Q4 2018 Earnings Call

Company Participants

- Frank K. Clyburn, Executive Vice President, Chief Commercial Officer
- Kenneth C. Frazier, Chairman & Chief Executive Officer
- Robert M. Davis, Executive Vice President-Global Services & Chief Financial Officer
- Roger M. Perlmutter, Executive Vice President & President-Merck Research Laboratories
- Teri Loxam, Senior Vice President-Investor Relations & Global Communications

Other Participants

- Alex Arfaei, Analyst, BMO Capital Markets (United States)
- Andrew S. Baum, Analyst, Citigroup Global Markets Ltd.
- Christopher Schott, Analyst, JPMorgan Securities LLC
- David R. Risinger, Analyst, Morgan Stanley & Co. LLC
- Geoffrey Meacham, Analyst, Barclays Capital, Inc.
- Jason M. Gerberry, Analyst, Bank of America Merrill Lynch
- Seamus Fernandez, Analyst, Guggenheim Securities LLC
- Steve Scala, Analyst, Cowen & Co. LLC
- Tim Anderson, Analyst, Wolfe Research LLC
- Umer Raffat, Analyst, Evercore ISI
- Vamil K. Divan, Analyst, Credit Suisse Securities (USA) LLC

MANAGEMENT DISCUSSION SECTION

Operator

Good morning. My name is Darla, and I will be your conference operator today. At this time, I would like to welcome everyone to Merck's Fourth Quarter 2018 Sales and Earnings Conference Call. All lines have been placed on mute to prevent any background noise. After the speakers' remarks, there will be a question-and-answer session.

Thank you. I would now like to turn the call over to Teri Loxam, SVP, Investor Relations and Global Communications. Please go ahead.

Teri Loxam {BIO 17997503 <GO>}

Thank you, Darla, and good morning. Welcome to Merck's fourth quarter and full year 2018 conference call. Today, I'm joined by Ken Frazier, our Chairman and Chief Executive Officer; Rob Davis, our Chief Financial Officer; and Dr. Roger Perlmutter, President of Merck Research Labs who will each have prepared remarks. In addition, I am joined by Mike Nally, our new Chief Marketing Officer; and Frank Clyburn, our new Chief Commercial Officer who will both be available for the Q&A portion of the call.

Before I turn the call over to Ken, I'd like to point out a few items. You'll 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 of these in our press release. We have also provided a table in our press release to help you understand the sales in the quarter for the business units and products.

I would like to remind you that some of the statements that we make during today's call 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 2017 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. You can see our SEC filing as well as today's earnings release on merck.com.

Finally, similar to last quarter we have posted a presentation to the Investor section of merck.com which highlights some of our financials from the quarter and the year. With that, I'd like to turn the call over to Ken.

Kenneth C. Frazier {BIO 1391636 <GO>}

Thank you, Teri. Good morning and thank you all for joining the call. In 2018, Merck distinguished itself through its strong performance across its businesses. Perhaps most significantly, our full year results demonstrate that our strategy to be the premier research-intensive biopharmaceutical company is working. The investments we've made in R&D over the past several years and our commercial execution have culminated in the highest top and bottom line growth the company has seen in years, and we expect our momentum to carry over into 2019.

At its core, Merck is a science-driven organization motivated by a quest to improve human and animal health. We've spent the last several years reinvigorating our labs; investing in three new research centers in South San Francisco; Cambridge, Massachusetts; and London; and refocusing our efforts on creating truly differentiated medicines that help solve big health problems for now and the future. This unwavering commitment to science and innovation enables us to retain the best

talent in the industry to drive our strategic priorities and to continuously enhance our pipeline of medically significant treatments and vaccines.

Our clinical and commercial execution in the IO space has further separated KEYTRUDA from its competition, and our leadership in oncology is further bolstered by the growth prospects for Lynparza and Lenvima. GARDASIL is not only driving meaningful growth for the company after a decade on the market but is also instilling optimism around the world that this vaccine could help prevent and maybe eliminate certain HPV-related cancers. We are confident in our broad portfolio of market-leading products and our diversified high-potential pipeline which includes significant innovations in oncology, vaccines, and other specialty and hospital care along with a robust industry-leading Animal Health business. In fact, Merck has one of the broadest and most promising pipelines we've had over the past two decades. In summary, we're excited by our progress, our pipeline, and our future. We are energized by the work that we do and, most importantly, by our ability to help patients around the world while also creating sustainable long-term growth and strong shareholder returns.

Before I turn the call over to Rob, I'm pleased to announce that we will be hosting an investor event on June 20 during which we will provide an update on our strategic progress and outline how Merck will continue to deliver innovative science and create value for all of our stakeholders. We'll be back to you with the details on location and other logistics, but we ask that you save the date. Now, I'd like to turn it over to Rob for more color on our financial and operational performance. Rob?

Robert M. Davis {BIO 6955931 <GO>}

Thanks, Ken, and good morning everyone. Please note that my comments today will be on a non-GAAP basis. Our results in 2018 reflect strong execution across our key growth pillars, focused investment in our pipeline, and disciplined expense management. We achieved meaningful top and bottom line growth and we also executed important business development transactions, initiated and expanded capital expenditure programs to increase our manufacturing capacity, and returned additional value to shareholders through increased dividends and share repurchases. We believe our company is well-positioned to achieve future growth. And as our 2019 guidance shows, we expect the recent momentum in our business to continue as we execute on our growth pillars and invest in R&D while remaining disciplined in our allocation of resources.

Turning to our fourth quarter results, total company revenues were $11 billion, an increase of 8% year-over-year excluding exchange with strong growth in both our Human Health and Animal Health businesses. Human Health revenues increased 8% ex exchange to $9.8 billion led by key products in our oncology, vaccines, and hospital and specialty businesses. In oncology, KEYTRUDA's sales exceeded $2.1 billion this quarter, extending the unprecedented launch of this foundational therapy and solidifying Merck as the clear market leader in renal oncology with continued strong future growth prospects. Global growth was primarily driven by higher use in first-line non-small cell lung cancer, and utilization remains strong across the breadth of our indications including melanoma, head and neck, bladder, and MSI-high

cancers. We're seeing strong uptake in squamous non-small cell lung cancer in the U.S. where a good portion of newly diagnosed patients are now receiving either KEYTRUDA as monotherapy or in combination with chemotherapy following the approval of KEYNOTE-407 in October. In total, in the U.S. we now have 15 approved indications and are approved in 10 different tumor types overall plus a pan tumor approval in MSI-high patients.

