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PRESENTATION

Operator

Good morning. My name is Grace Lakra, and I'll be your conference operator today. At this time, I would like to welcome everyone to the Merck & Co. Q1 Sales and Earnings Conference Call. (Operator Instructions) Thank you. I would like to turn the call over to Peter Dannenbaum, Vice President of Investor Relations. Please go ahead.

Peter Dannenbaum - *Merck & Co., Inc. - VP of IR*

Thank you, Grace, and good morning. Welcome to Merck's First Quarter 2022 Conference Call. Speaking on today's call will be Rob Davis, President and Chief Executive Officer; 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 items from our non-GAAP results and provide 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 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 in the 2021 10-K, 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, 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 - *Merck & Co., Inc. - President, CEO & Director*

Thanks, Peter. Good morning, and thank you for joining today's call. Before I get started, let me take a moment to speak about the ongoing crisis in Ukraine.

We're hopeful for an immediate and peaceful resolution to the Russian invasion of the country, and we support the Ukrainian people and stand with them, and recognize what a terrible tragedy this represents. Merck is making every effort to protect the health and safety of our employees and to ensure essential medicines and vaccines continue to reach patients. In addition, we are dedicating meaningful resources to address the humanitarian crisis in the country through multiple channels.

Turning to our business. We continue to deliver across our key strategic priorities in the first quarter. We're sustaining the strong business momentum we delivered in 2021 with robust top and bottom line growth. We've also achieved significant clinical advancements across our research pipeline and successfully integrated Acceleron.

Now moving to our results. We've had a strong start to 2022, achieving very strong top and bottom line growth. Commercially, we continue to execute well across a broad set of key growth drivers most notably, KEYTRUDA, GARDASIL and Animal Health. Our performance reflects robust underlying demand for our derisked innovative portfolio and reinforces the importance of our science-led strategy.

LAGEVRIO, our COVID-19 antiviral treatment, was a significant contributor as well. But even excluding these sales, our top line growth was still a very healthy 19% versus last year.

On LAGEVRIO, we've accelerated broad global access, and it's now established as an important tool for patients and health care providers to address the ongoing pandemic. Since receiving emergency use authorization in December, we've delivered approximately 6.4 million courses to more than 30 countries. The success we are achieving is reflected in our updated 2022 guidance, which demonstrates our expectation for another year of strong growth and overall business momentum.

Our oncology business is benefiting from the continued rollout of new and important indications, including in earlier lines of therapy. Global demand for GARDASIL remains strong and growth will benefit from increased supply as a result of the significant investments we are making to expand manufacturing capacity, and our Animal Health business remains positioned to grow at above-market rates.

Longer term, we remain confident in our ability to deliver strong revenue growth and operating margin expansion through 2025. We're preparing for the post-KEYTRUDA LOE period by continuing to strengthen the levers we have and building upon them in order to deliver long-term growth.

In oncology, we remain committed to building on the foundational position that we have achieved with KEYTRUDA, and we aim to expand our presence in this key therapeutic area and to establish an enduring leadership position. In addition, we'll continue to maximize the opportunities we see for our durable growth drivers, such as GARDASIL, our pneumococcal portfolio and Animal Health through our proven commercial execution.

Beyond our existing portfolio, business development remains a key priority. We remain highly focused in our pursuit of the best external innovation and will be appropriately aggressive when great science and value align. We have a strong track record of business development, but we know we need to do more. And we believe we are well positioned to quickly deploy capital towards the right strategic assets as they present themselves. And finally, we'll continue to advance our broad pipeline across key therapeutic areas in order to deliver medically important innovations to patients.

We've taken important steps to provide increased transparency into the opportunities we see in our portfolio and our business, including through two recent investor events. Earlier this month, we provided a detailed description of our growing cardiovascular portfolio and pipeline. At Merck,

we're focusing our efforts where the needs are greatest and where we have the best opportunity to positively impact patients' lives, including in heart failure, pulmonary arterial hypertension, thrombosis and atherosclerosis.

We've made significant advancements across our CV pipeline and believe our broad, differentiated portfolio can have meaningful impacts on patients' lives with at least 8 potential new approvals by 2030. We're confident that these important innovations have the potential to be meaningful growth drivers for Merck well into the next decade.

And in February, we hosted our inaugural ESG event which highlighted our activities in our 4 priority areas of access to health, employees, environmental sustainability and ethics and values. Our ESG efforts are grounded in our company's values, and we look forward to building on Merck's legacy of operating responsibly going forward.

Before I close, I'd like to take a moment to recognize Dr. Roy Baynes, who has announced his retirement after 8 years at Merck. Roy has been instrumental in helping Merck become a leading oncology company, particularly through his leadership in the development of KEYTRUDA. We wish Roy the best in his future endeavors, and we're confident that he leaves behind an outstanding team and program. I'm pleased to report that Dr. Eliav Barr was appointed to succeed Roy. Eliav not only has deep experience having served in several research capacities throughout his more than 2 decades at Merck, but also has an unwavering commitment to patients, consistent with Merck's purpose to save and improve lives.

In summary, we've begun 2022 with strong operational momentum, and I want to express my sincere thanks to our employees worldwide for their continued focus and commitment. We remain confident in our fundamental strategy, our growth prospects and in our ability to deliver significant benefits for patients and value to shareholders well into the future.

