potential opportunity for that[ph] events in the pediatric setting, which represents a larger market segment.

To conclude, there is continued momentum in our business, driven by demand and strong commercial execution, and we are well positioned as we move through the end of the year. The growth in the third quarter underscores our confidence in the underlying strength of our business and global demand for innovative medicines and vaccines, and we look forward to driving that growth long into the future.

With that, I'll turn the call over to Caroline.

Caroline Litchfield {BIO 20934609 <GO>}

Thank you, Frank. Good morning. Our team drove exceptional financial performance in the third quarter. The investments we are making in our strong portfolio and pipeline as well as in business development are helping us deliver outstanding near-term performance, while also positioning us to continue to deliver important innovations and long-term value to patients and shareholders.

Now turning to our third quarter results. Total company revenues were $13.2 billion, an increase of 20% or 19% excluding the positive impact of foreign exchange. The remainder of my comments will be on an ex exchange basis. As Frank highlighted, our Human Health business achieved improving momentum, growing 17%. Our Animal Health business also delivered robust growth with sales increasing 14% driven by strong global demand across both companion animals and livestock. Companion animals sales increased 18% driven by global demand in parasiticides, including the BRAVECTO line of products as well as companion animals vaccines. Livestock sales increased 12%, reflecting strong global demand for ruminant and poultry products, including our animal health intelligence products.

I will now walk you through the remainder of our P&L, and my comments will be on a non-GAAP basis. Gross margin was 76.8%, an increase of 0.3 percentage point, reflecting the favorable effect of product mix, partially offset by higher manufacturing costs. Operating expenses increased 11% to $4.7 billion, this was driven by investments in our key growth pillars, particularly in support of return to care activities and in our early and late-stage pipeline, including molnupiravir. Other expense increased by approximately $200 million, reflecting highest tension settlement costs. The effective tax rate was 13%, a decrease of 1.4 percentage point driven by discrete items. Taken together, we earned $1.75 per share an increase of 26%.

Turning now to our 2021 non-GAAP guidance. While the pandemic continued to impact many regions around the world, health systems and patients have largely adapted and we assume this trend will continue. Our guidance assumes, the Acceleron transaction will close during the fourth quarter, subject to the successful completion of the tender offer and regulatory approval and does not include potential sales or earnings from molnupiravir. The underlying strength of our business enables us to narrow and raise our expected revenue range to $47.4 billion to $47.9 billion, representing growth 14% to 15%, including a positive impact from foreign exchange of approximately 1.5%, using mid-October rates.

Our gross margin is expected to be approximately 76.5%. We continue to expect operating expenses to grow at a high single-digit rate. In other income and expense, we expect expense of approximately $450 million. We expect our full year tax rate to be between 14% and 14.5%. We assume $2.54 billion shares outstanding. Taken together, we are raising and narrowing our EPS range to $5.65 to $5.70, reflecting significant growth of 25% to 26%. This range includes a positive impact from foreign exchange of approximately 2% using mid-October rates.

As you consider your models, there are a few areas to focus on. Starting with molnupiravir revenue, we expect the global opportunity to be approximately $5

billion to $7 billion through 2022, including $0.5 billion to $1 billion expected to be realized this year. This assumes emergency use authorization in December. As a reminder, we will share any profit equally with our partner Ridgeback. Merck is responsible for recording global revenues and costs and will reflect the profit share within cost of sales.

For GARDASIL, we have had excellent momentum driven by strong demand and benefits from the step function increase in supply we are achieving this year. Fourth quarter sales will be lower than the third quarter due to normal seasonality and timing effect. However, we expect the growth in the quarter to remain very robust.

Animal health has had exceptional growth in the first three quarters of the year, driven in part by the pandemic effect on pet adoption and pet spending. In the fourth quarter, we will anniversary that effect, and we expect a more normalized year-over-year growth rate as a result.

Our operating margin in the third quarter benefited from very strong revenue performance, including the normal seasonality of our vaccines business. As we move through the fourth quarter, we expect operating margins to normalize due to this seasonality and phasing of spend. More broadly, as we look out to 2024, we remain confident in our revenue potential and continue to believe it is underappreciated, and we remain on track to achieve our 2024 operating margin target of greater than 42%. Our capital allocation priorities remain unchanged.

We will continue to invest in the business to drive the many significant near and long-term growth opportunities we see in our derisk portfolio and rich pipeline. We also continue to execute on our business development strategy, including our announced acquisition of Acceleron. We will pursue additional, value-enhancing and strategic business development opportunities, and we retain significant balance sheet capacity to do so. We remain committed to the dividend with the goal of increasing it overtime. To the extent we have excess cash, we will return it to shareholders through share repurchases.

