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PRESENTATION

Operator

Good afternoon. Welcome, ladies and gentlemen, to AstraZeneca's Q3 results analyst conference call.

Before I hand over the call to AstraZeneca, I'd like to read the Safe Harbor statement. The Company intends to utilize the Safe Harbor provisions of the United States Private Securities Litigation Reform Act of 1995. Participants on this call may make forward-looking statements with respect to the operations and financial performance of AstraZeneca. Although we believe our expectations are based on reasonable assumptions, by their very nature, forward-looking statements involve risks and uncertainties that may influence the factors that could cause actual results to differ materially. Any forward-looking statements made on this call reflect the knowledge and information available at the time of this call. The Company undertakes no obligation to update forward-looking statements.

I will now hand the call over to Mr. Pascal Soriot.

Pascal Soriot - AstraZeneca PLC - CEO

Hello, everyone. I'm Pascal Soriot, CEO of AstraZeneca. Welcome to the year-to-date and the third-quarter 2016 results conference call and webcast for investors and analysts. The presentation is also posted online for you to download. We plan to spend about half an hour on the presentation and then leave plenty of time for Q&A. In total, we have a full hour together.

(Caller instructions)

Please turn to Slide 2. This is the usual Safe Harbor statement.

Moving to Slide 3. This is the agenda. Today I'm joined by Mark Mallon, Executive Vice President for Global Product and Portfolio Strategy, Medical Affairs and Corporate Affairs. Today marks a special welcome to Mark Mallon, who recently took over the strategic marketing function from Luke Miels, who is now responsible for the European business. Mark Mallon was previously Head of International. Also with me here today, Marc Dunoyer, our CFO, and Sean Bohan, Executive Vice President for Global Medicines Development and our Chief Medical Officer.



Moving to Slide 4. The third quarter of 2016 continued broadly in line with our expectations and we are on track for the year. The total revenue decline reflected the loss of exclusivity for Crestor and quarterly US Symbicort impact on gross-to-net adjustments, the lack of FluMist sales, and one-off events in emerging markets. Mark Mallon will cover this in detail later.

The new AstraZeneca, which is -- which are the three main therapy areas and established medicines in emerging markets, grew 6% in the year to date. Tagrisso became our biggest lung cancer medicine during Q3, larger than Iressa. And Farxiga continues as the global leader in the SGLT2 class, with 42% volume share, taking the number one spot among AstraZeneca medicines in diabetes overall.

Strong execution continues in the emerging markets. We are a solid number two in China where we're growing the fastest and then we are much ahead of the market. In Russia, we are number three overall.

EPS is supported by active cost measurement and also benefited from a non-recurring intergovernment tax agreement. We saw our R&D investments fully stabilizing despite continued investment in the strong pipeline. SG&A costs further reduced, in line with our commitment. Given the tailwinds and headwinds in the quarter, we maintain full-year 2016 guidance.

Finally, as we strive towards building a more sustainable business, I'm pleased that AstraZeneca was recognized as a Dow Jones sustainability leader in the Pharmaceuticals/Biotechnology/Life Sciences industry group. This is an area of our Company, which is often overlooked.

Moving to Slide 5. The pipeline continued its progress in Q3 with a number of examples of what science can do. In Oncology, Faslodex achieved Japanese submission for first-line receptor-positive metastatic breast cancer based on the FALCON trial. Lynparza SOLO-2 trial read out very positively in second-line treatment of advanced ovarian cancer and we are looking forward to presenting the data as soon as possible.

Tagrisso saw its regulatory submission in lung cancer accepted in China, where it was also granted priority review. We decided to withdraw the EU regulatory submission for cediranib in ovarian cancer and we didn't make the primary endpoint in the Phase III trial for selumetinib in KRAS-mutated lung cancer.