In ex U.S. markets, first-line lung is the key driver of growth mostly due to further uptake of our monotherapy indication and PD-L1 high expressers following reimbursement approvals around the world. In Europe, we're off to a great start launching the chemo combo in non-squamous patients following approval of KEYNOTE-189 last September. We are already seeing adoption in select markets such as Germany where reimbursement begins upon approval and we will be working through the reimbursement process in other major European markets throughout this year. Growth in Japan remains robust and we're very pleased with the recent approval of five new indications across lung, adjuvant melanoma, and MSI-high cancers. Finally, in September we launched KEYTRUDA in metastatic melanoma in China which will be an important market for the brand going forward as we pursue additional indications. Overall, we remain very confident in the long-term growth potential for KEYTRUDA based on increased utilization and currently approved indications and our expectation of additional approvals worldwide.

We also remain very encouraged by the progress and potential of both Lynparza and Lenvima in partnership with AstraZeneca and Eisai respectively. Lynparza growth this quarter was driven by continued uptake in ovarian and breast cancers as well as launches in new markets such as Japan and China. In the United States, across all tumors Lynparza leads the PARP inhibitor class with over 50% total patient share. We're excited by the earlier than expected U.S. approval of SOLO-1 and look forward to bringing this treatment to more women with ovarian cancer. Growth for Lenvima reflected strong performance in hepatocellular cancer following recent launches in the U.S., Europe, and more recently China. Performance in Japan remains strong with Lenvima being used in a vast majority of hepatocellular patients.

Turning to vaccines, we have a significant and innovative portfolio. Our vaccines business reflected strong worldwide demand for GARDASIL which achieved sales of over $800 million this quarter. Health systems worldwide continue to support increased immunization with GARDASIL with the goal of reducing the incidence of certain HPV-related cancers. Growth this quarter was driven by strong uptake from our recent launch in China as well as increased demand in Europe given the move towards more gender-neutral vaccination programs. Sales of GARDASIL also grew in the U.S., mostly reflecting the difference in quarterly phasing of public sector purchases last year.

Our hospital and specialty business was led by BRIDION where growth in the U.S. reflects continued strong demand. BRIDION sales approached $1 billion for the year and we remain confident in the potential for additional future growth.

Looking now at our Animal Health business, we again saw strong growth this quarter with revenues increasing 11% to $1 billion excluding exchange. Growth was driven by our broad portfolio of inline and newly launched products with companion animal products growing 16% and livestock sales growing 8%, both excluding exchange. Companion animal growth was driven by sales of vaccines, while livestock benefited from increased sales of swine and poultry products. Animal Health segment profits were $387 million in the fourth quarter, an increase of 16% excluding exchange compared to the prior year. Our Animal Health business continues to perform well and we view it as a key pillar of Merck's future growth. We continue to invest in new product development and launches and recently announced the acquisition of Antelliq which will establish Merck as a leader in animal identification and monitoring, one of the fastest-growing parts of the animal health industry.

Turning to the rest of our P&L, gross margin was 75% in the quarter. The increase of 70 basis points versus the fourth quarter of 2017 was largely due to the favorable impacts of product mix this year and manufacturing variances related to the cyberattack that negatively impacted last year. This increase was partially offset by other headwinds such as lower prices and catch-up amortization of sales milestones, primarily related to the earlier than expected approval of SOLO-1.

Operating expenses of $4.8 billion increased 1% year-over-year, including a favorable 1 percentage point impact from foreign exchange. Investments in our oncology and vaccines clinical development portfolios as well as our discovery efforts drove the increase in R&D, while SG&A remained relatively flat. Our tax rate of 22.5% for the quarter was 720 basis points higher year-over-year, reflecting a true-up of our full year tax rate due to our mix of earnings. Taken together, we delivered earnings of $1.04 per share, an increase of 11% excluding exchange.

Now, let's turn to our outlook for 2019. We remain confident in both our near and long-term prospects for revenue growth notwithstanding expected headwinds from price, foreign exchange, and pressures on our mature and LOE products. For 2019, we expect full year revenue of $43.2 billion to $44.7 billion, which represents 2% to 6% growth driven by strength in our key growth pillars across oncology, vaccines, hospital and specialty as well as Animal Health. This range assumes an approximately 1 percentage point negative impact from foreign exchange using mid-January rates.

We expect our gross margin to be roughly flat year-over-year. As we previously communicated, we believe tailwinds, including improved product mix, will generally be offset by headwinds including lower prices, royalty payments, fluctuations in FX, and the continued amortization and collaboration milestones.

We expect our operating expenses to increase year-over-year at a low to mid-single-digit rate with continued disciplined management of SG&A allowing for a meaningful further investment in R&D to capitalize on our pipeline opportunities. We expect our tax rate to be between 18.5% and 19.5% for the full year. We project average diluted shares outstanding to be approximately 2.58 billion for 2019. Taken together, we expect EPS to be between $4.57 and $4.72 including an approximately 1

percentage point positive impact from foreign exchange at mid-January rates. This would represent approximately 5% to 9% bottom line growth.

Before concluding, it's worth mentioning that our 2019 EPS guidance assumes that our other income and expense line will be roughly zero in 2019. Due to an accounting standard implemented in 2018, we now recognize unrealized gains and losses related to our investments in equity securities into other income and expense.

Based on current market conditions for our investment portfolio, we have assumed a negative impact from our equity investments in OIE in our guidance. We also expect higher net interest expense given our cash and debt balances and given current interest rates. Market movements clearly create additional volatility as we move through the year, and we will continue to give you updates as we move forward.