To conclude, Merck continues to make exceptional progress on its commitment to drive growth and values for patients and shareholders. We remain in a position of financial and operational strength, which will enable us to deliver on that promise now and well into the future.

With that, I'd now like to turn the call over to Dean.

Dean Y. Li {BIO 21985278 <GO>}

Thank you, Caroline. Good morning, everyone. It is a pleasure to be here to provide a summary of progress made since our last quarter call. I will provide an update on our oral antiviral candidate molnupiravir, highlight the proposed Acceleron acquisition, shed light on recent progress with islatravir and finish with the synopsis of notable regulatory milestones and clinical updates from across the pipeline.

The need for additional treatment option remains key in combating the COVID-19 pandemic. Interim analysis from MOVe-OUT or Phase 3 study evaluating molnupiravir inaccurate, non-hospitalized patients with mild-to-moderate COVID-19, showed an approximately 50% reduction in the risk of hospitalization or death compared to placebo. Of note, through day 29, no deaths were reported in patients who received molnupiravir compared to eight deaths on placebo. This is the first oral antiviral for respiratory virus. It demonstrate benefits based on robust clinical outcomes and the first to show a meaningful five-day window for therapeutic interventions after symptoms.

Based on these positive results and at the recommendation of the interests advanted data monitoring committee, and in consultation with the FDA, recruitment into the study was stopped early.

In light of these findings and given the urgency to address the pandemic, our teams work tirelessly to submit a robust package to the FDA for EUA within 10 days of receiving data. We look forward to discussing the EUA submission at an upcoming meeting of the Antimicrobial Drugs Advisory Committee scheduled for November 30. And in the interim, we continue to engage with the FDA to support its review. Applications have also been submitted to multiple regulatory agencies around the world.

I do wish to take a moment to thank the investigators, patients and their families for their participation in the MOVe-OUT study. I am also grateful to our collaborators that Emory University, Ridgeback and Merck's internal teams for the incredible work done in conducting this program during a very challenging time.

A comprehensive vaccination strategy remains the best sustainable means confront this COVID-19 pandemic. Timely intervention following symptoms onset with an oral agent that can be self-administered at home, may provide an additional meaningful option for patients, healthcare systems and public health, which could make a significant and positive impact on the pandemic.

Based on a variable viral sequence data, molnupiravir showed consistent efficacy against the Gamma, Delta and new COVID-19 variants. As a reminder, we continued to actively recruit participants in the MOVe-AHEAD trial, which is evaluating the safety and efficacy of molnupiravir and preventing the spread of COVID-19 within households as a post-exposure prophylactic with a plan read out in the spring of 2022.

Now turning to the proposed Acceleron acquisition. Acceleron has an excellent scientific category which has yielded important treatment for anemia in adult patients with certain rare blood disorder. Their lead clinical candidates that targets that has the potential to be a foundational asset as an add-on therapy for the treatment of pulmonary arterial hypertension, and provide a complimentary addition to our growing cardiovascular pipeline. As such, following the close of the deal, our strategy would be to advance the wide-ranging Phase 3 clinical program.

Now, on to the portfolio and pipeline. starting with HIV. We continue to generate clinical data that reinforces the foundational potential islatravir in HIV. At the European AIDS Conference in London this week, we presented data from the Phase 2 study, evaluating doravirine and islatravir, and previously untreated adults with HIV infections, which demonstrated continued maintenance and viral suppression through a 144 weeks.

We also recently reported positive topline results from two pivotal trials, evaluating a once-daily oral regimen of doravirine and islatravir in switch setting in adults with HIV infection who are virologically suppressed on other HIV therapy regimen. At 48 weeks, both trials met their primary efficacy end-point per percentage of participants with levels of HIV RNA greater than or equal to 50 copies per milliliter, demonstrating comparable efficacy with those receiving the comparator antiretroviral therapy. We plan to prevent these findings and upcoming medical conference and incorporate the data into global regulatory submissions.

This week, we also announced the start of the Phase 2 clinical study, evaluating a once-weekly oral combination of islatravir of lenacapavir and people living with HIV who are virologically suppressed on an antiretroviral therapy.

We have made great progress in our collaboration with Gilead and look forward to reporting on future developments including our long-acting injectable co-formulation.

Next on to VAXNEUVANCE. We received a positive opinion for VAXNEUVANCE from the European Medicine Agency's committee for medicinal products for human use, an individual 18 years of age and older. And more recently in the U.S., the CDC's ACIP voted unanimously to provisionally recommend VAXNEUVANCE followed by PNEUMOVAX as an option for pneumococcal vaccination in adults 65 years and older as well as for adults age 19 to 64 with certain underlying medical conditions with both patient populations being studied in our clinical trials.

