Q4 2022 Earnings Call

Company Participants

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

Other Participants

- Andrew Baum, Citi
- Carter Gould, Barclays
- Chris Schott, JPMorgan
- Colin Bristow, UBS
- Evan Seigerman, BMO
- Geoff Meacham, Bank of America
- Louise Chen, Cantor Fitzgerald
- Mohit Bansal, Wells Fargo
- Steve Scala, Cowen and Company
- Terence Flynn, Morgan Stanley
- Tim Anderson, Wolfe Research
- Umer Raffat, Evercore ISI

Presentation

Operator

Welcome to the Merck & Co Q4 Sales and Earnings Conference Call. At this time, all participants are on a listen-only mode until the question-and-answer session of today's conference. (Operator Instructions). This call is being recorded, if you have any objections, you may disconnect at this time.

I would now like to turn the call over to Mr.Peter Dannenbaum, Vice President, Investor Relations. Sir, you may begin.

Peter Dannenbaum {BIO 20569031 <GO>}

Thank you and good morning. Welcome to Merck's fourth quarter 2022 conference call. Speaking on today's call will be Rob Davis, Chairman 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 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'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 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 {BIO 6955931 <GO>}

Thanks, Peter. Good morning, and thank you for joining today's call. 2022 was an exceptional year for Merck. Our science-led strategy is working, and I couldn't be more proud of what our team has delivered scientifically, commercially and operationally. We're focusing on what matters and keeping the patient at the center of everything we do.

We made significant progress in 2022 advancing our broad pipeline, with important internal success complemented by a portfolio of strategic acquisitions, collaborations and partnerships. We have moved with speed and urgency to drive strong progress. And we have provided increased transparency into several of our long-term opportunities, including for GARDASIL, for our cardiovascular pipeline, and more recently, from newer assets that leverage our leadership position in oncology. We enter 2023 with even greater confidence that we're creating a sustainable engine that will bring forth innovation and generate value for both patients and shareholders over the long-term.

Turning first to our results. The business is performing extremely well. The growth we've experienced in 2022 reflects a sustained track record of fundamental strength from our de-risked key growth pillars. We begin the year with confidence that we'll maintain this strong underlying growth, after taking into account the significant impact LAGEVRIO had during the height of the pandemic last year, and are pleased to reflect this in our 2023 initial guidance.

Importantly, our pipeline is advancing with significant progress across several late-stage programs. In oncology, we have expansive research efforts, including our ambition to move treatment into earlier stage settings where there is a higher potential for more favorable longer-term outcomes for patients. In December, along with our partner Moderna, we were pleased to announce highly encouraging Phase 2 results for a personalized mRNA therapeutic cancer vaccine in combination with KEYTRUDA in the treatment of adjuvant melanoma.

We're excited by the potential that this combination may have for patients across a range of tumor types. And last week, we were pleased to receive FDA approval for KEYTRUDA for the treatment of certain patients with early-stage non-small cell lung cancer following resection and platinum-based chemotherapy, which Caroline and Dean will speak to.

In cardiovascular, we're exploring candidates across a broad range of diseases and have made substantial progress from just one year ago. At the American College of Cardiology conference, we will present data from the STELLAR trial evaluating sotatercept in pulmonary arterial hypertension and from the Phase 2 trial of MK-0616, our oral PCSK9 inhibitor, and we will also host an investor event to discuss these programs.

In vaccines, Instituto Butantan in Brazil, with whom we are collaborating for vaccine development, reported very encouraging topline results for their candidate for the prevention of dengue. These data will inform future development of our dengue vaccine, V181, and our efforts to address this critical public health challenge.

Finally, through our business development efforts, we brought in four programs which will have Phase 3 trial starts in 2023 and which have the opportunity to contribute meaningful growth during the latter half of this decade and into the next. We are following our disciplined approach to business development, and we'll act when scientific opportunity and value align. We have more to do, but I feel very good about the progress we've made in 2022 and we believe that all of these efforts will lead to real benefits for patients and, in turn, for shareholders.

We enter 2023 with confidence in the innovation engine we are building and our ability to deliver sustainable value for patients well into the next decade. We will continue to execute on our de-risked assets and act with urgency to advance and grow our pipeline. We are doing all of this with an approach to sustainability that is closely aligned to our overall business strategy. I'm very confident in the short and long-term outlook of our company, and I look forward to providing future updates.

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

Caroline Litchfield {BIO 20934609 <GO>}

Thank you, Rob. Good morning. As Rob noted, 2022 was an exceptional year for our company. We delivered excellent topline growth of 22% driven by strength across our key pillars of Oncology, Vaccines and Hospital, as well as a significant

contribution from LAGEVRIO. Our Animal Health business delivered strong operational growth, which was offset by foreign exchange. These results are a testament to the profound impact our medicines and vaccines are having on patients globally, which are enabled by our dedicated teams who are executing with excellence to deliver these important innovations. We are confident in the health of our business, give our outlook for continued strong underlying growth.

Now, turning to our fourth quarter results. Total company revenues were $13.8 billion, an increase of 2%. Excluding the impact from foreign exchange, the business delivered strong operational growth of 8%. The remainder of my revenue comments will be on an ex-exchange basis. Our Human Health and Animal Health businesses continued their strong growth increasing 9% and 6%, respectively

Now, turning to the fourth quarter performance of our key brands. In Oncology, KEYTRUDA grew 26% to $5.5 billion driven by strong global demand for in-line indications as well as continued global expansion from new approvals. In the U.S., KEYTRUDA grew across all key tumor types and continues to benefit from uptake in earlier-stage cancers including triple negative breast cancer, as well as in certain types of renal cell carcinoma and melanoma.