In summary, we delivered strong performance in 2018. While 2019 continues to be another important investment year for R&D, we expect the operational momentum across our growth pillars combined with disciplined resource allocation to deliver another year of meaningful top and bottom line growth as well as operating leverage. Longer-term, we remain confident in our ability to drive strong sales growth and meaningful operating margin expansion. Our dedication to innovation and continued execution allow us to sustainably deliver for the patients we serve and, in turn, creates significant shareholder value.

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

Roger M. Perlmutter {BIO 3077183 <GO>}

Thanks, Rob. As outlined in our press release, the fourth quarter was an especially productive period for Merck Research Laboratories, marking the climax of what was an extremely busy year. Beginning first with KEYTRUDA, during the fourth quarter we obtained three new indications in the United States, first for the first-line treatment for patients with metastatic squamous non-small cell lung cancer in combination with carboplatin and either paclitaxel or nab-paclitaxel based upon the results of the KEYNOTE-407 trial; second, for the second-line treatment of hepatocellular carcinoma in patients who have previously been treated with sorafenib; and third, for the treatment of adult and pediatric patients with recurrent locally advanced or metastatic Merkel cell carcinoma, a rare skin cancer.

Separately, and based on the results of our KEYNOTE-054 study, which was conducted with the European Organization for Research and Treatment of Cancer, the European Commission approved KEYTRUDA for the adjuvant treatment of stage III melanoma with lymph node involvement in patients who have undergone successful tumor resection. Meanwhile in Japan, we obtained five new KEYTRUDA approvals at the end of December, including the first approval based on our KEYNOTE-042 trial for KEYTRUDA monotherapy in patients with non-small cell lung cancer whose tumors contain greater than or equal to 1% of malignant cells expressing the PD-L1 biomarker. Data from KEYNOTE-042 are also under review in

the EU and in the United States where submission of additional data resulted in an extension of the PDUFA date by three months to April 11 of this year.

Our other cancer programs also advanced meaningfully in the fourth quarter. In collaboration with our colleagues at AstraZeneca, we gained FDA approval for Lynparza as maintenance treatment for patients with advanced ovarian, fallopian tube or primary peritoneal cancer who experienced complete or partial response to first-line platinum-based therapy and whose tumors contain deleterious or suspected deleterious germline or somatic mutations in BRCA1 or BRCA2 gene. This approval is based on data presented last fall at the European Society for Medical Oncology meetings from the SOLO-1 trial.

We continue to see very positive results across our oncology portfolio including the success of our KEYNOTE-181 trial testing KEYTRUDA monotherapy in the second-line treatment of advanced or metastatic esophageal or gastroesophageal junction carcinoma with a 31% reduction in the risk of death as compared to traditional chemotherapy in patients whose tumors express the PD-L1 biomarker with a combined proportion score of greater than or equal to 10. This is the first demonstration of an improvement in the overall survival in esophageal gastric malignancy through immunotherapy. Data from the study were presented at the ASCO GI meeting in January and has been submitted for regulatory review.

During the fourth quarter, we also announced the results of our KEYNOTE-426 trial combining KEYTRUDA with Pfizer's axitinib in the first-line treatment of renal cell cancer as compared with sorafenib treatment. Data from this study in which improvements in overall survival, progression-free survival, and overall response rate were demonstrated have also been submitted for regulatory review.

Progress has been made in other disease categories as well. For example, the FDA granted priority review with a PDUFA date of July 16 for our novel anti-microbial agent MK-7655A which combines a new chemical entity, relebactam, with imipenem, thus blocking the activity of the bacterially expressed β-lactamase that would otherwise inactivate imipenem. This represents an important advance in the struggle to control antibiotic resistance. We're also active on the business development front joining with colleagues at NGM Biopharmaceuticals to advance MK-3655, a highly selective Phase 2 monoclonal antibody directed against the FGF receptor 1c β-Klotho receptor complex for the potential treatment of non-alcoholic steatohepatitis.

Our vaccine programs also progressed during the fourth quarter. At the end of the quarter, for example, we announced a collaboration with Instituto Butantan on the development of vaccines to protect against dengue virus infection. Instituto Butantan is currently conducting a Phase 3 study in Brazil with their vaccine candidate while our own related dengue virus vaccine showed promise in an earlier Phase 1 study. Finally, we commenced a rolling BLA submission for V920, our investigational vaccine designed to protect against infection with the Zaire strain of Ebola virus. We continue to provide tens of thousands of doses of this vaccine to the World Health Organization to assist in the battle to contain an Ebola outbreak in the Democratic Republic of the Congo. We hope that through the important work of

governmental and non-governmental agencies and in part as a result of our V920 vaccine that it will be possible to bring this very serious Ebola outbreak under control in the near future.

Now, my colleagues and I will take your questions.

Teri Loxam {BIO 17997503 <GO>}

Thanks, Roger. Darla, we will get started on questions. I just wanted to remind everyone to try and keep their questions to a maximum of one to two so we can get as many people on the call as possible. So with that, we'll turn it over to questions.

Q&A

Operator

Your first question is from Seamus Fernandez with Guggenheim.

Q - Seamus Fernandez {BIO 7525186 <GO>}

Thanks very much for the question. So my first question is for Ken and my second is for Frank and Roger. Ken, can you just help us understand the core areas of focus for potential M&A or business development to bolster the Merck pipeline, and maybe if you could just kind of give us a general sense of areas of interest and perhaps even the range? Obviously, lots of questions around the current mega cap M&A that's occurred in recent days. And then for Frank and Roger, can you just maybe each of you kind of characterize the key opportunities near and longer-term to sustain or perhaps even accelerate the KEYTRUDA opportunity? We're seeing amazing growth in that franchise but, again, we're just trying to get a sense of the key new opportunities, whether it be kidney cancer as a core opportunity or perhaps somewhat longer-term in the adjuvant setting. Thanks so much.