Vaccine performance is multi-dimensional and includes eliciting a strong immune response as well as providing coverage for important disease stereotypes.

Our two dose regimen accomplishes the best of both by eliciting a robust immune response across the 15 serotypes in VAXNEUVANCE including serotypes 3 as well as providing the broader serotype coverage among current pneumococcal vaccine options of which four that are unique to PNEUMOVAX. Furthermore, VAXNUEVANCE has the most extensive clinical development program of the newly licensed PCV. This includes completed or ongoing evaluation among those with certain chronic or an immunocompromised onditions that increased accessibility to and severity of pneumococcal disease.

We also announced positive topline results for VAXNEUVANCE from the pivotal new ped study, evaluating immunogenicity, safety and tolerability in the pediatric setting and have submitted an application to the FDA. Evidence indicates the incorporation

of serotypes 22F and 33F as well as strong immunogenicity against stereotype 3 as a potential to play an important role in the prevention of pneumococcal disease in infants and children. These three serotypes represent more than a quarter of all cases of invasive disease in children under the age of five. We will present full results at an upcoming scientific congress.

And finally to oncology. The rich flow of data from our clinical development programs across tumor types continue. We maintain momentum in the development of new treatment options for women's cancer with the approval of KEYTRUDA plus chemotherapy with or without bevacizumab for recurrent or metastatic cervical cancer based on data from KEYNOTE-826. This study showed a meaningful 36% reduction in the risk of death. This is the first anti-PD-1 combination treatment option for patients in the first line setting, and together with our industry-leading human papillomavirus vaccine, GARDASIL and GARDASIL 9, we are uniquely positioned to address certain unmet needs in cervical cancer with a focus on both prevention and treatment.

And ESMO in September, we presented final results from KEYNOTE-355, our study of KEYTRUDA in combination with chemotherapy for advanced triple-negative breast cancer, which showed a reduction in the risk of death by 27%. KEYTRUDA is the only immuno-oncology agent approved in metastatic triple-negative breast cancer. This, along with additional data presented across endometrial and ovarian cancers, reinforces the remarkable progress being made in our broad women's cancer portfolio.

We're also making enrolls in new cancer types, including prostate cancer. With our partners at AstraZeneca, we announced positive results from the Phase-III propel study for the frontline treatment of metastatic castration-resistant prostate cancer. This study demonstrated that little farther in combination with abiraterone, significantly delayed disease progression regardless of biomarker status.

This is the first PARP inhibitor to demonstrate clinical benefit in radiographic progression-free survival in combination with a new hormonal agent in this setting. We are encouraged by the study and the potential to help increasing number of men diagnosed with metastatic castration-resistant prostate cancer. Results will be presented at an upcoming Medical Meeting and submitted to regulatory authorities globally.

Next to renal cell carcinoma, which represents an important area of expansion. In August, we received FDA approval for WELIREG, a first in class F2 alpha inhibitor therapy for the treatment of adult patients with Von Hippel-Lindau disease who require therapy for associated renal cell carcinoma, central nervous system, hemangioblastomas or pancreatic neuroendocrine tumors, not requiring immediate surgery. This approval provides us a beachhead as we evaluate WELIREG potential in broader RCC indications and beyond.

Also an RCC in partnership with Eisai, following FDA priority review, we received approval for the combination of KEYTRUDA and Lenvima, and the frontline setting based on results from the KEYNOTE-581 trial. This brings forth an important new first-line treatment option for patients with advanced RCC. We are also rapidly expanding programs into earlier lines of therapy. During the quarter, the FDA granted priority review for our application for KEYTRUDA as an adjuvant therapy for patients with RCC at intermediate-high or high risk of recurrence following nephrectomy or following nephrectomy and resection of metastatic lesions from the KEYNOTE-564 study.

Additionally, we received priority review for KEYTRUDA for the treatment of patients with surgically receptive high-risk stage two melanoma, based on results from the KEYNOTE-716 study, that showed an improvement in recurrence free survival compared to placebo. Both of these studies demonstrate the benefit of expanding the use of KEYTRUDA to earlier stages of disease, allowing us to extend treatment benefits and more patients sooner. We look forward to decision on both studies by the end of the year.

To conclude, I am proud of the progress across our broad pipeline and look forward to providing further updates on our scientific progress in the future.

Now, I turn the call back to Peter.

Peter Dannenbaum {BIO 20569031 <GO>}

Thank you, Dean. Grace, can you please start the Q&A portion of the call.

Operator

Absolutely.