In Cardiovascular & Metabolic Diseases, Brilinta was approved in Japan but did not meet the primary endpoint of showing superiority to standard of care for clopidogrel for peripheral artery disease. The open combination of Farxiga and Bydureon was shown to be superior in Phase III compared to each of the monotherapies. And we also saw acceptance in the US, as promised, for the re-submission of ZS-9, our new potential medicine for hyperkalaemia. We're looking forward to swift review by the FDA.

In Respiratory, Benralizumab delivered its fourth positive Phase III efficacy trial in severe and controlled asthma. We'll make a regulatory submission for Benralizumab this quarter. Benralizumab is expected to become an important medicine for patients with asthma and potentially COPD as well as an important medicine for our business, broadening and deepening our offering in the respiratory market.

Finally, together with our partner, Eli Lilly, we obtained a Fast Track Designation for the BACE inhibitor in Alzheimer's disease. While early in Phase III development, the BACE inhibitor is an excellent example of the improved R&D productivity, which also makes us confident about the forthcoming inflection point for our strategy as well as we annualize -- sorry, the loss of Crestor exclusivity.

Please turn to Slide 6. Staying on loss of Crestor exclusivity, this chart illustrates how our Company is rapidly changing from a pipeline-driven strategic transformation and focused on three main therapy areas. Year to date, we saw a large impact from losing Crestor exclusivity in the US and we are also still seeing some impact from Nexium and Seroquel.

Further, we are also moving beyond the US CDC's recommendation to not use FluMist this season, for example. And as you can see, the impact of these patent expiries has been ongoing for a number of years now. As we annualize the negative impacts, our focus on three main therapy areas, Oncology, Cardiovascular and Metabolic Diseases and Respiratory will help us return to growth.



Oncology is growing rapidly through the launches of Lynparza and Tagrisso, with more to come from the pipeline. Also, other medicines like Faslodex are doing well. CVMD benefits from global growth of Brilinta and our type 2 diabetes franchise, in particular, Farxiga. Brilinta will soon approach \$1 billion annual blockbuster sales on a moving basis.

Respiratory was impacted in the quarter but is a growth platform with a combination of marketed and pipeline medicines like Benralizumab. When we add this all up, including established medicines in the emerging markets, we grew 6% product sales in the year to date and 3% in the quarter. The underlying quarterly growth rate, though, was actually 6% when you adjust for the items mentioned earlier.

It's important to realize that the emerging new AstraZeneca is a growing business in competitive markets, with existing medicines and pipeline to sustain the growth into the future, and that 6% year-to-date growth is achieved without the full impact of the launch of new products that are emerging out of our pipeline. We are in the early phase of those new launches, so we really look forward to a strong growth rate in the years to come.

Before I hand over to Mark Mallon for the growth platforms, I would like to thank all of my colleagues for their contribution during Q3 and 2016 so far. We have lots of talented people that work incredibly hard on returning our Company to sustainable growth. With this, over to you, Mark.

Mark Mallon - AstraZeneca PLC - EVP of Global Product and Portfolio Strategy, Medical Affairs and Corporate Affairs

Thanks, Pascal. Please turn to Slide 8. Our growth platforms continued to demonstrate strong growth in the year, despite a softer Q3. The combined revenue from our six growth platforms represented over 60% of our total revenue.

Momentum was clearly seen in diabetes, Brilinta, and importantly, in new oncology. For the first time, new oncology sales reached almost a \$0.5 billion, which is very exciting.

Please turn to Slide 9. Now, with the performance in diabetes, Japan and Brilinta continuing to be resilient, I will only touch on these growth platforms briefly. Instead, we'll focus today on the emerging markets, respiratory and new oncology.

Please turn to Slide 10. Turning next to emerging markets, we remain on track with our long-term goals despite a softer Q3. Underlying quarterly growth was kept at high single digits, adjusting for an adverse impact from healthcare spending cuts in Saudi Arabia and the reduction of our activities in Venezuela.