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

Caroline Litchfield - *Merck & Co., Inc. - Executive VP & CFO*

Thank you, Rob. Good morning. As Rob highlighted, we have had a very strong start to 2022 with exceptional performance in both revenues and earnings. These results further demonstrate that our focus on science and innovation at the core of our strategy, enabled by excellent execution of our dedicated colleagues across the globe, is delivering value for patients, customers and investors.

Total company revenues were $15.9 billion, an increase of 50%. LAGEVRIO contributed $3.2 billion in revenues. Excluding LAGEVRIO, the base business delivered very strong growth of 19%.

The remainder of my comments will be on an ex-exchange basis. Our human health business continued its strong momentum. Excluding LAGEVRIO, the human health business grew 21%, driven primarily by our key pillars as well as the reduced impact of the pandemic. Our Animal Health business also delivered above-market performance with sales increasing 9%, driven by growth across both companion animals and livestock segments.

Now turning to the first quarter performance of our key brands. In oncology, KEYTRUDA grew 27% to $4.8 billion, reflecting continued robust global demand and the expansion into new indications. In the U.S., KEYTRUDA continues to demonstrate strong growth across all key tumors and is benefiting from recent launches in earlier-stage cancers, including triple-negative breast, renal cell carcinoma and melanoma. KEYTRUDA is currently approved to treat 5 indications in earlier-stage cancers, and we are excited about the potential opportunity to expand into adjuvant lung cancer based on the encouraging data from KEYNOTE-091.

We continue to be confident that KEYTRUDA's robust clinical data, combined with physicians' familiarity and experience with the product, will support expanded use and patient benefit in early-stage disease. In the metastatic setting, KEYTRUDA continues to maintain its leadership position in non-small cell lung cancer, capturing 8 out of 10 eligible new patients.

Outside the U.S., KEYTRUDA's growth continues to be driven by lung cancer and the ongoing launches in head and neck cancer and renal cell carcinoma.

Lynparza remains the market-leading PARP inhibitor. Our alliance revenue grew 20%, driven by uptake in metastatic breast cancer. We are also excited by the expanded opportunity in early-stage breast cancer, following the recent FDA approval based on the OlympiA study. Further, we look forward to potentially reaching a broad prostate population based on the PROpel study.

Lenvima alliance revenue also had very strong growth, driven by uptake following the launches of KEYNOTE-581 in advanced renal cell carcinoma and KEYNOTE-775 in metastatic endometrial cancer, where we are seeing encouraging new patient share trends across each of these tumor types. Lenvima growth also benefited from increased demand in hepatocellular carcinoma in China and certain onetime items.

We are also excited by the launch of WELIREG for patients with certain VHL-associated tumors. WELIREG continues to generate strong interest among scientific leaders, providers and patients. Although still early in its launch, WELIREG has had strong uptake, providing a treatment option to the significant unmet need for these patients. We are working to potentially extend its reach to broader RCC indications in the future.

Our vaccines portfolio again delivered excellent performance led by GARDASIL, which increased 60% to $1.5 billion. Outside the U.S., significant growth was driven by strong underlying demand across key geographies, particularly China as well as increased supply. In the U.S., sales increased due to the timing of CDC purchases.

Global demand for GARDASIL remains robust, supported by strong clinical and real-world data as well as efforts to increase the recognition of GARDASIL as a vaccine that can help prevent certain HPV-related cancers in both females and males.

In our hospital acute care portfolio, BRIDION sales grew 20%, driven by the ongoing recovery in surgical procedures during the quarter and continued strong leadership of the neuromuscular blockade reversal agent class.

Our Animal Health business delivered another quarter of robust growth, with sales increasing 9%. Companion animal sales increased 13%, driven by global demand in parasiticides, including the BRAVECTO line of products as well as vaccines. Livestock sales increased 7% due to higher demand in ruminants and poultry.

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 70.7%, a decrease of 5.9 percentage points, driven primarily by higher LAGEVRIO sales. As a reminder, we share profits from LAGEVRIO equally with our partner Ridgeback, which is reflected within cost of sales and reduces our gross margin percentage. Gross margin this quarter also reflects the favorable impact of product mix, offset by higher manufacturing costs.

Operating expenses increased 7% to $4.8 billion as we continue to prudently invest behind our growth drivers and pipeline. Other expense was approximately $140 million. Our tax rate was 14%. Taken together, we earned $2.14 per share.

Turning now to our 2022 non-GAAP guidance. As a reminder, at the request of the SEC, certain companies in our industry, including ours, have made changes to non-GAAP reporting. We will no longer exclude significant expenses for upfront and milestone payments related to collaborations and licensing agreements as well as transactions accounted for as asset acquisitions from non-GAAP results.

As a result, $1.7 billion of R&D charges primarily related to the acquisition of Pandion are now included in our recast 2021 non-GAAP results. This increased R&D expense by $1.7 billion and decreased non-GAAP EPS by $0.65. There was no impact to the first quarters of 2021 and 2022.

Our 2022 guidance does not assume any significant transactions that would have previously been excluded from non-GAAP. So this could change in the future quarters if we execute business development which is a strategic priority.

The underlying strength of our business enables us to raise and narrow our full year guidance. We now expect revenue to be between $56.9 billion and $58.1 billion, representing growth of 17% to 19% or 11% to 12%, excluding LAGEVRIO and the impact from foreign exchange. The projected impact from foreign exchange includes an incremental headwind of approximately $200 million using mid-April rates, resulting in a full year negative impact of just over 2%.