KEYTRUDA continues to have a profound impact on patients, including in earlier-stage cancers, where there is greater potential for better outcomes. We are excited by the recent approval of KEYNOTE-091, which represents KEYTRUDA's seventh indication in earlier-stage cancers. Early lung cancer detection and screening remain an important unmet need. It is our ambition, along with others to improve lung cancer screening rates to levels similar to other tumor types, such as breast, where screening programs are more routine.

While we are committed to addressing this unmet need, we anticipate a more gradual near-term uptake from this indication. In the metastatic setting, KEYTRUDA maintains its leadership position in non-small cell lung cancer, which gives us confidence that we are well-positioned to positively impact patients in the earlier setting.

Outside the U.S., KEYTRUDA growth continues to be driven by uptake in metastatic indications, including non-small cell lung cancer, head and neck cancer and renal cell carcinoma as well as recent launches in earlier-stage cancers, including certain types of high-risk, early-stage triple negative breast cancer and renal cell carcinoma.

Lynparza maintains its leadership of the PARP inhibitor class. Alliance revenue grew 14% primarily due to continued demand in certain patients with high-risk, early-stage breast cancer. Lenvima Alliance revenue grew 9% driven by increased uptake in the treatment of certain patients with advanced renal cell carcinoma and advanced endometrial cancer in the U.S.. Lastly, WELIREG is performing in-line with our expectations, and we are proud of the impact it is having on adult patients with certain VHL-associated tumors.

Our vaccines portfolio delivered growth with GARDASIL increasing 6% to $1.5 billion, driven by strong demand in major ex-U.S. markets, particularly China. In the U.S., sales decreased primarily due to CDC purchasing patterns. Vaccines sales also benefited from the pediatric launch of VAXNEUVANCE, which is off to an encouraging start, with revenues also benefitting from inventory stocking.

In our Hospital Acute Care portfolio, BRIDION sales grew 7%, driven by an increase in market share among neuromuscular blockade reversal agents and an increase in surgical procedures. Hospital Acute Care sales also benefitted from the resupply of ZERBAXA, which started in the fourth quarter of 2021.

Our Animal Health business delivered another solid quarter, with sales increasing 6% reflecting strategic price actions and volume growth. Livestock sales grew 12% driven by increased demand in ruminants and poultry products. Companion animal sales were negatively impacted by supply challenges for certain vaccines and a reduction in vet visits in October, which improved during the quarter.

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 75.7%, an increase of 0.9 percentage points due to favorable product mix and foreign exchange. Operating expenses increased 8% to $5.7 billion, reflecting increased investments to support our portfolio and growing pipeline. Other income was $86 million, reflecting the return on pension plan assets and capitalized interest, which was largely offset by net interest expense. Our tax rate was 15.6%. Taken together, earnings per share were $1.62.

Turning now to our 2023 non-GAAP guidance. The strength across our key pillars is expected to continue into this year. We project revenue to be between $57.2 billion and $58.7 billion, including approximately $1 billion from LAGEVRIO. Excluding the negative impact of LAGEVRIO and an approximate 2% negative impact from foreign exchange using mid-January rates, we expect strong underlying revenue growth of 7% to 10%.

Our gross margin is expected to be approximately 77%. Operating expenses are assumed to be between $23.1 billion and $24.1 billion, which includes $1.4 billion of research and development expenses related to our acquisition of Imago and the expansion of our collaboration with Kelun Biotech. As a reminder, our guidance does not assume additional significant potential business development transactions.

Other income is anticipated to be approximately $250 million. We assume a full-year tax rate between 17% and 18% and approximately 2.55 billion shares outstanding. Taken together, we expect EPS of $6.80 to $6.95. This range includes a negative impact from foreign exchange of approximately 4%, using mid-January rates. Our guidance reflects confidence in the continued strong growth across Oncology, Vaccines, and Animal Health.

As you consider your models, there are a few items to keep in mind. On revenues, we are confident in our ability to drive strong growth of GARDASIL, particularly in

international markets. Global immunization levels remain low, which creates a tremendous opportunity to benefit more patients. And we are improving supply, which positions us well to support the significant demand we are experiencing today and expect over the long term for this vaccine that prevents HPV-related cancers.

Other revenue is projected to decline significantly, primarily reflecting a smaller planned benefit from revenue hedges following the U.S. dollar strength last year, which resulted in an approximate $800 million benefit in 2022. Other revenue is also expected to be lower due to the discontinuation of third-party manufacturing sales to Johnson & Johnson.

On the rest of the P&L, we project a shift from other expense to other income, which is primarily attributable to an assumption that there will be no pension settlement cost as well as an expectation of lower net interest expense and higher joint venture equity income. This benefit is more than offset by an increase in the estimated tax rate, due to the unfavorable impact of the R&D capitalization provision as well as an approximate 1 percentage point impact related to Imago.

Now shifting to capital allocation, where our priorities remain unchanged. We will continue to prioritize investments in our business to drive near and long-term growth. We are excited about the significant progress our team has made to advance and augment our pipeline in 2022. In 2023, we will continue to invest in opportunities that will address important unmet medical needs and drive the next wave of growth for our company, including the initiation of many late-stage clinical trials across a broad set of novel candidates.