China maintained double-digit growth of 10% and around 15% if you adjust for Plendil, which was partnered. This was ahead of the overall Chinese market, and also Russia and Brazil continue to grow well at 13% and 5%, respectively, in the year to date. We are well-positioned to maintain growth in the near term with our established portfolio in emerging markets and the growth platforms.

Trends of better diagnosis, improved access and favorable patient dynamics bode especially well for our medicines in diabetes and respiratory. Please also note we have recently completed our regulatory submission for Tagrisso in China, which has the largest patient population of EGFR-mutated non-small cell lung cancers in the world.

Please turn to Slide 11. Our respiratory performance in the year to date was short of long-term expectations and reflected the impact of deliberate strategic decisions we took to sustain Symbicort's strong position in asthma and COPD markets and also to prepare for the launch of the exciting medicines, Bevespi and Benralizumab.

In the year to date, our respiratory sales declined by 2%, including decreases in the US and Europe of 11% and 7%, respectively. The underlying reasons I will talk about on a medicine by medicine basis. In contrast, emerging markets experienced growth of 17%.

In the year to date, Symbicort continued to grow volume share. However, sales were down 10%, reflecting developments in the US market and an adverse event impact from healthcare spending cuts in Saudi Arabia.

In the US, Symbicort volume growth was offset by a true-up related to past quarters and managed care access gains. These gains came despite the very competitive market. Improved access in the US will provide a platform not only for Symbicort but also for future launches of Bevespi and Benralizumab.

In Europe, Symbicort maintained its leadership in ICS/LABA market while facing continued pressure from both branded and analog competition.

In emerging markets, we maintained leadership in the overall respiratory market and our sales grew by 11%, with China growing by an impressive 33% and global sales of Pulmicort increased by 8%, driven by a 20% increase from emerging markets. Again, our China business for Pulmicort grew 21% during the period, where we continue in China to improve diagnosis, increase home nebulization, and overall treatment rates.

Please turn to Slide 12. Moving next to our diabetes franchise, sales grew 13% with a positive contribution from all regions. We believe the GLP-1 and SGLT-2 classes will continue to be the fastest growing in Type 2 diabetes, with all three major classes remaining highly competitive. Farxiga is the number one diabetes medicine in AstraZeneca now, with sales of \$220 million in the quarter and remains the global leader by volume in the SGLT-2 class and outgrowing the class.

Please turn to Slide 13. In Japan, we improved our performance in the third quarter despite a more than 6% mandated price cut earlier this year. We maintain a leading dynamic market share across our key existing therapeutic areas with Crestor, Nexium and Symbicort, all being leaders in their classes.

We're also very pleased with the strong launch of Tagrisso that leverages our existing oncology portfolio and infrastructure. We now have more than 2,400 patients on treatment and sales of \$43 million in the year to date. Our diagnostics partner insists -- anticipates an approval for blood-based testing in due course.

Please turn to Slide 14. Brilinta, moving on to Brilinta, we delivered 39% growth in the year to date. Q3 growth in the US was impacted by inventory stocking in the comparative period. We saw continued progress in Europe and in emerging markets, China continued to deliver strong performance and we are also optimistic for future growth, given the potential listing of Brilinta on the China National Reimbursement Drug List in due course.

Please turn to Slide 15. In just a few weeks, Tagrisso will be celebrating its one-year anniversary. Tagrisso today exceeds a \$0.25 billion in sales, which is reflective of successive launches in the US, in the EU and Japan. Tagrisso is now available to patients in more than 40 countries and we're expecting a China launch in 2017.

Tagrisso sales in the quarter rose, reflecting strong patient demand and successful commercial launches across multiple markets. The US availability of the blood-based test is very encouraging. And recently, the NCCN guidelines recommended T790 mutation testing for EGFR-mutated non-small cell lung cancer patients upon disease progression.

The current testing rates in the US are over 40% and with the new test, we're expecting improved patient access to Tagrisso. The performance of Lynparza also continued to be strong. As the leader in PARP inhibitors, we have now treated nearly 5,000 patients and launched in 30 countries, with seven ongoing reviews.