We are increasing our gross margin expectation to between 74% and 74.5%. We expect operating expenses of $20.3 billion to $21.3 billion. At the midpoint, this is consistent with what was implied by our prior guidance. We expect other expense of approximately $350 million. We assume a full year tax rate between 13.5% and 14.5% due to an increase in estimated U.S. taxes to be paid on foreign income. We assume 2.53 billion shares outstanding.

Taken together, we have increased our expected EPS range to $7.24 to $7.36, representing pull-through of the operational strength from our key pillars and operating expense leverage, offset in part by a slight reduction in the top end of our LAGEVRIO sales assumption, the increase in our tax rate and an incremental 1% headwind from foreign exchange using mid-April rates.

As you consider your models, there are a few areas to focus on. First, on LAGEVRIO. We are narrowing the range of our full year guidance to $5 billion to $5.5 billion. We have entered into supply and purchase agreements for approximately 10 million courses of therapy. Since authorization, we delivered 6.4 million courses of therapy, including 5 million in the first quarter. We expect approximately half of the remaining full year revenue from LAGEVRIO in the second quarter.

We continue to expect strong annual growth for GARDASIL, especially in ex U.S. markets, including China.

Finally, as a reminder, our other revenue line contains several items, including supply sales to Organon, which we began recording upon the completion of the spin-off last year and to Johnson & Johnson for its COVID vaccine. Also included are our revenue hedge and royalties. Other revenue in the first quarter also benefited from approximately $100 million in receipts relating to out-licensing agreements.

Our capital allocation priorities remain unchanged. First, we will continue to prioritize investments in our business and pipeline to drive near- and long-term growth. We will continue to be appropriately aggressive in augmenting our internal pipeline through strategic business development, and we intend to pursue additional value-enhancing opportunities. We remain committed to the dividend with the goal of increasing it over time. To the extent we have excess cash, we will return it to shareholders through share repurchases.

To conclude, we remain very confident in the growth of our business, driven by the global demand for our innovative medicines and vaccines. We are in a position of financial and operational strength, and our continued execution will enable us to deliver value to patients and our shareholders well into the future.

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

Dean Y. Li - *Merck & Co., Inc. - Executive VP & President of Merck Research Laboratories*

Thank you, Caroline. It is good to be here to provide an update on our progress.

In the first quarter, we continued to demonstrate progress in our pipeline. We made advances across multiple therapeutic areas, including oncology in both advanced and earlier stages of cancer as well as in cardiovascular disease and vaccines. I will also provide an update on LAGEVRIO.

In oncology, we continue to build upon our strong position and execute on our strategy to expand, deepen and extend benefits to patients and diversify our imprint on cancer. This past quarter, we achieved milestones from several tumor types as well as different stages of disease.

Notably, we continue to expand our treatment impact in earlier stages of disease, where we now have 6 approvals from the FDA, 5 for KEYTRUDA and 1 for Lynparza. At the European Society for Medical Oncology Virtual Plenary session last month, data from the KEYNOTE-091 or PEARLS trial, evaluating KEYTRUDA for the adjuvant treatment of patients with stage IB to IIIA non-small cell lung cancer following surgical resection were presented. At an interim analysis, KEYTRUDA has significantly improved disease-free survival in all-comers, one of the study's dual primary endpoint. The trial will continue to analyze the other dual primary endpoint of disease-free survival in patients whose tumors express high levels of PD-L1, which did not meet statistical significance at the time of the planned interim analysis. These latest data provide a strong signal for the benefit of KEYTRUDA in the adjuvant treatment study.

Additional ongoing studies in earlier stages of non-small cell lung cancer include KEYNOTE-671, which is evaluating neoadjuvant adjuvant therapy for patients with resectable II, IIIA and IIIB disease; KEYNOTE-867, which is studying stereotactic body radiotherapy with or without KEYTRUDA in adults with unresected stage 1 HER2 disease; and KEYLYNK-012, where we are studying KEYTRUDA in combination with Lynparza in stage III disease.

Following the approval of KEYTRUDA for the adjuvant treatment of patients 12 years and older with stage IIB or IIC melanoma following complete resection based on KEYNOTE-716, we announced that at a prespecified interim analysis, the study also met its secondary endpoint of distinct metastasis-free survival and showed continued improvement in recurrent-free survival compared to placebo. The data from KEYNOTE-716 reinforces the evidence for KEYTRUDA as adjuvant therapy for appropriate patients with stage IIB and IIC following surgery that help prevent recurrence of disease.

Now similarly, in the earlier-stage setting, along with AstraZeneca, we announced Lynparza was approved by the FDA for the adjuvant treatment of patients with germline BRCA mutations with HER2-negative high-risk early breast cancer previously treated with chemotherapy, either before or after surgery based on the OlympiA study. Further, in women's cancer, we received FDA approval for KEYTRUDA for the treatment of patients with microsatellite instability-high, or mismatch repair-deficient advanced endometrial carcinoma based on new data for KEYNOTE-158. Now this approval is the fourth gynecologic cancer approval for KEYTRUDA and marks the fifth approval derived from the KEYNOTE-158 trial, an innovative trial designed to evaluate the use of predictive tumor biomarkers in patients receiving KEYTRUDA for advanced solid tumors.