We remain committed to our dividend, with the goal of increasing it over time. We will continue to pursue the most compelling external science through value-enhancing business development to augment our internal pipeline, and will invest appropriately to maximize the potential of our R&D programs. Given the strength of our business and balance sheet, we plan to resume share repurchases, while ensuring we maintain ample capacity to pursue additional business development, which is the higher priority.

To conclude, we enter 2023 with confidence in our ability to execute on the important opportunities we have to deliver innovation to patients and sustain the strong underlying growth of our business 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. Today, I will provide notable updates since our last earnings call. We continue to make significant advancements and achieve important regulatory milestones. The fourth quarter marks the end of a successful year with progress made across oncology, vaccines, infectious diseases and cardiology.

Let me start with oncology. We remain committed to transforming the landscape of cancer therapy with an ongoing focus on treating earlier stages of disease. We are pleased by the recent approval of KEYTRUDA for the adjuvant treatment of adult patients with stage IB, II or IIIA non-small cell lung cancer following resection and platinum-based chemotherapy based on the results of KEYNOTE-091. This approval provides, for the very first time, an adjuvant immunotherapy option for this patient population with stage IB disease and regardless of PD-L1 status.

Beyond KEYNOTE-091, we have additional ongoing studies in earlier stages of non-small cell lung cancer including: KEYNOTE-671 evaluating KEYTRUDA with platinum doublet chemotherapy as neoadjuvant followed by adjuvant therapy in resectable stage II, IIIA and IIIB disease; KEYNOTE-867 evaluating KEYTRUDA in patients undergoing stereotactic body radiotherapy with unresected stage I or II disease; and KEYLYNK-012 studying KEYTRUDA in combination with Lynparza in stage III disease.

These trials are all part of our broader effort to treat earlier stages of cancers and further improve patient outcomes across tumor types, such as melanoma. Together with Moderna, we announced positive Phase 2 results for V940/mRNA-4157, in combination with KEYTRUDA, for the adjuvant treatment of stage III and IV melanoma in patients with high risk of recurrence following complete resection.

The combination demonstrated a statistically significant and clinically meaningful improvement in recurrence free survival versus KEYTRUDA alone. This investigational personalized neoantigen therapy utilizes mRNA technology and is specifically tailored to target the unique mutational signature of each patient's tumor. We plan to discuss the results with regulators and initiate Phase 3 trials in multiple tumors this year. Detailed results will be presented at an upcoming medical meeting.

We also announced positive results from the Phase 3 KEYNOTE-966 trial evaluating KEYTRUDA in combination with chemotherapy. This trial demonstrated an improvement in overall survival for the first line treatment of patients with advanced or unresectable biliary tract cancer. In addition, we announced positive topline results from the Phase 3 KEYNOTE-859 trial evaluating KEYTRUDA in combination with chemotherapy for the first-line treatment of patients with HER2-negative locally advanced unresectable or metastatic gastric or gastro-esophageal junction adenocarcinoma.

In November, we announced the acquisition of Imago Biosciences which closed last month. Imago's lead candidate, bomedemstat, is a potentially first-in-class orally available lysine-specific demethylase 1 inhibitor. It is currently being evaluated in multiple Phase 2 clinical trials for the treatment of essential thrombocythemia, myelofibrosis and polycythemia vera. The combined team is now focused on continuing to advance the ongoing clinical development programs.

At the American Society of Hematology annual meeting, data were presented from multiple pipeline candidates including: favezelimab, our anti-LAG3 antibody; zilovertamab vedotin, an antibody drug conjugate targeting ROR-1; and

nemtabrutinib, our oral reversible, non-covalent BTK inhibitor as well as KEYTRUDA. Updated Phase 2 data for bomedemstat in essential thrombocythemia and advanced myelofibrosis were also presented. We continue to deliver on our regulatory strategy.

In the European Union, along with our partner, Astra Zeneca, we announced the approval for Lynparza, in combination with abiraterone and prednisone, for the treatment of certain patients with metastatic castration-resistant prostate cancer based on the results of the PROpel trial. In China, based on the results of KEYNOTE-522 and KEYNOTE-394, we received approvals for KEYTRUDA in neoadjuvant, adjuvant high-risk, early-stage triple negative breast cancer and hepatocellular carcinoma, respectively.

With our partners Astellas and Seagen, we announced the FDA has accepted supplemental biologics license applications for KEYTRUDA with PADCEV, an antibody-drug conjugate targeting Nectin-4, for the first-line treatment of certain patients with locally advanced or metastatic urothelial cancer, who are not eligible to receive cisplatin-containing chemotherapy. The agency set a PDUFA date of April 21, 2023 for each application. Building on the clinical benefits observed with KEYTRUDA in combination with chemotherapy and antibody drug conjugates, we have focused on augmenting our tissue targeting candidates through business development.

We announced the expansion of our agreement with Kelun Biotech with the addition of up to seven preclinical antibody drug conjugates. The collaboration leverages technology with the potential to yield a new generation of candidates designed to precisely target and deliver potent anticancer agents to the tumor site. This follows previously disclosed agreements for two clinical stage candidates, including MK-2870, an investigational TROP2 targeting ADC we are planning to advance into Phase 3 trials this year.