The BRCA testing rates continue to grow, with rates now close to 70% in the US and Europe. With the positive trial readout of SOLO-2, we remain even more confident of the benefits patients can derive from Lynparza.

Now I'll hand it over to you, Marc.

Marc Dunoyer - AstraZeneca PLC - CFO

Thanks, Mark, and hello, everyone. I'm going to spend the next few minutes taking you through our performance for the year to date. Please turn to Slide 17. This first slide in my presentation shows our reported P&L performance in the year to date and in the third quarter.

Please turn to Slide 18. Looking closely at the core P&L, the total revenue decline of 3% in the year to date, reflected a 6% fall in product sales with the effect of losing exclusivity on Crestor in the United States, particularly impacting the performance in the third quarter. External revenue increased by 56% to \$1.4 billion, ahead of the total we delivered in the whole of 2015. This is in line with the commitment I gave at the start of the year.

Core gross profit declined by 3% in the year to date and excluding the impact of externalization, the core gross profit margin declined by 90 basis points to 83%. Despite the impact of the loss of US Crestor, our mix of sales and the growing element of specialty care medicines meant that our core gross margin in the third quarter remained stable at 84%.

Core R&D cost growth was stable in the third quarter, a good performance after the growth seen in the first half of the year. I do, however, now expect full-year core R&D to be ahead of last year. Core SG&A fell by 12% in the third quarter, and a 7% reduction in the year to date.

I'm delighted that we will deliver on our commitment to materially reduce core SG&A cost this year. Other operating income in the year to date was significantly behind that in the comparative period. We have, however, a number of disposal agreements that have been either closed or expected to close in the fourth quarter. These agreements will take full year other operating income to around the level achieved in 2015.

The core EPS performance in the third quarter of 2016 included a non-recurring benefit of \$0.36, resulting from agreements on transfer pricing between various tax authorities. This benefit delivered a year-to-date gross tax rate of 8%, which implies a potential full-year rate significantly below the range of 16% to 20% that I've talked about previously.

Please turn to Slide 19. As I've said many times before, cost discipline is a key focus for the business and we have made very good progress in the year to date. We are doing what we said we'd do and we are delivering on our commitment, producing results in line with guidance.

Looking at R&D cost, the chart shows sequential declines over recent quarters, despite the absorption of ZS Pharma and Acerta Pharma. Excluding the absorption, the R&D cost would have only increased by 1% in the year-to-date. In the third quarter, total core R&D costs were stable, despite the continued focus on a number of potential medicines in pivotal trials. The investment in the pipeline remains an absolute priority for us.

Turning to core SG&A cost. Efficiency savings in sales and marketing operations and reduction in IT cost underpin the restructuring program outlined earlier this year. Our US business has made particular progress this year. Core SG&A cost, as a percentage of total revenue, fell to 35% in the year to date, more than 2 percentage points lower than the comparative period.

Please turn to Slide 20. To conclude, I want to reiterate the guidance for 2016, which is at constant exchange rates. We continue to expect a low to mid-single digit percentage decline in both total revenue and core EPS. I plan to provide guidance for 2017 within our full-year result announcement in February next year.

Finally, I want to reconfirm our capital allocation priorities. These are unchanged today. We continue to strike a balance between the interest of the business, our financial creditors, and our shareholders.

After providing for investment in the business, supporting the progressive dividend policy and maintaining our strong investment grade credit rating, we'll keep under review any potential investments in value enhancing and immediately earnings accretive opportunities.

Thank you for listening. And I will now hand over to Sean.

Sean Bohan - AstraZeneca PLC - EVP of Global Medicines Development and Chief Medical Officer

Thank you, Marc. Hello, everyone. Let's start by taking a look at the encouraging progress we have made with the pipeline since our last update.