Next, the prostate cancer. Along with AstraZeneca, positive results were presented at the American Society of Clinical Oncology Genitourinary Cancers Symposium for the PROpel trial evaluating Lynparza in combination with abiraterone as a first-line treatment for patients with metastatic castrate-resistant prostate cancer with and without mutations in a group of homologous recombination or therapy. At a planned interim analysis, results showed an improvement in radiographic progression-free survival versus the standard of care. These early results also showed a trend towards improved overall survival. The trial will continue to assess this key secondary endpoint, and we plan to engage with health authorities to discuss the findings with the aim of bringing this important option to appropriate patients.

Prostate cancer represents a significant unmet need, and we are continually gaining important insights into the biology of the tumor. We are keen on making an impact for patients with late-stage disease.

Last month, we announced the discontinuation of the KEYLYNK-010 study, evaluating the combination of KEYTRUDA and Lynparza for the treatment of metastatic castrate-resistant prostate cancer. At an interim analysis, this study showed no evidence of superiority to abiraterone and enzalutamide with respect to overall survival and radiographic progression-free survival.

Our attention in metastatic castrate-resistant prostate cancer now shifts to KEYNOTE-921, a study exploring the combination of KEYTRUDA and chemotherapy; and KEYNOTE-641, which is evaluating the combination of KEYTRUDA and enzalutamide.

Outside of the United States, we continue to deliver on our regulatory strategy. Notable actions include positive CHMP opinions for cervical, MSI-high and early-stage breast cancer in Europe and approvals for the combination regimen of KEYTRUDA plus Lenvima for advanced renal cell carcinoma in Japan.

And finally, to coincide with ASCO, in early June, we are planning to host an investor event in Chicago. At our recent cardiovascular investor event, we showcased our growing portfolio of programs targeting a range of conditions, including atherosclerosis, heart failure, pulmonary arterial hypertension and thrombosis.

Following the completion of our acquisition of Acceleron Pharma, we are making strong progress in advancing the development of sotatercept, a potential first-in-class soluble activin receptor type IIA fusion protein. We recently completed enrollment for the STELLAR trial ahead of schedule. STELLAR is the first of 4 ongoing Phase III studies evaluating sotatercept. This progress reflects enthusiasm from investigators regarding this novel investigational mechanism.

For the first time, the 2022 American Heart Association, American College of Cardiology and Heart Failure Society of America, guideline for the management of heart failure included Verquvo, which we collaborate on with our partner, Bayer, as a Class IIB recommendation for the treatment

of stage C heart failure with reduced ejection fraction. The guideline highlights the submechanism of sGC such as Verquvo and the potential benefits of stimulating soluble guanylate cyclase and increasing cyclic GMP.

Based on evidence from the pioneering VICTORIA trial, Verquvo is the first drug specifically studied and approved for patients with worsening heart failure and the only drug recommended in the new guidelines for these patients.

Our ongoing VICTOR study is designed to expand on the evidence to date by evaluating Verquvo in patients with chronic heart failure and reduced ejection fraction who have not experienced a recent worsening heart failure event. Merck is uniquely positioned to meaningfully impact the treatment of patients with cardiovascular disease with at least 8 potential approvals by 2030, including Verquvo and stable heart failure and sotatercept as well as our pipeline of candidates, including an inhaled soluble guanylate cyclase stimulator, a Factor XI inhibitor and an oral PCSK9 inhibitor.

Next, the COVID-19 and LAGEVRIO. As the pandemic evolve, there continues to be regional surges in infection rates with the emergence of new COVID-19 variants. Now some of these strains are resistant to specific monoclonal antibody regimens and appear able to evade some vaccine protection, highlighting the importance of testing and the availability of antiviral option.

At the recent European Congress of Clinical Microbiology and Infectious Diseases, we presented Phase III virology outcomes data for MOVe-OUT, adding to the growing body of evidence for the antiviral properties of LAGEVRIO.

The PANORAMIC trial evaluating novel antivirals for early treatment, which is being sponsored by the University of Oxford and funded by the U.K. government and the MOVe-AHEAD trial evaluating LAGEVRIO for post-exposure prophylaxis are both ongoing. We are working collaboratively with the European Medicines Agency to provide additional data from these trials in order to secure an approval.

We remain confident in the safety and efficacy of LAGEVRIO in appropriate patients. In particular, we believe it's low propensity for drug-drug interactions makes it an important option for patients.

Next, on our pneumococcal programs. Earlier this month, the FDA extended the PDUFA date for the supplemental biologics license application for VAXNEUVANCE, our 15-valent conjugate pneumococcal vaccine in infants and children to July 1, 2022. The agency requested additional analyses of data, which we provided. Importantly, no new studies were requested.

Also in our pneumococcal program, we received breakthrough therapy designation for V116, our investigational PCV that is designed to target serotypes responsible for approximately 80% of the residual invasive disease in the older adult population and includes 8 unique serotypes not in currently licensed vaccine. We look forward to providing future updates.

In closing, I would like to thank Roy Baynes for his many contributions to Merck over the past 8 years. As we build upon his legacy, I'm constantly reminded of Roy's business wisdom and teaching, and I'm grateful to work with a remarkable team he has trained and mentored.