Peter Dannenbaum {BIO 20569031 <GO>}

(Operator Instructions)

Questions And Answers

Operator

(Question And Answer)

All right. (Operator Instructions) Your first question comes from the line of Umer Raffat of Evercore ISI. Your line is open, sir.

Q - Umer Raffat {BIO 16743519 <GO>}

To the Molnupiravir in the rest of the call. So I'll just ask on KEYTRUDA and adjuvant lung instead. Have you had an interim and does the stack [ph] plan allow for hierarchy where PD-L1 positives is first? And do you expect the benefit to show in patients that did and did not get adjuvant chemo? Thank you very much.

A - Robert M. Davis {BIO 6955931 <GO>}

Yeah. Thank you very much. That -- I appreciate the question. First, I just want to elevate for just a second, we are excited by the emerging data, the role of PD-1 and PD-L1 and the early treatment in adjuvant space. For us, we're gratified that in renal melanoma breast cancers just this year, there appears to be a great effect. And these are cancers where there are frequently employed methods for early screening. In relationship to lungs specifically, we enjoy a dominant position in lung cancer. And in lung cancer, the treatment of latter stage cancer is the predominant stage.

The data, as you somewhat allude to from other companies, indicate that in lung cancer, the PD-1 PD-L1 class, could be effective in early and adjuvant. In specific in relationship to the -- we have a number of early and adjuvant stage lung cancers, and it was enumerated in the slide.

KEYNOTE-091 is also known as the PEARLS trial. KEYNOTE-091 PEARLS is a collaborative study with the European Organization for Research and Treatment of Cancer. And Merck is a collaborate on this trial. This is an event-driven study and we are in active communication with EORTC. Together, we are waiting data from the IA2 before the end of the year. And I would hazard to guess that any public announcement from Merck would be announced at the beginning of the new year.

A - Peter Dannenbaum {BIO 20569031 <GO>}

Great. Thank you, Umer. Next question, please.

Operator

Thank you. Next up, we have Daina Graybosch from SVB Leerink. Your line is open.

Q - Daina Graybosch {BIO 20659414 <GO>}

Hi. Can I ask maybe a two-part question on Molnupiravir and how you're moving forward. The first is there's been some concerns publicly about the genotoxicity. I wonder if you could address the data you have that makes you not concerned about that. And then the second concern is maybe with resistance. And I wonder how you're thinking about the future and combinations, and whether that will be needed to prevent any resistance maybe from low compliance to Molnupiravir.

A - Dean Y. Li {BIO 21985278 <GO>}

Yes. Thank you for that question. This is Dean. I would just emphasize we are very confident in the safety profile of Molnupiravir based on our preclinical and clinical data. In relationship to the clinical data, I think most people recognize that in the interim analysis, we had a profound reduction in hospitalization on death -- or death

compared to placebo. And it was stopped early in -- by the guidance of the DSM-V and in consultation with the FDA.

And in that interim analysis, the incidence of any adverse effect was comparable in both Molnupiravir and placebo. And actually, if you look, there were fewer subjects in the Molnupiravir group who discontinued therapy due to an adverse event compared to the placebo group. In relationship to our confidence in the safety profile based on our extensive preclinical valuation, I think it's important to recognize that Molnupiravir is a nucleoside analogue that functions by creating errors in the genetic material of RNA viruses. These nucleoside analogues are often used in many other antiviral treatments, including HIV and hepatitis. And we have done a comprehensive non-clinical program to characterize the safety profile of Molnupiravir.

It's been written by other people, it's actually been written in the sort of scientific journals as well and we will be presenting all of this data I believe in the adcom that the FDA will be holding. But probably, the most important thesis of information is that in two distinct in vivo rodent mutagenicity assays, commonly called the Big Blue and the Pig-a, which are well characterized and considered to provide a robust measure of the ability of a drug or chemical to induce mutations in vivo. And in these studies, we're administering Molnupiravir for longer and higher doses than those employed in the human clinical trials. And the totality of the data from these studies indicate that Molnupiravir is not mutagenic or genotoxic in these in vivo mammalian systems. Now, we have shared these results throughout with the regulatory agencies worldwide and we'll continue to provide additional data as this process continues.

A - Peter Dannenbaum {BIO 20569031 <GO>}

Great. Thank you, Daina. And next question, please.

Operator

Thank you. Next up, we've Andrew Baum from Citi. Your line is open.

Q - Andrew Baum {BIO 1540495 <GO>}

Thank you. Questions for Frank on Molnupiravir just in relation to supply. It strikes me, given some of the published improvements in manufacturing and the four gram per patient dose. That 20 million looks like a very conservative estimate, given particularly the inclusion of third-parties, what could be achieved, given the dosing in the M-API? I'd like you to comment please on where you think the 2022 real supply could be?