We also expanded our collaboration with PeptiDream to include the discovery and development of peptide drug conjugates. This technology potentially provides for improved permeability and drug selectivity in targeting tumor tissue.

Next to our vaccines portfolio. We were encouraged by the progress scientists and clinicians at the Instituto Butantan in Brazil made in developing a single dose dengue vaccine candidate for registration in Brazil. We are collaborating with the team there to conduct a detailed analysis of these positive, topline Phase 3 results to determine next steps for our own dengue vaccine candidate, V181, currently in Phase 2 development. Merck's goal is to make V181 available outside of Brazil for populations at-risk for dengue.

As Caroline noted, we are receiving positive feedback from the field regarding the recent launch of VAXNEUVANCE in the pediatric setting and remain confident in our population-specific strategy for the prevention of pneumococcal disease.

VAXNEUVANCE offers strong protection, including in the first year of life, with robust immunity across all shared and unique serotypes. This is important because the incidence of invasive pneumococcal disease is greatest in the first year of life for children. Also, we are on track and look forward to the Phase 3 results from our V116 program for the protection of adults this year.

We, along with others in the industry, are making a real impact in our goal to help reduce cancer incidence. It was noteworthy that the American Cancer Society's recently published annual report on cancer facts and trends include the remarkable observation that there has been a 65% reduction in cervical cancer incidence in women 20 to 24years old, from 2012 through 2019.

It is this type of finding that further reinforces Merck's commitment to bringing forward treatment and prevention options to help patients with this devastating disease. As part of this commitment, we are encouraged by the role GARDASIL continues to play in helping to prevent certain HPV related cervical cancers.

Turning to the broader portfolio. With the continued impact of COVID-19 in China, treatment options are urgently needed to help reduce the incidence of disease and burden on healthcare systems. We were pleased, LAGEVRIO was granted conditional marketing authorization by China's National Medical Products Administration in December, for use in adult patients who have mild to moderate COVID-19 infection and a high risk of progressing to severe cases.

I wish to reinforce something Rob mentioned. Please mark your calendars for March 6th, where we will present detailed findings of the Phase 3 STELLAR trial evaluating sotatercept in patients with pulmonary arterial hypertension and the Phase 2 results for MK-0616, our oral PCSK9 inhibitor, at the American College of Cardiology in conjunction with the World Congress of Cardiology meeting in New Orleans. We will also host a live investor event to answer your questions.

We look forward to bringing sotatercept as an important treatment option to patients and are currently working towards submission of the data from the STELLAR trial. We are in discussions with the FDA about submission of the data on a rolling basis, which is likely to result in a potential approval in early 2024.

As we close out 2022, it is important to highlight that over the course of the year, we made strong progress across therapeutic areas, modalities, stages of development and multiple business development transactions.

In oncology, we obtained several important regulatory approvals globally for KEYTRUDA and Lynparza as well as advanced the number of programs evaluating earlier stage cancer regimens. In vaccines, we received an important approval in pediatrics for VAXNEUVANCE. And in addition, we were granted expanded authorizations in China and active recommendations were reinstated in Japan for GARDASIL. In HIV, we resumed our clinical development program for islatravir.

And finally, in cardiovascular disease, we made significant progress across our pulmonary arterial hypertension and hypercholesterolemia programs. Taken together, we continue to deliver on our strategy of advancing promising candidates across multiple therapeutic areas. We have strong momentum across our pipeline and look forward to providing further updates on our progress in 2023.

And now, I will turn the call back to Peter.

Peter Dannenbaum {BIO 20569031 <GO>}

Thanks, Dean. Kelly, we're ready to take questions now. We intend to end the call at 9 sharp this morning. So request that the analysts limit themselves to one question please.

Questions And Answers

Operator

(Question And Answer)

(Operator Instructions) Our first question is from Carter Gould from Barclays. Carter, your line is open.

Q - Carter Gould {BIO 21330584 <GO>}

Hi. Thank you for taking the question. Maybe just you made some comments around sort of uptake in the adjuvant setting after the most recent label update. Can you maybe just sort of set expectations there, and does that comment reflect any sort of assumptions around when we might see more mature data from the PEARLS study potentially this year? Thank you.

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

Yes, so I believe you're speaking about KEYNOTE-091. So I just want to take a broad view, and then the today view and the tomorrow view. So I would just count that the American Cancer Society 2023, it's really remarkable. They suggest that for between 1991 and 2023, there's a massive reduction in lung cancer, 58%, 36%, and KEYTRUDA has been critical in that story. And now we're moving to early lung. The label is broad. It is regardless of PD-L1 and it reflects the clinical trial where we demonstrated a 27% reduction. We're pushing into these earlier lines with other trials, but I think, for -- what we need to set for is two things. We need to make it much more easier with scientific innovation, other means to get to subcu -- I mean to get KEYTRUDA, and that's why we're very eager to push our subcu pembrolizumab with (inaudible) into Phase 3 this year.

But we also need to do a lot to improve adherence to establish guidelines, which currently only have 6% or so of individuals actually who should be screened -- being screened in the United States. So I think with that, we have work to do in relationship

to really taking this important advance and making it broadly available to individuals who should be getting screened.