Please turn to Slide 22. In the quarter, we made progress in oncology with a regulatory submission for Faslodex in Japan, to include the results in first-line treatment from the FALCON trial in the label. We completed the regulatory submission for Tagrisso in China and obtained a priority review



designation. China represents the largest market in terms of patient numbers for Tagrisso, due to the high prevalence of EGFR mutation in non-small cell lung cancer patients there.

We also saw a positive Phase III readout for Lynparza as a maintenance treatment in second-line platinum-sensitive relapsed BRCA-mutated ovarian cancer from SOLO-2. This trial showed significant progression-free survival benefit and provided additional evidence to support the use of Lynparza in this setting. On cediranib, we withdrew the regulatory submission in the EU based on questions raised by the EMA very late in the review process.

In cardiovascular and metabolic disease, we had a setback in EUCLID, with Brilinta not showing superiority over clopidogrel for peripheral artery disease based on a base composite cardiovascular endpoint consisting of cardiovascular death, non-fatal myocardial infarction and ischemic stroke. We are pleased, however, to report that we were able to move the ZS-9 program forward with an acceptance of the resubmission by the FDA. ZS-9 is now on track for regulatory decisions in the first half of 2017, both in the United States and in the EU.

The DURATION-8 trial combining Farxiga and Bydureon had a positive readout and showed improvement in hemoglobin A1c as well as lowered systolic blood pressure and weight loss versus each of the individual medicines. ZONDA also read out positively as the fourth Phase III efficacy trial, with Benralizumab for severe, uncontrolled asthma.

Finally, as Pascal mentioned earlier, we received Fast Track Designation from the FDA for the BACE inhibitor. As a reminder, the medicine is currently being tested in two Phase III trials in Alzheimer's patients.

Please turn to the next slide. Moving on to Tagrisso, we announced positive results for the AURA-3 trial in July and we're looking forward to sharing those data at the World Conference On Lung Cancer in December. Tagrisso can become the treatment of choice for all EGFR-mutation positive non-small cell lung cancer patients.

Key data readouts, such as the BLOOM and FLAURA trials in 2017, could help Tagrisso realize this ambition. As a reminder, BLOOM is a Phase I trial, evaluating the efficacy and safety of Tagrisso in patients with leptomeningeal disease. Unlike other tyrosine kinase inhibitors in the class, Tagrisso has the ability to cross the blood-brain barrier at therapeutic doses, which is proving more and more important. FLAURA is a Phase III trial in patients with first-line EGFR-mutated metastatic non-small cell lung cancer which, if positive, will enable use in this important setting.

Please turn to Slide 24. At ESMO, we presented updated safety and efficacy data on the Durvalumab monotherapy cohort from Study 1108 in non-small cell lung cancer, and head and neck cancer. These data points bode well for the ongoing Phase III trials with Durvalumab monotherapy as well as for the combination trials with Tremelimumab as they highlight Durvalumab as a highly active inhibitor of the PD1/ PD-L1 pathway.

In addition, we presented early data of Durvalumab, combined with a STAT3 inhibitor in multiple tumor types as well as the first OX40 inhibitor data in patients with advanced solid tumors. Activating OX40 boosts anti-tumor immunity by promoting the survival and proliferation of cancer fighting T-cells and could potentially become a third therapeutic intervention on top of PD-L1 and CTLA-4.

For Faslodex, we presented new data from the Phase III FALCON trial demonstrating superior median progression-free survival for Faslodex compared to anastrozole in the first-line treatment of post-menopausal women with locally advanced or metastatic breast cancer. As noted, we already achieved regulatory submission in Japan.

Lastly, a comparative analysis was presented of multiple diagnostic assays used to evaluate PD-L1 expression in head and neck squamous cell carcinoma on over 500 tumor samples. This head and neck comparative analysis is a complementary trial to a similar analysis on 500 non-small cell cancer tumor sample -- non-small cell -- lung cancer tumor samples presented at AACR, emphasizing our pioneering work in tumor biomarkers and assays comparisons.