And then second, perhaps, you could just comment on the appetite of Merck to use direct-to-consumer advertising or other promotion on Molnupiravir. I understand that promotion and advertising is allowed under an EUA. If you could confirm or deny, that would be great. Thank you.

A - Frank Clyburn {BIO 20654315 <GO>}

Yeah, Andrew, this is Frank. So a couple of things that I want to highlight is: First, we have a line of sight and we will produce 10 million courses this year, Andrew, in 2021. And as we have mentioned that we have line of sight and we will at a minimum double that in 2022. So to your question, we're going to do everything we can to increase the supply for this product. In addition, we have voluntary license, partners you have seen, and we also have a number of partners that we're working with to provide global supply. So rest assured, Andrew, we're going to try to do everything on the supply front.

On direct-to-consumer, I think it's a little bit early for us on that. We have not made a decision around that. We are really focused on doing everything we can to sign up agreements with governments, get the product available globally and we will be providing additional information as we go forward on Molnupiravir, but this is our number one priority for the company and it's something that we're really looking-forward to trying to help address the pandemic going-forward.

A - Robert M. Davis {BIO 6955931 <GO>}

Andrew, this is Rob, and I just want to make sure, because I listened to your question, and I think Frank hit it, but just to emphasize in case others on the phone aren't catching this, the 20 million we're expecting [ph] more than doubling what we can do next year, that is Merck's production. We are not including in any of those numbers the eight voluntary license partners in India, nor anyone in the [ph] Medicines Patent Pool signs up. So obviously, global production of Molnupiravir will be significantly more next year. We're just speaking to what volumes we will produce within Merck.

Q - Andrew Baum {BIO 1540495 <GO>}

Great.

A - Frank Clyburn {BIO 20654315 <GO>}

Let me just add one thing, because I recognize that this question is also somewhat linked to the other question that -- and it relates to how we think about Molnupiravir scientifically in the pandemic phase and there's going to be an endemic phase. And potentially, there could be other phases after that. But for the pandemic phase, I just want to emphasize we have the MOVe-OUT trial and then we'll have to see the potential in the move ahead to see whether we both have a treatment and a prophylaxis

In the endemic phase, when the pandemic somewhat recedes, it's highly likely that SARS-CoV-2 will become an endemic infection. And we all have to recognize, and it's related to the previous question, during this phase, there will be a large reservoir of individuals across the globe with high copy number of viruses in many of these individuals that may lead to a constant brewing of variants. So this question of resistance becomes very important.

It is important to emphasize that Molnupiravir has an extremely high barrier to resistance. It has broad efficacy across all SARS-CoV-2 variants to date. And in our

preclinical studies and preclinical studies of others, it not only has a broad efficacy across SARS-CoV-2 variants, but a broad variety of RNA viruses and probably the broadest than other -- than all other current mechanisms that we know being developed. I should emphasize this high barrier to resistance is critically important both in the pandemic and the endemic phase as has been highlighted. And I need to emphasize for this reason, we prioritize Molnupiravir over our other programs, including an external protease inhibitor, given the paramount importance we place on ensuring the highest barrier to resistance, given where we are in the world right now.

A - Peter Dannenbaum {BIO 20569031 <GO>}

Great. Thank you, Andrew. And next question, please, Grace.

Operator

Thank you. Next, we have Carter Gould from Barclays. Your line is open.

Q - Carter Gould {BIO 21330584 <GO>}

Hi, guys. Good morning. Thanks for taking the question. Unsurprisingly, I'm going to focus on (inaudible) too. I guess, maybe for Frank and Caroline, I'm just trying to understand exactly kind of what's baked into that guidance in terms of what's being distributed for next year between kind of your supply crossing that with the -- to your point, the supply in sort of low and middle-income countries with -- through the MPP. I acknowledge that there's going to be cured pricing, but it seems like you still becoming far short of distributing your full capacity. So any color on that front would be helpful.

A - Frank Clyburn {BIO 20654315 <GO>}

Yeah, Carter, this is Frank. I'll start and see if Caroline wants to add anything. So in our assumptions, and appreciate this is a very fluid situation, we do assume an Early Use Authorization in December of this year, and we are including the contracts that we already have in place as well as those that are underway. So we are comfortable with that $5 billion to $7 billion range through '22.

And just to re-emphasize, the numbers based on the agreements signed, those in line of sight and others that have high probability of execution. A couple of other things is, as we've mentioned and Rob reiterated, we will produce 10 million courses of therapy by the end of '21 and are committed to at least doubling that in '22. Our focus initially or it's important that it's on treatment with COVID-19. And you mentioned the broad global access, which does come with global tiered pricing around the world, and that's an important aspect that the pricing will be tiered based on affordability measures.