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

So Carter, maybe I can just add on a little bit about the commercial opportunity. As Dean said, this will be a slower ramp, because we have to drive more people to get diagnosed early so that we can get them the care they need. But just to give you some sizing of this, if you look at 2023, there are about 230,000 people who were diagnosed with lung cancer in the U.S. and the majority of that group was not diagnosed until they were in the metastatic setting. So if you think about it from a minority perspective, we would estimate about 120,000 people in the early-stage setting, of which, only a quarter will have resection or have surgery and be in the stage 1B to 3A, which is what our label indicates. So you're looking at about 30,000 patients who would be the addressable population. And then, obviously, of that group, historically, only about half of those patients have gone on to receive treatment in the form of chemotherapy or IO.

So that's obviously something we hope to change as we go forward because we think the outcomes will show that if you are resected, you should pursue KEYTRUDA in that setting, and it's our goal over time not only to drive more patients in that segment, but obviously, the more people we can get diagnosed early pre-metastatic, then actually we'll expand the population over time. So we see this is a meaningful opportunity long term that is going to take us time to ramp as we work to change the paradigm that's existed in the past.

A - Peter Dannenbaum {BIO 20569031 <GO>}

Thank you, Carter. Next question please, Kelly.

Operator

Our next question is going to come from Andrew Baum from Citi.

Q - Andrew Baum {BIO 1540495 <GO>}

Hi. Thank you. A couple of questions. Could you please address the demand of Merck's business to plug the holes associated with the KEYTRUDA LOE post 2028, alternatively instead, just build the exit growth rate and focus less on finding revenues to plug the hole as you think about your BD strategy? And perhaps quickly for Dean, could you just give us some guidance on the timing for the PFS analysis in the PD-L1 high greater than 50 cohort from KeyVibe-003? Should we expect it in the next 12 months? I know the total PFS read for the whole trial is somewhere in '24, but it strikes me you may have a separate analysis for that greater than 50 subgroup? Thank you.

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

Great. Well, maybe Andrew, I'll start off and that Carolyn or Dean want to jump in. But to give you a sense, obviously, we haven't given specific guidance to the LOE period. But just to ground everyone in the facts, KEYTRUDA in our expectation, will

lose exclusivity in the United States in 2028 and in China in 2028. It loses it in Europe in 2030, and in Japan in 2032. So obviously, by shorthand, we refer to '28, but the reality of it is over most of the markets, and KEYTRUDA increasingly is becoming, as you know, a global product, it's spread out. But as we look at where we sit today, I would say, we feel good about the progress we've made, we're confident that we're on a path to sustainable growth into the next decade. Obviously, we have more work to do. But I would just point you to a few proof points that I think support that.

First of all, as we talked about, in the last 18 months, we've made meaningful progress in our cardiovascular pipeline. We have eight potential approvals between 2025 and 2030. Obviously, the centerpiece of that is sotatercept and what we're seeing from the STELLAR data, which really was just quite phenomenal. If you look at that, we expect those products are portfolio of opportunity on an un-risk-adjusted basis to be in excess of $10 billion as you approach the mid-2030s. We recently discussed the fact that even the business development deals we've done that brought in new assets apart from KEYTRUDA, apart from Lynparza, Lenvima and WELIREG that themselves these new mechanisms I would point you to things like Orion and Imago. Those products along with what we see in the ABC space as a portfolio we think themselves have the potential for $10 billion or more of revenue as you get into the early to mid-2030s. So today, we sit there with the expectation that we are starting to make meaningful progress and that excludes all the work we're doing to bring an incremental value to patients on KEYTRUDA.

And obviously, as great as KEYTRUDA is, it still only has an overall response rate averaging around 30%. We need to deepen and drive better response. We're looking to do that through combinations and through other means to find ways to improve on KEYTRUDA. We're looking to continue to expand the new tumor types as well, and clearly, move into earlier lines of therapy where we believe we can start to move to a point that we can actually give people an extension of life, and hopefully, someday you get to a point that we talk about cancer is a chronic disease and not a fatal disease. Obviously, you have more to do there, but that is the aspiration, and we have a lot of efforts underway to do that through what we're doing in IO-IO combinations, IO-ABC combinations with our subcutaneous offering.

And then obviously, we're very excited recently about the deal we did with Moderna for the personalized cancer vaccine, which is really a therapeutic that we think in combination with KEYTRUDA, while we're starting it first in Melanoma, obviously, we believe has the potential to move into broader tumors. So that in of itself gives us a lot of confidence and we're doing similar activities with Lynparza, with Lenvima, and then obviously, WELIREG is in its early days. So if you look at the total of that and I haven't even gotten into our vaccines portfolio and what we see is excitement there. We feel like we've made a lot of progress. We have more to do, but that's why you hear me talk more about how do we build the sustainable engine to drive growth well into the next decade. And that really should be a focus point, because I'm confident, if we do that well, the LOE of KEYTRUDA will take care of itself. So Dean?

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

Yes. So there was a question on our TIGIT program, KEYTRUDA plus TIGIT. Just to remind everyone, we have nine ongoing trials, we have five Phase 3s. In fact, just

recently in December, we opened up KeyVibe-10, which is Phase 3 and in early melanoma. In relationship to KeyVibe-003, which I think is the question, we added the TPS greater than 50% as an endpoint. These are event-driven. And as the event drive to specifically and clinically meaningful data, we'll announce it appropriately.

Q - Andrew Baum {BIO 1540495 <GO>}

Great.

A - Peter Dannenbaum {BIO 20569031 <GO>}

Thank you, Andrew. Next question please, Kelly.

Operator

Our next question comes from Evan Seigerman from BMO. Evan, your line is open.