Please turn to Slide 25. This slide illustrates the key Phase III data readouts that you should expect to see from our mono and combo immuno-oncology portfolio through 2018. And as you can see, the majority of these trials are fully recruited. As previously communicated, and in line with recent changes in the head and neck cancer competitive landscape, including the approval in the US for PD-1 monotherapy for second-line treatment, we are unlikely to make a regulatory submission for the HAWK trial.



HAWK, which is a single-arm, Phase II trial was originally designed as a potential fast-to-market opportunity and we expect to have data internally available during Q4. Last month, we confirmed that the FDA had placed a partial clinical hold on the enrollment of new patients with head and neck cancer in clinical trials of Durvalumab as monotherapy and in combination with Tremelimumab or other potential medicines.

All trials are continuing with currently enrolled patients. The partial clinical hold on new patient enrollment related only to head and neck cancer. Trials for Durvalumab in different cancer types as monotherapy or in combination with Tremelimumab or other potential medicines are progressing as planned, with pivotal data in lung cancer anticipated in the first half of 2017. We have submitted our analysis of the observed bleeding events to the FDA and we expect to hear back in the next fortnight.

Turning to MYSTIC, we remain fully confident in the trial design. Both progression-free survival and overall survival are primary endpoints that can demonstrate the benefit of treatment of our IO medicines. The MYSTIC trial could potentially provide a monotherapy label for Durvalumab, despite enrolling all comer patients and has the potential to analyze PD-L1 positive and PD-L1 negative tumors on a separate basis.

There is an option to amend the definition of PD-L1 positivity as long as the trial remains blinded with no analysis performed. In making this decision, there is flexibility to consider internal as well as external data. The MYSTIC trial enrolled over 1,100 patients with the last patient having commenced dosing in Q3. As you know, the first data on progression-free survival is expected during the first half of 2017, with data on overall survival expected in 2018 at the latest.

Please turn to Slide 27 -- I'm sorry, 26. Turning to diabetes. We recently saw promising data from a combination of Farxiga and Bydureon in the DURATION-8 trial. We saw decreased hemoglobin A1c levels in addition to a reduction in both weight and blood pressure compared to each medicine individually. These results on glycemic parameters and cardiovascular risk factors supported continued testing in patients with Type 2 diabetes who suffer from obesity, hypertension, and hyperlipidemia.

Additionally, we are investigating two new trials with Farxiga, looking at the long-term outcomes on CKD and CHF in patients with and without Type 2 diabetes. These two outcomes trials are in addition to the DECLARE outcomes trial for Farxiga that is fully recruited with data expected latest in 2019 as well as the EXSCEL outcomes trial for Bydureon, with data expected latest in 2018.

Please turn now to Slide 27. In respiratory, we recently presented the data from the SIROCCO and CALIMA Phase III clinical trials for Benralizumab at the ERS meeting. This data was also published in the Lancet. The data demonstrated the potential benefit of adding Benralizumab to standard of care therapy for patients with severe uncontrolled eosinophilic asthma.

We observed a reduction in exacerbation rates of up to 51% compared to placebo. There were also significant improvements in lung function and asthma symptoms, both key secondary endpoints. In terms of lung function, these improvements were observed after the first dose and sustained throughout the duration of therapy.

These results were obtained with once every eight-week dosing of Benralizumab, using a pre-filled syringe for subcutaneous injection, which may be more convenient for patients than other IL-5 options currently available. As previously mentioned, regulatory submissions in the US and EU are expected before the end of the year.

Finally, let me finish by highlighting two exciting and innovative first-in-class biologic medicines in our respiratory pipeline. First is Tralokinumab, an anti-IL13, currently in Phase III trials, for severe uncontrolled asthma. We expect top line data during the second half of 2017. And, Tezepelumab, an anti-TSLP, which is in Phase II development and is expected to read out with top line data in the first half of next year.