If our post-exposure prophylactic trial is successful, as Dean was highlighting, with an expected readout in spring, there is potential upside to these estimates. Furthermore, throughout 2022, we do not assume to your question, and all of the suppliers use, as such, we have the ability to fulfill additional demand. We also do

assume that there will be other oral antivirals in the market and we have to see how that unfolds. And we look forward to provide you some additional detail and clarity as we learn more over the next couple months.

A - Peter Dannenbaum {BIO 20569031 <GO>}

Great. Thank you, Carter. Next question, please, Grace.

Operator

Thank you. Next, we have Steve Scala from Cowen. Your line is open.

Q - Steve Scala {BIO 1505201 <GO>}

Thank you. Merck views its competitive position in pneumococcal vaccines as strong, but ACIP did not appear to agree, fueling the cost benefit of the 20-valent as superior, even one assuming it was ineffective against serotype 3. So where does Merck think ACIP errored? And how does Merck change that narrative? Thank you.

A - Robert M. Davis {BIO 6955931 <GO>}

Of course, we're very confident of our V114 VAXNEUVANCE. There's two places that's where we're advancing it. It's an adult and pediatrics. As you know, the pediatric market, and I'll let Frank speak to it, is quite robust market. And we're advancing our program. We have submitted to the FDA and we hope to hear back from them in short order. So we're very focused in the pediatric.

In relationship to the adult, the critical issue for us in relationship with ADL, [ph] is that we -- as I said in the prepared comments, I think it's very important to give the best coverage in terms of serotype, but not just by immunogenicity, by actually studying clinical events, especially in those patients who are compromised or at-risk or have some other condition that might increase their susceptibility to have invasive pneumococcal disease. And we think that clinical data and the way that we studied it in these patient populations directly, we have not extrapolated from immunogenicity. We've actually studied it as something that's critically important as one looks at the true efficacy of the vaccine. Frank, do you want to answer?

A - Frank Clyburn {BIO 20654315 <GO>}

Yeah, the only thing I want to add is, actually, we were very pleased that it was unanimous approval for the sequence of VAXNEUVANCE and PNEUMOVAX. And we feel though that the sequence offers patients really with the broadest coverage, with strong immune responses against serotypes that are responsible for two-thirds of pneumococcal disease in adults, as well as the ACIP did highlight that the regimen was both cost-effective as well as cost-saving in the 65-plus patient population. And then as Dean mentioned, we're also really excited about the opportunity for VAXNEUVANCE in the pediatric segment, which we believe is the larger market opportunity. So overall, from our perspective, we feel really good about the ACIP's recommendation.

A - Peter Dannenbaum {BIO 20569031 <GO>}

Thank you. Steve. Next question, please, Grace.

Operator

Thank you. Next, we have Geoff Meacham from Bank of America. Your line is open.

Q - Geoff Meacham {BIO 21252662 <GO>}

Morning, guys. Thanks for the question. You touched a little bit with Molnupiravir during the first quarter, [ph] but how do you think about it virtually versus the booster strategy for vaccines? Would you expect any more formal guidelines from CDC from other sales authority about how might Molnupiravir fit into the algorithm? Thank you.

A - Frank Clyburn {BIO 20654315 <GO>}

I'll maybe try this. Geoff, I apologize, you were kind of garbled, so I'll repeat what I think your question was and then you can clarify if I got it wrong. I think your question was this is the first oral antiviral, but obviously we continue to have out there vaccines that are important as really the first line, and do we think there's any discussion on how this will fit into the regimen? I don't think we can really comment on how advisory committees, the FDA or others, the CDC would look at that. But what I will tell you from our perspective that first and foremost, people should be vaccinated, that it continues to believe what we think is the right answer.

We see our therapy as something that is an important addition to the armamentarium. And obviously, there are places where people cannot get the vaccine or unfortunately if people get vaccinated and have breakthrough virus. So there's definitely a need for this. But it is in collaboration as a complement to the vaccine and not in place of it. That's our perspective. We'll let the government speak to their own.

A - Peter Dannenbaum {BIO 20569031 <GO>}

Great. Thank you, Geoff. Next question, please, Grace.

Operator

Thank you. Next, we have Chris Schott from JPMorgan. Your line is open.

Q - Chris Schott {BIO 6299911 <GO>}

Great. Thanks so much for the question. I'm just going to get my hands around GARDASIL and the results in the quarter. So can you just clarify or quantify a little bit how much of the $2 billion in sales this quarter was stocking versus underlying demand? And maybe more broadly, are we still in a position where demand is exceeding supply I guess on a global basis as we think about the recent capacity expansion? And I guess I'm trying to get my hands around like, will there be another

step up in sales for this franchise as we look out to 2023 and beyond with the new facility coming online? Or is the capacity efforts you made so far kind of addressing most of the demand that's out there? Thanks so much.