A - Kenneth C. Frazier {BIO 1391636 <GO>}

Thanks, Seamus. Let me start by saying, again, that business development remains an important priority for us. First and foremost, we look for those scientific innovations that we believe will enhance our pipeline because we believe that's what's important ultimately to drive long-term growth and value for shareholders. In that regard, we don't try to pre-determine what therapeutic areas are best. We want to find the best science and match it up to the best opportunities to help people, and that's how we go about it. And I'll remind you that we were very active last year in BD. We did about 60 transactions spanning licensing and technology deals, clinical collaborations. We did the collaboration with Eisai, we did the acquisition of Viralytics which expands our early immuno-oncology pipeline, we did the Antelliq acquisition. So again, I think what we want to do given our strong balance sheet is to actively look across the entire spectrum of assets across therapeutic areas to create the strongest portfolio. I'll close by saying we continue as we've said for years to want to focus on the kinds of deals that we can add with minimum disruption to our

ongoing scientific efforts, so we have not really been focusing primarily on the large mega mergers that you referred to.

A - Teri Loxam {BIO 17997503 <GO>}

And Roger, why don't you start on the second question around KEYTRUDA key opportunities and we can turn it over to Frank for the commercial portion?

A - Roger M. Perlmutter {BIO 3077183 <GO>}

Right. Seamus, thanks for the question. First of all, I think it's important from a context point of view, and you know this, that we're still at an early point in the development of KEYTRUDA. So keep in mind that it's just a little over four years since the first indication was obtained in the United States in 2014, and in that sense the indications are still rolling out. KEYTRUDA as I've said and as you know is the first truly broad-spectrum antineoplastic agent introduced into clinical practice with 15 indications and more coming, and many of those indications have not yet been broadened around the world, and Frank will have a chance to talk about that. So there's a great deal of opportunity to do good in helping patients around the world.

But beyond that, we've continued to work on a strategy in which we first demonstrate activity with monotherapy in different tumor types. And the monotherapy studies are essentially complete – we have a few more studies coming through – but then move forward in combination studies while simultaneously advancing from salvage therapy, third-line, second-line to first-line, adjuvant, neoadjuvant, and all of those studies are going on. And we are expanding into new areas and, in addition, in combination with other agents, both those that have already been introduced into practice, into renal cell carcinoma, and in addition our own pipeline. So there's just a huge set of opportunities.

Looking forward, I think, as I mentioned, the data that we presented in esophageal gastric cancer in January at ASCO GI and the renal cell data which will be presented in mid-February from the KEYNOTE-426 study are special highlights, but there are going to be a lot of presentations coming forward. There's a lot of new data coming up and we'll have a chance to talk about some of that, for example, in advance at ASCO. It's early days but a lot of expansion opportunities. And Frank, I think you can talk about that.

A - Frank K. Clyburn {BIO 20654315 <GO>}

Seamus, good morning. And to echo Roger's point, we have actually a very early stage launch going on and I just wanted to reiterate especially outside the U.S. for lung cancer. We're right now launching KEYNOTE-189 and we're just in the early stages of that launch. So if you look at our ex-U.S. growth, in fact this quarter ex-U.S. growth was over 86% and that just shows the early progress that we're making not only with our monotherapy but early on with our combination in lung. In addition, we have a number of other opportunities. You heard us announce the approvals in Japan. We're very excited about the opportunity that we have in China with our second-line melanoma indication, and we have a broad program that we are building in China. In addition to that, we have significant opportunities as you've heard from Roger with regards to our renal cell carcinoma data that we're looking

forward to presenting, KEYNOTE-426, at ASCO GU. We're also excited about triple-negative breast cancer. We presented our data now for KEYNOTE-048 for head and neck cancer with first-line chemo combination, gastric cancer and others. So we're very excited about our current indications and expanding those around the world as well as the significant amount of data readouts that are going to be coming in the future that we think will provide very significant growth not only this year but in the long run.

A - Teri Loxam {BIO 17997503 <GO>}

Great. Thanks for the questions, Seamus. Darla, we'll move on to the next one, please.

Operator

It's from the line of Steve Scala with Cowen.

Q - Steve Scala {BIO 1505201 <GO>}

Thank you. A couple questions. Ken, I was interested in your comment that Merck has one of the most broad pipelines in the past two decades, and this is quite a statement given Merck's rich research history. What are we missing externally that Merck sees internally, and will June 20 be the opportunity for us to learn a lot more about the pipeline? And secondly, Merck's pneumococcal vaccine I believe received breakthrough designation in children but not adults. Is this an issue of timing or did FDA deliberately not grant the 15-valent product breakthrough in adults? Thank you.

A - Kenneth C. Frazier {BIO 1391636 <GO>}

So thank you for your question, Steve. I continue to believe that Merck's longer-term revenue growth prospects are underappreciated in large part because people don't see the pipeline the way we do, so let me try to answer your question. So we see tremendous future growth not only in KEYTRUDA, Lynparza, and Lenvima but we have behind it a formidable internal pipeline of assets in oncology – over 20 unique mechanisms. In the vaccine world, we think the GARDASIL opportunity is really significant going forward, but behind that are opportunities in next-generation pneumococcal, RSV, CMV, dengue, and other areas of lung that we look forward to.

As we also look beyond that, we just announced positive Phase 3 data for ZERBAXA, our antibiotic for hospital-acquired ventilator-acquired pneumonia which we believe to be very a sizable opportunity to go with our leading portfolio of hospital products including BRIDION. The Afferent compound which we acquired a couple years ago is now being studied in a Phase 3 in chronic cough (30:09) Bio collaboration is just another example of that, not to mention great novel assets in HIV and neuroscience. So to answer your question, I actually look forward to the June opportunity for us to talk about what it is that we see in our pipeline. I will say that we are genuinely excited. We see the opportunities for us to invest across a broad area. And again, we look forward to speaking to you in more detail on June 20.

A - Roger M. Perlmutter {BIO 3077183 <GO>}

Right. This is Roger. With respect to the breakthrough destination, yes, we did receive breakthrough designation in pediatrics for the V114 pneumococcal conjugate vaccine, and the reason was because of the very meaningful clinical data that we obtained demonstrating the balanced response across all 15 serotypes represented in that vaccine. We have very strong data in the adult segment as well, and it's really a matter of timing with respect to how we interact with the agency. Just to remind you, breakthrough designation provides a mechanism whereby you can have more frequent consultation interaction with the agency on late stage trials, and keep in mind that V114 is already in eight Phase 3 studies that will be reading out this year or next year. So there's already a very substantial head of steam on this program.