One of those mentees, of course, is Eliav Barr. Eliav's experience and commitment to Merck's purpose of saving and improving lives makes him the ideal leader of our global clinical development program. Eliav has a wealth of experience, holding leadership roles across an array of therapeutic areas during his 27 years at Merck, including vaccine, infectious disease and oncology. I look forward to continuing to partner with Eliav to build upon Merck's legacy of innovation and breakthrough science.

And now back to Peter.

Peter Dannenbaum - *Merck & Co., Inc. - VP of IR*

Thank you, Dean. Grace, if you could please begin the Q&A. (Operator Instructions) Thank you.

QUESTIONS AND ANSWERS

Operator

(Operator Instructions) Your first question comes from the line of Carter Gould from Barclays.

Unidentified Analyst

This is [Edward] on for Carter. We wanted to ask about GARDASIL. If you could talk about any impact you're seeing in China, either from a demand perspective or disruptions to manufacturing. And in that context, should we think about cadence -- or should we think about cadence over the year being notably different than in the years past? There's just a lot of different [constants] in play. So any color there would be helpful.

Caroline Litchfield - *Merck & Co., Inc. - Executive VP & CFO*

Carter, this is Caroline. Thank you very much for the question. GARDASIL continues to be a great growth driver for our company globally, including China.

Specific to China, we saw strong performance in the quarter, and we expect continued strong performance as we go through this year. We have significant demand in China. And as they're [off-play] as a result of COVID and potentially lockdown in one part of the country, we have the ability to ensure that we're supplying more of the GARDASIL doses to other parts of the country. So we're therefore not anticipating a significant impact to our GARDASIL performance in China as a result of what we're seeing in Shanghai at this moment in time.

As it pertains to our supply chain, our company has a very robust supply chain. And we have plan A and plan B, if there are any interruptions in the supply chain. So we, again, have no concerns for the reliability of our supply chain, but we remain vigilant and focused on the situation at hand.

Operator

Next up, we have Mohit Bansal from Wells Fargo.

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

Congrats on the quarter. So one question you are getting a lot is how do you feel about potential challenge from a competitor or for PD-L1 and TIGIT combo, potentially looking better than KEYTRUDA in first-line PD-L1-high lung cancer? Do you see this as a major threat, especially looking at the Phase II data from that competitor TIGIT?

Dean Y. Li - *Merck & Co., Inc. - Executive VP & President of Merck Research Laboratories*

Thank you for that question. So I just wanted to emphasize the question focuses on the addition of another checkpoint inhibitor, TIGIT on top of PD-1. And this is a strategy to sort of deepen the response of PD-1 and PD-L1. I think it will be very important to see that data and look at the contribution of components.

And really, we're -- we have a TIGIT program that we're also advancing in non-small cell lung cancer and small lung cancer. So the field will have to sort of see as the data evolves, how much does TIGIT add to PD-1 in the lung space. But I do want to make a broader sort of comment, which is you'll see movements in TIGIT, there was recently movement in PD-1 and CTLA-4 and PD-1s and LAG-3. What you recognize as each of those combinations, what they do is if you're able to show a benefit of the additional agent, it doesn't have as broad of an impact as PD-1 has in many different tumors.

And so one of the things that I think is important to highlight is our strategy is not to just be invested in LAG-3, not to be just invested in CTLA-4, not to be just invested in TIGIT, but to be invested in all 3 and to focus them in specific tumor types.

Operator

Next up, we have Seamus Fernandez from Guggenheim.

Seamus Christopher Fernandez - *Guggenheim Securities, LLC, Research Division - Senior Analyst of Global Pharmaceuticals*

So just really wanted to focus in on sotatercept and the 6-minute walk test as the primary endpoint. If you guys could just help us understand what is being done in the clinical trial to really manage closely the risk that sort of a subjective endpoint represents? Or is your confidence that the magnitude of the difference that you saw in the Phase II will comfortably cover the challenges of the 6-minute walk test that we've seen in some other studies given some placebo responses that raised levels of concern? So just love to get your thoughts there.

Dean Y. Li - *Merck & Co., Inc. - Executive VP & President of Merck Research Laboratories*

Yes. So thank you so much for that question in relationship to sotatercept. So just to reemphasize, we have 3 different trials, all driving towards somewhat different outcomes, the 6-minute walk, which is the STELLAR trial. There's also time to clinical worsening, and then there's also even harder outcomes past that. And as you point out, each one of those is sort of ratcheting up what sotatercept can do.

In relationship to the first one, which is STELLAR, which is related to what you said, the 6-minute walk test, where we saw actually quite impressive data and relationship to the Phase II. We have very committed patient groups as well as sites who are very well trained in how to do these trials. And the Phase II was really nice data. And the fundamental issue is that we are confident that many of those same sites that were involved with the Phase II are involved with Phase III. So I think we're confident we'll see what that data is.

But the best predictor of how well we can manage those trials is really the best indicator is the Phase II, and we're using there many of the same sites and the investigators. So we have great confidence in them.

Operator

Next, we have Chris Schott from JPMorgan.

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

Maybe just a two-parter around kind of corporate structure. I guess first, business development landscape, I know you talked about this as a priority. I guess it's been another kind of quarter of weak equity market performance in the biotech side. So I guess, are you seeing any change in willingness on the part of some of the targets to engage or any resets in valuations that could enable some of these business development kind of activities to move forward?