A - Caroline Litchfield {BIO 20934609 <GO>}

So Chris, this is Caroline. I'll start and I'll hand over to Frank. So in the quarter, as you know, we've had an exceptional quarter and that's driven by strong global demand and the step-up we had in supply. We also did benefit from CDC timing, and that was approximately $125 million of buy-in in the third quarter of this year. And that contrast to a buy-out actually in the third quarter of 2020. So year-over-year, we feel we've benefited by approximately $180 million to the results. Now, in terms of how we see this going forward, we've very excited about the opportunity. We see opportunities for increased supply through '22 and beyond, as we see those capacity come online. But let me hand over to Frank to talk about the demand that we have.

A - Frank Clyburn {BIO 20654315 <GO>}

Yeah, Chris, thanks for the question. A couple of other things I do want to highlight is we think about GARDASIL and this is something we've been discussing for a while as both the near-term results as you mentioned with the long-term prospects. First, I want to highlight that only 9% of, we say it, the eligible cohort globally has been vaccinated. So Chris, I start there and say this -- we still have significant opportunity. And if you think about markets such as China, if you think about the approval in Japan, if you think about the gender neutral opportunities that we have in Europe as well as other age cohorts in adult, mid-adult in the US, because we feel that there's significant opportunity for continued GARDASIL

As you saw a step-up in our supply, we will continue to see that. It'll be a little bit more modest pace in next year. But rest assured as we bring on the two new bulk manufacturing facilities in '23, this is why we feel that the long-term growth prospects for GARDASIL are very significant and can be a key growth driver for the company going forward.

A - Peter Dannenbaum {BIO 20569031 <GO>}

Thank you, Chris. Next question, please, Grace.

Operator

Thank you. Next up, we have Tim Anderson from Wolfe Research. Your line is open.

Q - Tim Anderson {BIO 3271630 <GO>}

Thank you. A question on additional M&A, so maybe for Rob. On the Acceleron investor call you held, I asked whether Merck would do more M&A, given that (inaudible) taking a rating debt downgrade, and you were very frank in your answer and you said yes, but the company has not been willing to kind of quantify what debt -- additional debt that would potentially be -- that would trigger a downgrade. My understanding is that another $10 billion cash deal would be enough to trigger a

one-notch downgrade. And if it was something like $30 billion cash deal, that could be a two-notch downgrade. So my new question here is, would Merck actually do the deal big enough to cause a two-notch rating downgrade? Thank you.

A - Robert M. Davis {BIO 6955931 <GO>}

Yeah, I appreciate the question. And I would start more high-level, do we continue to pursue additional business development? The answer is yes. It will be driven as it has always been based on what we see as the compelling scientific opportunity where we see signs addressing unmet need that is strategically aligned with us and where we can bring value. So that is unchanged.

And as we look at capacity, I would just say we believe we have the firepower to do, frankly, any deal as it's out there that we would have strategic interest in doing. The balance sheet will not be a great limiter for us. We have very strong balance sheet capacity. I don't think we want to get into trying to get specifics. Some of your numbers, frankly, were quite a bit off actually, but I don't want to start getting into those kind of specifics, because it depends on rating agencies, it depends on the target. Cash flow is coming from the target. So with that, I think important message is balance sheet capacity is not going to be a limiter for us.

A - Peter Dannenbaum {BIO 20569031 <GO>}

Thank you, Tim. Next question, please, Grace.

Operator

Next up, we have Seamus Fernandez from Guggenheim. Your line is open.

Q - Seamus Fernandez {BIO 7525186 <GO>}

Great. Thanks for the question. So just a quick one on the earlier stage pipeline. I'm a little surprised you guys are presenting your first oral PCSK9 inhibitor in a late-breaker at AHA in two weeks. But it isn't included in your pipeline summary. Could you just help us understand why not? And just as a follow-up to that, when might we hear more about the earlier stage pipeline? Will this be at an R&D Day in 2022? What's the right time to start, I guess, showing a little bit more of the earlier stage pipeline that Merck's been building over the last three to four years via acquisition and then internally? Thanks.

A - Robert M. Davis {BIO 6955931 <GO>}

Yeah, this is Rob. Maybe I'll let Dean just comment specifically on the oral PCSK9, then I can give the comment on the additional transparency question in answer.