A - Teri Loxam {BIO 17997503 <GO>}

Great. Thank you. We'll move on to the next question please, Darla.

Operator

It's from Andrew Baum with Citi.

Q - Andrew S. Baum {BIO 1540495 <GO>}

Many thanks. A couple of questions please. Some of the industry lobbies has championed net pricing given the announcements last night. So Frank and Ken, could you talk to the Merck assessment of the proposal, particularly probably if it goes through, how you see the risks as well as the potential positives and the spillover in terms of the commercial book of business when? And then secondly to Roger, I note that you recently initiated a trial of olaparib in tissue-agnostic setting with HRR mutated tumors who are resistant to refractory or gold standard treatment. The question is, number one, is that trial fileable given the advanced nature of the patients? And number two, the size of that patient population depending on what biomarker you use could be very substantial. Could you talk to how large that population may be in a percentage of addressable relapsed/refractory patients? Many thanks.

A - Kenneth C. Frazier {BIO 1391636 <GO>}

Thank you, Andrew. Let me start with your first question about the HHS rebate proposal. Let me start by saying we share the administration's goal of lowering out-of-pocket cost for patients. That's critical for patients, it's critical for our business. As you know, unfortunately the current pharmaceutical supply chain includes various misaligned incentives that serves to support middleman while often neglecting patients. We are evaluating the specific proposal released by the administration late yesterday and we're hopeful that it will achieve this shared goal of ensuring patients have affordable access to innovative medicines.

A - Roger M. Perlmutter {BIO 3077183 <GO>}

Yeah. And Andrew, I think you were asking a question – we're having a little bit of trouble hearing you here, but you were asking a question about a Lynparza study which was a tissue-agnostic study. And again, this is part of the broader rollout of our Lynparza analysis because what we found with Lynparza, as I think everyone

recognizes is that the breadth of activity of Lynparza is greater than we expected. First of all, any DNA repair, a variety of DNA repair defects, defects in the molecule's recombination, seem to sensitize cells through Lynparza. But even in cell types in which those defects are not recognizable, there's evidence, accumulating evidence that we're seeing clinical responses. So we're beginning to think of Lynparza having much broader activity, and that's particularly the case when we look at Lynparza in combination with KEYTRUDA and other agents. So you can expect to see broader studies of Lynparza in a variety of different settings both outside of the hormone responsive tumors and as well in combination with other agents. I hope that helps.

A - Teri Loxam {BIO 17997503 <GO>}

Great. Thanks, Andrew. We'll move on to the question please, Darla.

Operator

Your next question is from Chris Schott with JPMorgan.

Q - Christopher Schott {BIO 6299911 <GO>}

Great. Thanks very much for the questions. My first question was just on longer-term margin expansion and just expenses in general. I guess as we think about the low to mid-single-digit OpEx growth in 2019, is that a reasonable growth rate to think about on a go-forward basis for Merck or should we think about spending starting to moderate as we look out to 2020 and beyond? I know in general there's been a lot of discussion around kind of the magnitude of operating margin expansion, so any color on that front would be helpful. And my second question was just – is focusing a little bit more on the launch dynamics in first-line lung, specifically in the U.S. I guess, can you just give us a sense of where we are at this point in terms of share of new starts? And are there any additional areas for growth within the lung market and I guess where you must focus on from a commercial standpoint as we think about just that indication playing through in the U.S.? Thanks very much.

A - Teri Loxam {BIO 17997503 <GO>}

Thanks, Chris. So let's start with Rob.

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

Yeah. Thanks, Chris. And to your question on long-term margin expansion, so as I said in the prepared remarks, we continue to believe we will see meaningful operating margin expansion as we go forward. But as we've been talking about, given the fact that we have such a wealth of opportunity right now in R&D, you start with KEYTRUDA and look at just what this drug could be and how unprecedented it is, we want to make sure we're investing fully behind that as well as with Lynparza and Lenvima. Those programs are now in full swing, not to mention our vaccines program. So as we've indicated, we do think you're going to see sales growth continue. And with that, you're going to see R&D grow in the near-term faster than sales over the next couple of years as we really get to the bolus of that with R&D slowing down to a rate slower than sales thereafter, and SG&A will continue to be managed very tightly.

It's nice to see frankly that even despite the fact that we're making meaningful investments in R&D in 2019, we're actually going to see operating margin expansion in 2019. So that actually is really I think a result of what we've done from disciplined expense management across the organization to make sure we can put back all of our resources into the important programs in R&D. But as we've talked about, we do have a long-term margin expansion. It will be driven mainly by operating expense moderating versus sales. We do continue to believe SG&A will be managed very tightly. And then you'll see R&D slow down after we get out of the next couple of years. So that's really what we're driving.

A - Teri Loxam {BIO 17997503 <GO>}

Great. Thanks, Rob. Frank, we'll have you comment on the first-line lung market.

A - Frank K. Clyburn {BIO 20654315 <GO>}

Chris, we are seeing significant share of newly diagnosed first-line non-squamous non-small cell lung cancer patients that do not have an abnormal EGF or ALK gene. Based off of KEYNOTE-189, we've seen that penetration very rapidly in the majority of the segments in the non-squamous non-small cell lung cancer setting. We do have room for further penetration in particular in the PD-L1 patient population in the U.S., and that's where the team is focused. And also, we are seeing very rapid uptake with our KEYNOTE-407 approval the end of October, and we're penetrating the squamous cell carcinoma patient also very significantly. So I think in the U.S., I would say it's really in the PD-L1-negative population where there's opportunity for further growth in the non-squamous patients.

I would highlight outside the U.S., and just to reiterate, that we're very early on in the launch outside the U.S. in lung cancer. In fact, most of our growth outside the U.S. is primarily being driven off of the PD-L1 high express patient population on KEYNOTE-024. So we're just rolling out our chemo combinations around the world and anticipate significant growth outside the U.S. in lung.