Q - Evan Seigerman {BIO 18922817 <GO>}

Hi, guys. Thank you so much for taking the question. I would love to just talk to what might make MK-2870 a better TROP2 targeting ADC versus those that we've seen from Gilead and Astra and Daiichi? Also do you still believe that it's too difficult to combine an ADC plus IO in a fixed-dose combination? Thank you.

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

Yes. So let me just state, I -- we'll be starting a whole series of Phase 3 trials this year. I really appreciate your question. For me, the critical thing is whether it be an ADC or whether it be a RAF inhibitor, in solid tumors, especially as you want to advance in solid tumors where IO has been important, the combination benefit of the two becomes really important. So we're very excited to be pushing for our TROP2-ADC. I can get into the details of the molecules and the linkers and the payloads and the DARs, but really the better sort of thing is, I believe that this year we will be presenting our Phase 2 studies.

And at the end of the day, that'll be the most convincing data to provide to you as to why we think we have an important play with our TROP2-ADC, but it's also the play of that TROP2-ADC in relationship to adding it to an IO agent. We think that is an important considerations when thinking about any cancer-killing mechanism in solid tumors.

A - Peter Dannenbaum {BIO 20569031 <GO>}

Great. Thank you, Evan. Next question please, Kelly.

Operator

Our next question comes from Louise Chen from Cantor. Louise, your line is open.

Q - Louise Chen {BIO 6990156 <GO>}

Hi, thanks for taking my question here. So I wanted to know how you're thinking about your Phase 3 trial design for your oral PCSK9? And how will that design really highlight the competitive advantages of your product? Thank you.

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

Thank you very much. So first, I don't want to get ahead too much of our March 6 Investor Meeting where we'll showing the data that we have in relationship to the oral PCSK9 and sotatercept. I will just sort of emphasize what we're trying to accomplish, and what we're trying to accomplish is we are trying to accomplish the most potent LDL lowering oral pill for lowering cholesterol. There should be no coaching, there should be very little need to interact with the healthcare system, which makes it reach very easy and very accessible, not just in the U.S, but globally. And we need to do it at a price point of what I would call a branded oral medicine would be in order to maximize the access.

In relationship to Phase 3, there's a general sort of view of how that is. One is you would drive it because LDL lowering is such a clean biomarker, so that's something. But one would also have to, at the same time, drive towards outcomes, which is also going to be important. So our Phase 3 trial design is informed by what the history of the field has been and what the FDA's regulatory sort of outlines have been for others.

A - Peter Dannenbaum {BIO 20569031 <GO>}

Great. Thank you, Louise. Next question please, Kelly.

Operator

Our next question comes from Tim Anderson from Wolfe Research. Tim, your line is open.

Q - Tim Anderson {BIO 3271630 <GO>}

Thank you. If I could ask you a question on V940, the cancer vaccine. What tumor types outside of melanoma do you already have any positive human data and even if those are earlier stage? And if you don't have any human data in non-melanoma tumor types, can you talk about animal data? I'm trying to obviously think about what Phase 3 trials you may be starting in 2023 with that product? Thank you.

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

Thank you very much. So you're speaking about the wonderful partnership that we have with Moderna in the personalized cancer vaccine. I just want to preface everything. What we've released is top-line data in melanoma. That data will be presented sometime in the near term where we present the data that we have for melanoma. And we have work to do to move that into Phase 3. So I -- we have a lot of work to do just in melanoma. I'm not going to speak ahead of what human data we have outside of that, but I would say two things that are really important. One is, one can watch which of the tumors have sensitivity to an immune approach and one

can watch about the clinical development with KEYTRUDA to sort of map out where you would think about doing that.

The second issue that I would emphasize is that when we're talking about an IO-IO strategy, which often people speak about. I view this personalized neoantigen therapy as an IO-IO strategy with KEYTRUDA. And the reason I want to emphasize that is, there is a view that we are beginning to develop that IO-IO strategies may be especially useful in early cancer stages, and you see that in our interest in our combination projects related to checkpoint inhibitors, but also in relationship to personalized neoantigen therapies. And so we think that, that around that we are going to advance and the critical component for us to be able to advance that is to advance KEYTRUDA as a monotherapy in those indications, because it creates a base for us to actually do these clinical trials.

A - Peter Dannenbaum {BIO 20569031 <GO>}

Great. Thank you, Tim. Next question please, Kelly?

Operator

Our next question comes from Geoff Meacham from Bank of America. Geoff, your line is open.

Q - Geoff Meacham {BIO 21252662 <GO>}

Great. Good morning, guys. Thanks for the question. Dean, on subcu KEYTRUDA, can you talk about the cadence of data this year? And what you're ultimately looking for from a risk benefit perspective as you evaluate different technologies? And Rob, I wasn't sure where this program ranks and kind of your strategic priorities across IO? Thank you.

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

So thank you very much for that question. I think it's on we'll be -- when we talk about starting 10 to 15 Phase 3 clinical trials just in oncology, this subcu program is a critical component to that, and we will be starting those Phase 3s this year. What are we seeking to achieve? I've talked about the early cancer space. The early cancer space I think is really important just from a medical standpoint of where we can intact really the outcomes of patients, we can remarkably improve that.