And then Rob, just a kind of a maybe tangential question on that is broadly across the pharma group, I think we've been seeing asset divestitures of nontraditional pharma businesses. I know you viewed Animal Health as more core to the company. But have your thoughts evolved at all, I guess, as your time as CEO and when you look at your implied kind of core pharma valuation given where some of the animal health multiples trade? So just any incremental perspective there would be appreciated.

Robert M. Davis - *Merck & Co., Inc. - President, CEO & Director*

Great. Chris, thanks for the questions. On the BD landscape question, the short answer is we are not seeing a fundamental shift in seller expectations as of this point. I think as time continues, if we see the market reset to become more permanent and more importantly, if the IPO market continues to be challenged for biotech companies, that might change over time as companies become more cash constrained. There are some smaller players that do have cash challenges. So I think that's where you could see movement first. But fundamentally, we've not seen a change in the landscape yet. We'll have to continue to watch.

With regards to the Animal Health business, our view continues to be that the Animal Health business, as you said, is core to the company. It's core to our strategy as part of a growth driver for the company. But as we've always said, we look at this regularly. We always are challenging ourselves to ask what is the long-term value creation opportunity of this business in our hands relative to what would it be outside of the company. And on a long-term view, we continue to believe it is best in our hands as part of the company. But if that situation evolves, we obviously will continue to be objective in how we analyze that. But we do not look at the short term the arbitrage opportunity for us. It's more about the long-term value creation, and that has not changed as of now.

Operator

Next up, we have Chris Shibutani from Goldman Sachs.

Chris Shibutani - *Goldman Sachs Group, Inc., Research Division - Research Analyst*

If I could ask a question on KEYTRUDA, the strength, particularly out of the U.S. this quarter. If you could help us with some of the underpinnings there.

And relatedly, longer term, 2025, I think you framed how KEYTRUDA, your objective is to have -- I guess the wording changed slightly. You were previously looking for 30% coming from adjuvant with your focus framed around the U.S. If I'm reading it correctly, you brought in the framework here to now think about it as 25% on a global basis. Maybe update us on where you feel you are in terms of making progress towards achieving those objectives of the adjuvant revenue contribution.

Robert M. Davis - *Merck & Co., Inc. - President, CEO & Director*

Yes. So Chris, this is Rob. Maybe I'll take the first part of the question, then Caroline can jump in for the second part. On the strength of the growth we're seeing in the United States, this is really a testament to what we've been talking about all along, which is as we continue to roll out new indications, we are continuing to see our share grow as the leading I-O agent. And importantly, I would highlight that the growth we saw among other things in the quarter, continuation of our position in renal cell carcinoma, continuation of the growth we're seeing in head and neck. In RCC, obviously, being a first-line treatment in the metastatic setting as well as now having adjuvant therapy as well, we've covered pretty much the waterfront of RCC, and we have the opportunity to continue to grow there.

But the standout frankly, for the quarter, and it's, I think, really important to understand is triple-negative breast cancer, both in the metastatic setting and in the adjuvant setting. We are seeing incredible growth in that space and it's something that we feel very proud of because I think we're going to have a meaningful difference there. The reason I highlight that is both -- if you look at the adjuvant opportunity there and this growth we're getting as well as I mentioned, in adjuvant RCC, I think it just reinforces what we see as the future, which is the growth contribution from the earlier lines of therapy long term. But with that, maybe Caroline can be specific to some of the guidance we've provided.

Caroline Litchfield - *Merck & Co., Inc. - Executive VP & CFO*

So to Rob's point, we are extremely excited about the opportunities we have for adjuvant and the impact that, that has on patients. We initially shared that we expected 50% of our growth to come from adjuvant, representing 30% of the U.S. business. We have now extended that to say 50% of the growth will come from adjuvant, representing 25% of our global business in the year 2025.

And to Rob's point, our early introductions into the earlier-stage cancers with 5 indications now in KEYTRUDA are putting us on a very good course to have this impact.

Operator

Next, we have Umer Raffat from Evercore ISI.

Umer Raffat - *Evercore ISI Institutional Equities, Research Division - Senior MD & Senior Analyst of Equity Research*

Maybe let me touch up on molnupiravir real quick. I think the total utilization to date is about 200,000 courses through mid-April. And it looks like, at least based on third-party data sets, that the Pfizer regimen is getting used 8 to 10x more than molnupiravir. So I guess my question is, if only a couple hundred thousand courses have been used through mid-April and 3.1 million courses were contracted to U.S., is there any recourse for U.S. to return a chunk of these courses back? And I'm asking because some of these sales have been recorded in P&L. I just want to make sure they're permanent sales.

Robert M. Davis - *Merck & Co., Inc. - President, CEO & Director*

Yes. I'll let Caroline maybe address this.

Caroline Litchfield - *Merck & Co., Inc. - Executive VP & CFO*

So Umer, thanks for the question. First, let me start. We're proud of molnupiravir, LAGEVRIO and the impact that it can have on the world. And it has impact to the comments that Dean made given its importance, especially in patients that have drug-to-drug interactions.

The data that we have access to suggest that we have actually had utilization by 500,000 patients globally at this stage. We have shipped 6.4 million courses as of now. Both shipments represent expectations for utilization over a period of time. And we're actually seeing extremely strong utilization, especially in ex U.S. markets, where the statistics you quote are actually reversed in some of the markets. We have a very strong market share. So as we sit here today, we've guided on the $5 billion to $5.5 billion based on the contracts that we have in hand, and we are confident in that in our financials.