A - Teri Loxam {BIO 17997503 <GO>}

Great. Thanks for your questions, Chris. We'll move on to the next caller, please.

Operator

It's from David Risinger with Morgan Stanley.

Q - David R. Risinger {BIO 1504228 <GO>}

Thanks very much. So I just wanted to go back to the margin opportunities beyond 2019. It seems like Merck is increasingly becoming more of a specialty-focused company. And to that end, many specialty biopharma companies can generate higher margins simply because they don't need the primary care infrastructure and the other costs associated with a much broader portfolio. And so could you discuss opportunities to further streamline Merck's cost structure in future years as you continue to pivot the company? And then second, with respect to the data on February 16, the abstracts are coming out on Monday, February 11, at 5 pm. So will we

see the key data in the abstract release or will we really have to wait for the data on February 16? Thank you.

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

All right. Dave, thanks for the question. Maybe I'll take the first part and then Roger can take the second part. So as you look at the profile of the business given the mix of our portfolio, you are correct that as we go forward we continue to believe that there is an opportunity to shift as we move to the more specialty-focused business to continue to optimize the resources we have around primary care. I think the important point though is this isn't a new thing for us. In fact, when we pointed this out in the past we've actually been able to grow on EPS basis through the years even when we didn't have sales growth. At the same time, we were standing up an oncology franchise from scratch and investing meaningfully into R&D. And so we did that because we have already started really harvesting some of the primary care resources we have in the marketplace primarily through selling forces. We've been reducing selling forces over the last several years to be able to do that. And there's opportunity for us to continue to do that going forward, that's why we do believe that we're going to continue to see SG&A get better as a percentage of sales despite the fact that we're already at an industry best-in-class position with the fact that we still have the primary care resources in place, although less than they used to be. So that is an opportunity that's out there and we're going to be driving it over the next couple of years as we move forward. So that is something you should look for as we go forward.

I think the thing that's important to note is while we're getting the favorable impact from mix obviously given the strong volume growth and margin you get from positive mix, we do have the headwinds at the gross margin line that we've talked about that's going to cause gross margin to be roughly flat. So the operating margin expansion we're going to see will come from that SG&A leveraging we're talking about as well as the R&D I mentioned earlier.

A - Teri Loxam {BIO 17997503 <GO>}

Roger, you want to comment on...?

A - Roger M. Perlmutter {BIO 3077183 <GO>}

Right. And David, you're referring on February 16 to the renal cell carcinoma data from KEYNOTE-426. Of course, February 16 is also the PDUFA date for the KEYNOTE-054 study in adjuvant melanoma, but I think you're referring to the KEYNOTE-426 data. And the complete data of course will be presented then. There will be an abstract that appears beforehand. The abstract has some data and, depending on what you view as key, there's some material in it. We're eager to gain publication also of the complete analysis just as soon as we can. So there will be various different parts of the data coming out, but the main presentation on February 16 is the part that I would focus on.

A - Teri Loxam {BIO 17997503 <GO>}

Thanks for your questions, Dave. Darla, we'll move on to the next caller, please.

Operator

It's from Umer Raffat with Evercore ISI.

Q - Umer Raffat {BIO 16743519 <GO>}

Good morning. Thanks so much for taking my questions. First, perhaps Roger, I feel like there's a trial which hasn't come up very much at all on Merck conversations which is your stage 3 lung trial, KEYNOTE-799. And it's my understanding that it's a first-line trial within stage 3 which would potentially position KEYTRUDA before the current label for IMFINZI. However, what I noticed with your slide today it calls it a second-line trial. So I just wanted to clarify that, A. And B, on the pneumococcal vaccine side I know there's a couple of Pfizer patents which you guys have prosecuted in the past and now appealing. And my question is as it stands currently and let's say the appeal doesn't go favorably, do you have the freedom to operate? Thank you very much.

A - Roger M. Perlmutter {BIO 3077183 <GO>}

Okay. With respect to KEYNOTE-799 just to provide a higher altitude context for this, from the very beginning our concern with respect to administering KEYTRUDA in the setting of radiotherapy has been pneumonitis. And we know that from a variety of different studies previously that we had come to associate proximity of radiotherapy with KEYTRUDA administration with more inflammation in the lung. So KEYNOTE-799 has an important safety component which is the administration of KEYTRUDA in combination with chemotherapy plus radiotherapy in different cohorts. But the question of whether or not pneumonitis exceeds 10%, that's really an important issue. The actual study population is a population that has undergone resection but is not widely disseminated – sorry, let me get this right. The actual population is a population of individuals who have lung cancer that is radio-responsive, potentially radio-responsive, and who can receive that in a first-line environment because they won't have received prior systemic chemotherapy. So that was your question.

A - Kenneth C. Frazier {BIO 1391636 <GO>}

And your question with respect to V114, let me say that we continue to believe that we will have freedom to operate in that space. And recently, the IPR ruling from the PTAB was in our favor on a number of the patents that we have challenged, so we'll see what goes on as we move forward.

A - Teri Loxam {BIO 17997503 <GO>}

Great. Thanks. We'll move on to the next question, please.

Operator

It's from Tim Anderson with Wolfe Research.

Q - Tim Anderson {BIO 3271630 <GO>}

Thank you. A couple of questions. Going back to the very first line of questioning on your pipeline and then the perception by investors of late-stage enemies that tends to run on the thin side, here you and Bristol potentially share a common thread which is all the heavy spending in IO has maybe crowded out other R&D programs. So the question I had in this context is something that we asked you maybe about a year ago. When is R&D spending on KEYTRUDA going to peak? About a year ago you suggested that wasn't very far off qualitatively, but it was never quite clear to me what that meant, and I know with all the combination programs maybe it doesn't peak any time soon. So that's the first question.

Second question is just on your triple-negative breast adjuvant trial. Update on timing of seeing those results and how would you characterize the riskiness of that trial in terms of achieving a positive readout. Would you say it's low or medium or high risk?

A - Teri Loxam {BIO 17997503 <GO>}

Sure. Let's start with Rob to talk about the cost first.