If you're going to go in the early space, whether it's neoadjuvant or adjuvant, from my clinical training, working with lung cancer doctors and oncologist, our ability to limit the need for individuals to constantly come to infusion centers is very important, and we need to have the scientific innovation to do that. In doing that, we have to think carefully about how do we give as much optionality cu three weeks, cu six weeks in that subcu regimen, and that's what we're trying to drive to in our Phase 3 trials. Rob, did you want to answer anything else?

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

Well, I appreciate the question, Geoff. I think Dean covered it well. This is a very important part of our overall strategy as we think about moving the earlier lines of therapy and then to drive convenience and access for patients, which is -- it's very important. So it's meaningful and it's something we're going to pursue as fast as we can.

A - Peter Dannenbaum {BIO 20569031 <GO>}

Thanks, Geoff. Next question please, Kelly.

Operator

Next question comes from Mohit Bansal from Wells Fargo. Mohit, your line is open.

Q - Mohit Bansal {BIO 18070890 <GO>}

Great. Thank you very much for taking my question. I think, I have a big particular question regarding IO-IO combinations and the development strategyies there. Because the common criticism is that many of these big Phase 3 studies were started with -- after less than robust Phase 2 data, and that's why they failed to show benefit in Phase 3. I mean, looking at your data in Phase 2, they are single-arm data as well. So can you just help us understand what gives you confidence that this is the right strategy to move forward? And wouldn't it be better to do some kind of Phase 2 trial where you are -- you have pembro as a control? Thank you.

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

Yes, thank you very much. I'll just emphasize that as a general rule, the way that I have begun to develop my view of IO-IO strategies is that IO-IO strategies are very important to pursue. I think that IO-IO strategies plus other therapies that kill cancers may be especially important in the metastatic. But IO-IO strategies in the early stage could be quite impactful. And so as I've just said, we have advanced our IO-IO strategy. We've advanced it with TGIT, CTLA4 and LAG3, so another component part that I would just say is, I don't know that there's one single addition to KEYTRUDA that will have as -- the breadth of KEYTRUDA.

So we've been a little bit selective there. And I think the movement of IO-IO not just in the metastatic space, but especially in the early space will become important. And the ability to do that requires your first IO of that IO-IO to be approved in the early space. And that is why we are so excited about moving into early spaces with KEYTRUDA, because that allows us to execute in an IO-IO strategy in early-stage cancer.

A - Peter Dannenbaum {BIO 20569031 <GO>}

Thanks, Mohit. Next question please, Kelly.

Operator

Our next question comes from Chris Schott from JPMorgan. Chris, your line is open.

Q - Chris Schott {BIO 6299911 <GO>}

Great. Thanks very much. I think you mentioned that you're looking to review share repo and it does -- it seem like maybe Rob some of your recent business development commentary has been skewed towards smaller deals or collaborations. So can you just put into context what you view as an appropriate level of leverage for Merck? And should we be thinking about kind of cash generation beyond that level as maybe going towards repo going forward? And I think just slipping in really quick second one. Just help me on FX, I think you're talking about 2% headwind, most of your peers aren't seeing much given the recent weakening of the dollar. Just are there any currencies that stand out we should be keeping in mind there? Thanks so much.

A - Caroline Litchfield {BIO 20934609 <GO>}

So Chris, this is Caroline. First to talk to share repurchase. As we've stated previously, it's our goal as a company to deploy our cash first and foremost behind the business opportunities we have within the company, as well as augment that with business development. We have turned on the share repurchase program given the strength of our business and our balance sheet. But we'll be ensuring we have ample capacity to pursue business development, which is the higher priority and is a better generator of growth and value creation.

We have a portfolio of CDs that we are reviewing, and we will continue to do so and hope to have news that we'll be sharing in the future. So priority remains CD, invest in the business, but to the extent there is excess cash, we will return that to shareholders through the share buybacks. We will maintain an appropriate leverage for our company. We are very comfortable operating at the credit rating we are at, and would expect to sustain that kind of level as we go forward.

From a foreign exchange perspective, in 2022, we were extremely successful as a company in blunting the impact of foreign exchange with our revenue hedging program. The underlying impact of foreign exchange to our business in 2022 was approximately 6% on the top line, 10% on the bottom line. But with our effective hedging program, which brought revenue on the other revenue line of approximately $800 million that blunted the impact to 4% on the top and 4% on the bottom.

As you rightly note, as we look at 2023, we expect the underlying impact of foreign exchange will be around 1 percentage point on the top and the bottom line. What is impacting the guidance that we've given is we obviously don't expect as significant hedge gains in 2023, which means that the overall impact from foreign exchange year-over-over is expected to be 2% on the top and 4% on the bottom.

A - Peter Dannenbaum {BIO 20569031 <GO>}

Great. Thank you, Chris. Next question please, Kelly.

Operator

Our next question comes from Terence Flynn from Morgan Stanley. Terence, your line is open.

Q - Terence Flynn {BIO 15030404 <GO>}

Great. Thanks so much for taking the questions. I know you guys typically don't give product-level guidance, Caroline. But I was wondering if you can speak at a high level about your vaccine franchise this year? Obviously, you have new capacity coming on for GARDASIL, but you also talked about the pediatric opportunity for VAXNEUVANCE. So just wondering how we should think about those this year? And then one follow-up for Dean on sotatercept. I know you're talking to the FDA now. Are you still confident that that single trial will be sufficient for approval or is there a possibility you could need data from the other ongoing studies? Thank you.