Operator

Next, we have Daina Graybosch from SVB Leerink.

Daina Michelle Graybosch - *SVB Leerink LLC, Research Division - Senior MD of Immuno-Oncology and Senior Research Analyst*

I have another one on KEYTRUDA in early stage. Can you please talk to how the success of Opdivo plus chemotherapy in neoadjuvant lung cancer changes your expectations or strategy for the early-stage opportunities in lung cancer and then in the other tumor?

Dean Y. Li - *Merck & Co., Inc. - Executive VP & President of Merck Research Laboratories*

Yes. Thank you very much for that question. In relationship to sort of just earlier stage in lung cancer, I think it's really important to emphasize, there's a series of different ways to approach it. One is neoadjuvant adjuvant. One is adjuvant. And I just think all of these signals just demonstrate throughout a variety of different studies just the impact that PD-1s can have.

So our point of view of it is it shouldn't change our strategy, it should just make our strategy pretty comprehensive. The fundamental thing is we have KEYNOTE-091, which is in the adjuvant, so that's post-surgery, and that's usually given by a medical oncologist. The disease-free survival was positive in all-comers regardless of PD-L1. There was a trend to TPS greater than 50%, but not statistically significant. And OS, it was a favorable trend regardless of PD-L1. So we'll be letting that data mature as we continue to discuss with the FDA.

But going to your point, it's not just KEYNOTE-091. It's KEYNOTE-671, it's KEYNOTE-867, it's KEYLYNK-012. It's all in the earlier stage. So our desire to really push that earlier stage is going to be, if anything, our commitment towards that is even greater.

The one thing I would just add in relationship to some of the comments that Caroline and Rob made is that I think it's very important to think about melanoma renal cell carcinoma and triple-negative breast cancer, where at least my experience being in the hospital, there's a concept of really looking at that earlier stage. And I think uptake may be sort of built in the medical system.

I think all of us, including us and other companies as well as patient advocacies and medical centers are going to have to require diligent investment to really, really maximize the important scientific impacts of KEYTRUDA and PD-1s and PD-L1s in the early lung space.

Operator

Next, we have Andrew Baum from Citi.

Andrew Simon Baum - *Citigroup Inc., Research Division - Global Head of Healthcare Research and MD*

I'd just like to thank Roy for all the contributions and insights over the years. The question is on your Factor XI monoclonal. Given your background in cardiology, and I'm sure you keep familiarity with hemostasis team. There's clearly been a number of indications where the DOACs were unsuccessful compared to warfarin for both efficacy and safety, potentially speaking to different underlying mechanisms for thrombosis and a different indication as I'm thinking about [ESS], I'm thinking about mechanical heart valves. Given what you know about Factor XI biology and the intrinsic pathway nature of the inhibition, what indications would you actively avoid or be somewhat cautious about taking a Factor XI inhibitor into, be it yours or someone else's?

Dean Y. Li - *Merck & Co., Inc. - Executive VP & President of Merck Research Laboratories*

Yes. So let me just step back for just a moment. The benefit risk of whether it's platelet or coagulation factors in terms of clotting is something that's actually very topical in the news. I would just emphasize for years, for probably a decade or more, aspirin has been just everywhere. And recently, people realize the benefit risk, one has to be very careful. There has been a major change in the guideline. So that impacts how I think about it.

The other sort of thing that impact is, if you look at Factor XI, the fundamental advantage of that is that you can get blockage of the coagulation cascade with, by genetic, very little impact in relationship to adverse effect. And so for me, the critical thing is to prove that as quickly as possible. So we immediately go where is the problem, where thrombosis and bleeding is both impacted there. And so that's why we ran the end-stage renal disease.

But I could see in the future mechanical devices, one of my favorite sort of things is left ventricular assist device. I think that will continue to need to be monitored in the future. So that's a place where the risk of bleeding and the risk of thrombosis is really high.

Where we have chosen to be a little bit careful is, for example, broader sort of things such as atrial fibrillation and the risk relationship to stroke because we look at the Factor X as very effective. There are bleeding complications, but to make a safety argument for it, you're talking about a very, very large trial. So we are racing to places where the benefit risk of thrombosis and clotting and bleeding, where that differential would make something like a Factor XI have the biggest impact.

Operator

Next, we have Louise Chen from Cantor.

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

I wanted to ask you about your pneumococcal conjugate vaccine. And how you think your more targeted approach will be a competitive advantage versus the one-size-fits-all that we're seeing now? And is there any precedence to what you're doing with V116 and 117? And maybe just lastly, how will you make that message clear to physicians since if everything goes as planned, you'll have several PCVs on the market?

Dean Y. Li - *Merck & Co., Inc. - Executive VP & President of Merck Research Laboratories*

Yes. First of all, we need to get the data to demonstrate that we have an advantage in the different patient populations. But I think you point out a really important point, which is essentially what we're trying to do is, for lack of a better word, we're -- if you want to call it, precision-targeted vaccinations, right? So the fundamental thing is V114 is adult approved and we're driving towards a pediatric approval for the 15-valent. And so that will be in the pediatric population.