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

Yeah. Good morning, Tim. With R&D, so if you look at what's driving the bulk of our clinical spend right now, it is still KEYTRUDA but it's actually now more combination studies than it is monotherapy studies. A lot of the monotherapy clinical studies are already starting to peak and come off. So really right now, what's driving it is the combination studies and then in addition to that, importantly, the investments in Lynparza and Lenvima will be peaking over the next couple of years, too. So if you look at total R&D, it is being driven by those, and then obviously our vaccines programs are contributing as well. So those are the major categories and we do think though the bolus of KEYTRUDA-related studies and the broader Lynparza and Lenvima studies will peak in the next couple of years. So when we've been talking about that threshold happening, it's really those programs that are driving that change where we do think you'll see R&D slow down as we move forward. Obviously, though, the good news from a long-term perspective is Roger keeps turning over new positive thing, so we always have to moderate as we have opportunity to invest. But the good news is we have a great pipeline, we're investing behind it, and we're going to invest fully. You should see it peak in the next couple of years.

A - Teri Loxam {BIO 17997503 <GO>}

Great. And Roger, you want to address the second question?

A - Roger M. Perlmutter {BIO 3077183 <GO>}

Right. I believe, Tim, you're referring to the KEYNOTE-522 study which is a neoadjuvant study, and we did have the opportunity to see early data from the KEYNOTE-522 study. We had the chance to share those data with the agency and we and they agree that it is important to get additional data with a longer term follow-up, so that's what we're waiting for that study. And once we have those data

available we'll have a chance to look at it more carefully and then of course share with you.

A - Teri Loxam {BIO 17997503 <GO>}

Great. Thanks for your questions, Tim. We'll move on to the next question.

Operator

It's from Vamil Divan with Credit Suisse.

Q - Vamil K. Divan {BIO 15748296 <GO>}

Hi, great. Thanks so much for taking my questions. So, one, appreciate the color you gave on the lung cancer side and the commercial uptick there. I'm just trying to understand the adjuvant melanoma and also the front-line renal indications. Obviously, we need to see the full data on the labels. Was there anything specific or unique with those two indications that may make the uptake faster or slower than what we've seen so far in lung cancer? And then the second one just going back to the topic of drug pricing. If you can just share what you're assuming in terms of net pricing growth in the U.S. in 2019 for your guidance. And also sort of related to that question, in terms of KEYTRUDA if you can just sort of share your net pricing assumptions U.S., Europe, and also China would be very helpful. Thanks.

A - Teri Loxam {BIO 17997503 <GO>}

So let's start with Frank on the adjuvant mel and RCC and maybe you can just comment broadly on pricing for KEYTRUDA before we turn it over to Rob for the other pricing question.

A - Frank K. Clyburn {BIO 20654315 <GO>}

Vamil, in adjuvant mel we mentioned we're actually just starting approval in Europe for adjuvant melanoma. We do think this is a good opportunity for us. We have established a very strong foothold in metastatic melanoma so we think this is a good opportunity to expand into adjuvant melanoma. As Roger mentioned, we're waiting on our PDUFA date for adjuvant melanoma in the U.S. and we think we will be competitive there as well.

With regards to RCC, we're excited about the opportunity. The study was done across all risk groups and we're looking forward to sharing the data in the next several weeks, but we think that this will be a very important opportunity in RCC upon approval.

As far as KEYTRUDA goes with regards to pricing, we don't give out specific guidance from a pricing perspective. But in the ex-U.S. markets, we're seeing very strong reimbursement for KEYTRUDA based off of the very strong value proposition that we have, and we feel as though we're positioned very well from a reimbursement perspective outside the U.S. And then, in the U.S., we also feel as

though we're positioned very well with regards to reimbursement, especially because KEYTRUDA is reimbursed in Part B currently.

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

Good morning, Vamil. To your question on the guidance, while our guidance range does assume multiple scenarios, we don't require any additional pricing in the United States to meet our guidance range.

A - Teri Loxam {BIO 17997503 <GO>}

Great. And we're going to try to squeeze in a few more questions here. I know we're getting closer to the top of the hour. Next question please, Darla.

Operator

It's from Jason Gerberry with Bank of America.

Q - Jason M. Gerberry {BIO 17237298 <GO>}

Hey. Good morning and thanks for taking my question. Maybe just, Frank, just a follow-up on a couple of Vamil's questions here. So in adjuvant melanoma, just curious. In lung, you enjoy a first-mover advantage. In adjuvant melanoma, Bristol already has roughly 70% share. So just kind of curious how you think you can make inroads if you think the first-mover advantage is really that important or if you think you can actually capture share. And then my second question just on front-line renal. In the U.S., and maybe you're drawing from your experience in other tumor settings, are payers mandating that they'll only reimburse the specific studied combinations? And the reason I ask is I'm wondering if there's an advantage at all in terms of how these different TKI combinations will be used. Will physicians ultimately migrate to using different TKIs which they're more familiar with or more commonly used or if there's going to be a winner takes all with potentially the study that gets there first with TKI? Thanks.

A - Frank K. Clyburn {BIO 20654315 <GO>}

Yeah. So all things being equal, you would like to be first in most of the indications. However, we have experienced in several cancer types where we were not first. So I'll point you to bladder where we actually launched fifth in the U.S. and we now have the leading market share in bladder cancer, and really it was because of the strong data with KEYNOTE-045 and the overall survival benefits. So really, the oncologists are going to look first and foremost to the data and we feel as though KEYNOTE-054 has a very strong dataset and we feel as though we'll be competitive.

The other thing I would also say is that in the community especially in the U.S. because of the breadth of our program and because of the use in lung cancer, in head and neck, and now in gastric and other cancer types, we feel as though the community is very familiar with using KEYTRUDA. They're giving us very strong feedback on the profile of KEYTRUDA, and we think that's going to help us not only in adjuvant mel but also being second in renal cell carcinoma. And then the last one I'll mention on renal cell carcinoma is when we share the data in the next several

weeks, we feel as though, as Roger has highlighted, we've top line having overall survival benefit, progression-free survival benefit, and strong response rates. So usually the oncologists will make a choice based off of the data they see and we're looking forward to, upon approval, competing in RCC.