A - Caroline Litchfield {BIO 20934609 <GO>}

Thank you for this questions. So the guidance that we've provided for 2023 is underpinned by very strong revenue growth of 7% to 10% when you exclude the impact of LAGEVRIO and foreign exchange. The drivers of that growth are our key pillars of oncology where we expect continued impacts of patients and growth, given the portfolio of indications we have in KEYTRUDA, Lynparza and Lenvima. Vaccines, as you rightly note, driven by an acceleration expected in the growth of GARDASIL as we have new supply coming online, as well as an acceleration in our VAXNEUVANCE performance, especially given the strong data we have for the pediatric setting.

And we expect continued growth, strong growth in our animal health business. There's some headwinds against that, that we talked about with LAGEVRIO, with foreign exchange and with an increased level of pricing expected, especially in Europe, due to changes to B tax scheme in UK and not in Germany. But overall, very confident in the underlying growth of our business and good to oncology vaccines and animal health.

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

Yes. So again, March 6 clinical trial data for sotatercept will be more fully discussed. I think it will be very impactful data and I have no indication at this point that we will need a readout from any other trial from a clinical standpoint to support our filing to the FDA for sotatercept.

A - Peter Dannenbaum {BIO 20569031 <GO>}

Thank you, Terrance. Next question please, Kelly.

Operator

Our next question comes from Colin Bristow of UBS. Colin, your line is open.

Q - Colin Bristow {BIO 17216671 <GO>}

Hey, good morning and thanks for taking the questions. I guess, I'll piggyback on a couple of the others. On TIGIT we've obviously seen some competitive data recently, and then we have some Phase 3 competitor read out this year. Just what is your level of enthusiasm this class currently, and just what underpins that in terms of the data we've seen? And then just second on GARDASIL. Are you able to give any more granularity on the timing and levels of additional supply that will be coming online with respect to new manufacturing facility? Thank you.

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

Yes. Well, thank you for that question. In relationship to TIGIT, I mean, we're very confident on our molecule, as I've said, we have nine ongoing five Phase 3 trials, pushing the boundaries of what pembro can do or PD-1 can do with another IO agent has been something that's very important for the field. And the way that I can simply answer your question about the confidence in the molecule is, we just opened an additional KeyVibe study, a Phase 3 study in the earlier stages of cancer for this IO-IO combination.

A - Caroline Litchfield {BIO 20934609 <GO>}

And for GARDASIL, we as you know have driven productivity in the existing manufacturing facilities we have, and we have two new facilities coming online over the course of '23, '24. So it will be a progressive ramp. But I'll reiterate we're expecting an acceleration in our growth during 2023.

A - Peter Dannenbaum {BIO 20569031 <GO>}

Great. Thank you, Colin. Next question please, Kelly.

Operator

Our next question comes from Umer Raffat from Evercore. Umer, your line is open.

Q - Umer Raffat {BIO 16743519 <GO>}

Hi, guys. Thank for taking my question. There's a story in New York Times last week, which mentions Merck has a patent estate of 180 patents on KEYTRUDA. And I'm curious since your 10-K only points to the earliest patent expiry date of 2028, can you speak to the types of patents encompassed in this 180 patent estate? And is it reasonable to assume that your true patent estate on KEYTRUDA goes well past 2035? Thank you.

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

Yes, so I would just want to elevate the question a little bit. The focus of what we're trying to do is, we're trying to drive the concept of inhibition of checkpoint inhibitors can really have a profound effect throughout cancers in all stages and all tumor types. We can't talk about expand into different tissue types and stages, deepen in combination and extend with routes of delivery, routes of administration and frequency. And these innovations are critically important to make sure that this life-saving sort of treatment is available and we are confident in those innovations of

providing benefit to patients and we have filed, where appropriate, intellectual property for that.

A - Peter Dannenbaum {BIO 20569031 <GO>}

Thank you, Umer. Last question please, Kelly.

Operator

Our last question comes from Steve Scala from Cowen. Steve, you line is open.

Q - Steve Scala {BIO 1505201 <GO>}

Thank you. Novartis said yesterday that it believes the treatment of cardiovascular disease is moving towards infrequently administered injectables as opposed to orals citing very poor compliance with orals. They probably have a good point because the Merck PCSK9 could be associated with GI issues and other issues, which may make oral delivery a challenge. So I assume you disagree is that because indeed your oral PCSK9 is very well tolerated and clean or do you disagree for other reasons? Thank you.

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

We'll be talking about the detailed data from the PCSK9. We believe that it's very clean. But I'll just step back. As a cardiologist who trained in late 80s and 1990s, the ability to have an oral drug that lowered LDL cholesterol was impactful for the world. Yes, every oral drug regardless of what therapy it is, has a compliance, sort of it's very important to maintain compliance. What we're trying to do is to create the most LDL cholesterol lowering pill ever made that does not require constant interactions with the healthcare system. We think that, that access is actually one that's very important, not just in the U.S., but also globally. And this is personally speaking as someone who practiced as early -- as recently as five years ago. If I had an oral PCSK9 LDL lowering pill back then, I would be prescribing it with the other three to four oral pills that I'm prescribing an individual.

A - Peter Dannenbaum {BIO 20569031 <GO>}

Thank you, Steve. And thank you everybody for your thoughtful questions. Please follow-up with me and the IR team if you have anything additional, and we look forward to staying in touch. Take care.

Operator

That concludes today's call. Thank you for participating. You may disconnect at this time.