A - Dean Y. Li {BIO 21985278 <GO>}

Yeah, specifically, in relationship to the oral PCSK9, it is going to American Heart Association. It is flipping into Phase 2, and that's why we often in our pipeline lead it as Phase 2, but we're trying to demonstrate increased transparency by showing something that's about to enter that. The presentation at the American Heart

Association I think will be well-attended. I think trying to create an oral PCSK9 has been a holy grail in the cardiovascular field for some time and has not been achieved, and we believe we have achieved it. It is about that product, but it's also about the ability of Merck to do things that other people can't do. And when one looks at how we've created that molecule, one can immediately ask yourself, wow, what is that capacity, what is that technology that allows them to do that for PCSK9, what other targets could they be doing as well? Bob.

A - Robert M. Davis {BIO 6955931 <GO>}

Yeah, so thank you. And as Dean highlighted, we tend -- our view is that as things move from Phase 1 into Phase 2, that's when we'll start discussing it. So this is just in that process. And I would highlight, and Dean did get into it, but there's a lot of -- we have other assets in the cardiovascular space that also either have moved or moving into Phase 2. That's why we really see our cardiovascular pipeline as a growing area of excitement and strength, and why we were so excited about the complementary nature that Acceleron is to that pipeline.

And as you asked about the transparency, our intention -- the next area we'd like to highlight is cardiovascular, because I can tell you I'm excited about what we have. We got a lot going on, but I don't think it's appreciated. Obviously, we would like to wait to see the Acceleron deal completed, so we can include their assets in that discussion and that will come as soon as we can figure out when that will happen, either later this year or early next year.

Beyond that, I was very pleased with what we did when we gave added visibility to our HIV pipeline, the excitement we have around is islatravir. That's foundational drug. Oncology continues to have just multiple shots on goal both with KEYTRUDA and a growing number of new mechanisms. We've highlighted that. And once we get past the cardiovascular, I assume we'll start to talk about our CNS portfolio, because we also have a lot in the neurology space, so I think it's pretty exciting. So our view is to do it area-by-area as things start to move into those Phase 2 realm, and we'll bring it forward as quickly as I can with cardiovascular being first once Acceleron is done.

A - Peter Dannenbaum {BIO 20569031 <GO>}

Thank you, Seamus. It's a little past 9:00. I think we have time for one more question. Next question please, Grace.

Operator

All right. Your last question comes from the line of Louise Chen from Cantor. Your line is open.

Q - Louise Chen {BIO 6990156 <GO>}

Hi. Thanks for taking my question here. So there are several players trying to bring lower price checkpoint inhibitors in the market. And do you believe that these discounted pricing strategies will have any traction, why or why not? Thank you.

A - Frank Clyburn {BIO 20654315 <GO>}

Hey, Louise, this is Frank and I'll take that from a couple of different angles. I know there's been discussion there, and I first want to make sure that we really continue to emphasize that oncology we see is really data-driven and the importance of strong clinical data and I think you have seen that position us well and also the wall of data that we've established with a product like KEYTRUDA. With 33 indications right now and just the familiarity in the growth that we're seeing across so many different cancer types that I was highlighting, we feel we are very well-positioned.

We also think that the regulatory hurdle for new entrants increases with additional KEYTRUDA approvals. And as positions continue to gain experience, we think that also you would have to have a broader structural change would be required in the US to adopt broadly. So our view is we'll continue to monitor the competitive landscape as we always do, but we feel very confident in KEYTRUDA and our growth prospects going forward.

A - Peter Dannenbaum {BIO 20569031 <GO>}

Great. Thanks, Louise. Rob, any final points?

A - Robert M. Davis {BIO 6955931 <GO>}

Yeah, maybe just a couple points. First, I want to thank and recognize our Marck employees across the globe for their hard work and dedication. With the pandemic, the way we've been able to execute really I think shows the best of who we are and I couldn't be more proud across all elements of our business; clinically, commercially, manufacturing, it's really phenomenal. So I do want to first recognize them, because I think that's important.

And hopefully, what you took from the call is this is an exciting time at Merck. We really have growing momentum and I can tell you growing confidence that we have the ability to grow not only in the near-term, but a growing portfolio of assets that set us up to be sustainably be an important contributor to human health and to continue to deliver significant value for our shareholders. We're more focused company. We're a faster growing company. We're working with urgency to achieve our mission and deliver for patients and shareholders. So hopefully, that came through.

And I'm also quite pleased with the amount of progress we've made in a short period of time. You've heard today good developments across businesses, with development -- good developments in delivering an incredibly strong quarter, moving fast with what we're doing with Molnupiravir, great results coming, there's islatravir in our broader oncology portfolio. So we're firing on all cylinders and I'm confident and proud of where we are, and I thank you for your time.

Operator

Thank you--

A - Peter Dannenbaum {BIO 20569031 <GO>}

Thank you very much.

Operator

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