A - Teri Loxam {BIO 17997503 <GO>}

Great. Let's move on to the next question, please.

Operator

It's from Alex Arfaei with BMO Capital Markets.

Q - Alex Arfaei {BIO 15433937 <GO>}

Great. Thank you and good morning [Technical Difficulty] (55:02) and Roger, could you please provide your thoughts or comments on KEYTRUDA lifecycle planning? Obviously, after JANUVIA's upcoming LOE you'll be more dependent on KEYTRUDA. I realize we're a few years away, but given your valuation and potential size of this product it does become an important investment consideration. And then for Frank, could you please provide your estimates of KEYTRUDA sales by indication in both U.S. and ex-U.S.? Thank you.

A - Kenneth C. Frazier {BIO 1391636 <GO>}

So the first question about KEYTRUDA, so obviously KEYTRUDA has been a winning franchise, obviously, for us and an important growth driver across all the opportunities that we have both as a monotherapy as well as a combination. But we continue to stress the fact that as we look at our future, we don't see ourselves as just a KEYTRUDA story. So I emphasized before the other pillars of growth including Lynparza and Lenvima in oncology, what comes after that with 20 unique mechanisms; the vaccines programs that we have; ZERBAXA; BRIDION; (56:10) the Afferent compound. We continue to think that even when we see an important drug like JANUVIA go off patent that Merck will have multiple sources of growth going forward. And then of course, it's really important to recognize that in addition to our internal pipeline we're continuing to seek to augment that pipeline with value creating, innovative external assets to business development. So we feel very confident about our ability to drive sustained revenue growth going forward, recognizing that a major patent expiration is coming.

A - Teri Loxam {BIO 17997503 <GO>}

Great. And we'll turn it over to Frank next.

A - Frank K. Clyburn {BIO 20654315 <GO>}

So in the U.S., and this is very directional data due to the claims data lagging several months behind, but approximately 65% to 70% of our use is non-small cell lung cancer, melanoma represents about 10%, head and neck is approximately 5%, bladder approximately 5%. And then we also are seeing good growth in the MSI-high agnostic indication that represents about 5% of our business, and then the all

other category or other indications represents about 10%. Outside the U.S., it's really hard to give specific breakdowns, but the majority of our use right now is in lung cancer.

A - Teri Loxam {BIO 17997503 <GO>}

Great. Thanks, Frank. So we're going to (57:28) get to our last question.

Operator

It's from Geoff Meacham with Barclays.

Q - Geoffrey Meacham {BIO 21252662 <GO>}

Good morning, guys. Thanks for the question. Frank, I want to get a bit more detail about the OUS dynamics for KEYTRUDA in lung. You guys saw good trends in 4Q but I wasn't sure if we're already at an inflection point based on the cadence of reimbursement. Maybe just it'd be helpful to go through how you see the pace of share gains in Europe in lung over the balance of the year. And then Roger, at a higher level how are you guys thinking about the balance of therapeutic areas in the pipeline? I mean, obviously you want to press your advantage in oncology, but is expanding other existing categories is a strategic priority or is there capacity for new a therapeutic category? Thank you.

A - Teri Loxam {BIO 17997503 <GO>}

Let's start with Frank.

A - Frank K. Clyburn {BIO 20654315 <GO>}

Sure. So in Europe, I'll give an example. So right now, we have reimbursement in most of the European Union for KEYNOTE-024, and that's where you're seeing a lot of the growth on our monotherapy indication. With KEYNOTE-189, we have reimbursement in Germany, Austria, and Netherlands and a couple of other markets, But we're very early on in getting an uptake for KEYNOTE-189 broadly in Europe, and I anticipate that will come throughout the year. Very similar ramp to what we saw back when we launched KEYNOTE-024, so think of that as the timing you should be thinking about for that ramp. In addition to that, as mentioned Japan we think is a very significant opportunity now with not only the approval of KEYNOTE-189 but KEYNOTE-407 and also KEYNOTE-042, so we think Japan provides a very good opportunity outside the U.S. And then as mentioned, we're in the very early stages in China with just our first launch in second-line melanoma, so we see also outside the US significant opportunities for growth there.

A - Roger M. Perlmutter {BIO 3077183 <GO>}

Yeah, and this is Roger. If I might, I'd say also today the CHMP announced that they adopted a positive opinion with respect to KEYNOTE-407 in Europe.

A - Frank K. Clyburn {BIO 20654315 <GO>}

Yeah.

A - Roger M. Perlmutter {BIO 3077183 <GO>}

And with that, of course reimbursement will be required. In most markets it will take some time, but it's going to advance that still further. In terms of balance of therapeutic areas, Geoff, certainly my interest is in having the greatest possible impact on improving and extending human life wherever we see that, and so we're not going to be bound to any particular therapeutic area. If you look at the kinds of things that we're doing, look at the work that's taking place in HIV right now. MK-8591 is an extraordinary molecule. We've got Phase 2 data in combination with doravirine. We hope we'll have an opportunity to present those data probably sometime around the middle of the year. And this is really a remarkable compound in terms of its potency, the durability of the treatment effect, and it changes the landscape in a lot of ways in terms of how you think about HIV treatment. That's a therapeutic area which doesn't get an enormous amount of attention externally but which we're putting a lot of effort into just as we're putting a lot of effort into other areas in infectious diseases. So there's a lot of work going on.

A - Teri Loxam {BIO 17997503 <GO>}

Great. Thanks.

A - Kenneth C. Frazier {BIO 1391636 <GO>}

So let me close by thanking you for joining us. We had a strong 2018. We're confident going forward in our execution, in our pipeline, and our future. We believe that we're well-positioned to drive sustained revenue growth. And we also expect meaningful operating margin expansion over time, and that's largely the result of a differentiated pipeline that we believe will actually position Merck well going forward. So thank you.

A - Teri Loxam {BIO 17997503 <GO>}

That'll conclude our call. Thank you, Darla. Thanks everyone.

Operator

Thank you. This concludes the Merck Fourth Quarter 2018 Sales and Warnings Conference Call. You may now disconnect.