In the V116, where we have a breakthrough designation, we're trying to demonstrate that we can target 85% of the residual serotypes. And I would just sit there and tell you it would be 8 unique serotypes in relationship to all the different currently approved ones. And I think that patient population, I reflect a little bit about COVID, but it's that older population that especially has the risk factors who you really want to make sure that, that whole population, that adult population is covered.

And so I do think the fundamental thing is we'll have to have the data, but our concept is the adult have a different set of serotypes and they need to be protected, and we'll have to get the data to demonstrate that. But I think if we can demonstrate it, the uptake will be quite good.

Operator

Next, we have Mara Goldstein from Mizuho.

Mara Goldstein - *Mizuho Securities USA LLC, Research Division - MD of Equity Research Department*

I'm just hoping maybe we can return for a second back to the question of novel targets in combination with KEYTRUDA. And maybe if you could just give us a very high level, perhaps rationale, for which targets you're looking at and which indications. And I'm referring here, obviously, two things like TIGIT, LAG-3, ILT3 and the like.

Dean Y. Li - *Merck & Co., Inc. - Executive VP & President of Merck Research Laboratories*

All right. So let me just sort of separate. So we always talk about expand, deepen and extend. And when we talk about deepen, we're trying to get a deeper response with PD-1s. And there's a series of things that we do with what I call non-I-O agents, which is chemotherapy. We're doing stuff with many other people as well as ourselves with ADCs. Our RAS programs are advancing. So we think that, that sort of combination, there's large precedent throughout our portfolio already, and there will continue to be. And that's also true with Lenvima and Lynparza.

The specific question I think you're driving to is combinations of I-O with I-O agents and LAG-3, CTLA-4 and TIGIT. So at least in our mind, we do recognize that there was demonstration of LAG-3 adding to PD-1 in melanoma. And I think that's an important signal for us. Where we focused our effort to LAG-3 is in MSS CRC. So we know that PD-1s work in MSI-high, and no one's really been able to crack MSS CRC. So that's very important and also in classic Hodgkin's. I would say, in relationship with CTLA-4, there was recent data with HCC.

I would make a comment that I think would make some of the people from Merck smile a little bit. We were the ones who actually did the study with PD-1 and CTLA-4 in relationship to lung. And we could not show a clear contribution of component of CTLA-4 over PD-1. So that is not a place that we think is an important place for patients, and that is not a place that we're going because we have -- we did the study to demonstrate that. Where we think there could be is, clearly, other people have recently released HCC. We're focused in, for example, in renal cell carcinoma. And then PD-1 and TIGIT, our initial focus is non-small cell lung cancer and also small cell lung cancer. And we're advancing a series of trials in that.

So I hope that gave a comprehensive view of LAG-3, CTLA-4 and TIGIT. In relationship to ILT4, other checkpoint inhibitors such as CD27 or in relationship to cytokines, I think the data that we're doing in earlier stages will have to play out for us to be able to answer that more completely.

Peter Dannenbaum - *Merck & Co., Inc. - VP of IR*

Great. Thank you, Mara. I think we have time for one more question, and Rob will have a few closing comments.

Operator

Last question comes from the line of Colin Bristow from UBS.

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

Congrats on the quarter. And I also wanted to say all the best to Roy. It's been really great working with you, and also congrats to Eliav. So I just wanted to piggyback on a GARDASIL question. Could you maybe just give us a little more detail on how you expect the GARDASIL supply to increase? And then maybe just help us think through what is the supply/demand mismatch right now? Some of your prior comments suggested that there may not be such. But I know you said supply has been an issue over the past sort of couple of years. So would love to get some expanded thoughts there.

Caroline Litchfield - *Merck & Co., Inc. - Executive VP & CFO*

Thank you for the question. This is Caroline. So let me start first with the supply/demand. There is significant demand for GARDASIL. This cancer-preventing vaccine in the HPV area has only reached today 9% of the global eligible population. So there is significant runway ahead of us to protect lives and to drive growth for Merck. Indeed, we've stated that we expect the revenue in year 2030 to be double the $5.7 billion we achieved in 2021. So we have significant opportunity ahead of us.

In order to achieve that opportunity, we are building new facilities that will be coming online from 2023, 2024 and 2025. So we're going to have a step-up in the level of supply to the market that will happen over that period.

Specific then to this year, we will see a continuation of the supply into the market as we did in 2021, albeit not quite at the same step-up that we achieved in 2021. So we remain really confident in our ability to drive strong growth for GARDASIL both in 2022 and the years to come.

Peter Dannenbaum - *Merck & Co., Inc. - VP of IR*

Great. Thank you, Colin. Rob?

Robert M. Davis - *Merck & Co., Inc. - President, CEO & Director*

Well, just let me say thank you for your time and your interest today. And I'd just like to conclude by again thanking the Merck team globally for their focus and commitment and really in driving the results you've heard about today, but in continuing to ensure we keep the purpose of the company front and center, which is to deliver for patients.

Hopefully, you get the sense, we are very confident in the business momentum we have. And I'd like to say as well, we are feeling better and better about the evolution of our pipeline and what you've heard today, we're starting to expand. We're doing all of the things we need to do. We have more to do, but we're making great progress. And that's why I have such confidence in the sustainability of our business long term. So we look forward to continuing to share these results with you to deliver for the patients that count on us and in turn, bring value to the shareholders.

So with that, I'd say thank you and have a great day.

Operator

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