Please turn to Slide 28 for a look at our forthcoming news flow. Looking at the rest of the year news flow, we plan to submit Tagrisso's AURA3 trial and our partner, FibroGen, is expected to initiate the rolling submission process for roxadustat in anemia in China during this quarter. There is the potential for up to nine regulatory submissions next year.



In oncology, we expect the first IO submission of the Durva and Treme combo as well as life cycle opportunities for Lynparza and Faslodex. We also see the potential for a blood cancer submission for acalabrutinib based on Phase II data, with the standard caveat that this is a fast-to-market strategy ahead of randomized controlled trial data.

Next year, we also plan to submit a new auto injector device for Bydureon, to improve both the patient experience and the competitive positioning of the medicine. We are very pleased with the progress of the late-stage pipeline.

And I will now hand you back to Pascal.

Pascal Soriot - AstraZeneca PLC - CEO

Thank you, Sean. Please turn to Slide 30. Before we end, let me summarize. Our financials are on track. Our guidance is unchanged and we are delivering on our commitments.

The second message for you is the pipeline is accelerating with 13 new potential medicines in Phase III or under registration. The oncology pipeline is progressing ahead of our own expectations, in particular, Tagrisso and the immuno-oncology programs.

Tagrisso is an excellent example of the new AstraZeneca and this product is going from strength to strength. We are looking forward to sharing forthcoming news flow for over the next 12 months that we think has the potential to transform our Company.

We'll now go to the Q&A.

QUESTIONS AND ANSWERS

Operator

(Operator Instructions)

Matt Weston at Credit Suisse. Matt, go ahead.

Matt Weston - Credit Suisse - Analyst

Thank you, Pascal. Two questions if I can. The first with respect to MYSTIC and the data that we saw at ESMO. I'd be very interested in Sean's views as to the confidence around the percentage of PD-L1 high patients that you've recruited into the study and also whether or not you are sure that your stratification has been as detailed as perhaps it needs to be given the surprise results from Bristol.

And then secondly, one for Marc around externalization revenue. Marc, consensus has externalization of \$1.3 billion in 2017 and another \$900 million of other operating income. I know that some of that is going to be recurring but a lot of it is also assumed to be upfront money on deals. If we go back and look at the deals that you've done recently, it seems that you're selling assets for about 2 times sales, plus a royalty income. So my question is, should we be looking to take an incremental \$1 billion out of the top line going forward to adjust for those gains coming in? Is that a reasonable assumption in terms of the legacy assets that you're likely to divest over that period?

Pascal Soriot - AstraZeneca PLC - CEO

Thank you, Matt. Before we answer the question, let me mention two participants who are also with us today. Mondher Mahjoubi, who Heads our Oncology Franchise, and Rob Iannone, who is our Head of Clinical Development for Immuno-Oncology, and they may participate in answering the questions. The first question, MYSTIC, Sean, you will cover and the second, Marc, you want to cover the externalization.

The only thing I would say about externalization, Matt, is that it's a bit early for us to give guidance on 2017. So apologies if we are not very, very specific addressing your question. The other point I would mention is when you look at 2 times sales, you really have to be careful when you look at those deals, because many of them are actually partnering deals and when we partner, we usually do not divest the entire product.

We actually divest a portion of the product, if you will, giving a margin to our partner to promote the product and accelerate the growth, an example of (inaudible). An example with our anesthetics business. So you cannot do an average across the whole portfolio. But let's start with MYSTIC. Sean, over to you.

Sean Bohan - AstraZeneca PLC - EVP of Global Medicines Development and Chief Medical Officer

Sure. Thank you for the question. The first part of the question had to do with confidence in having adequate representation at PD-L1 high patients in MYSTIC. I'll just go back with a little history on MYSTIC. MYSTIC is an all-comers trial in first-line non-small cell lung cancer. So we're enrolling both PD-L1 high and PD-L1 low patients.

You'll recall that earlier in the year, we changed MYSTIC. We did a couple of things. One is elevated overall survival to primary endpoint. And with doing that, we also significantly increased the size of MYSTIC from 700 to 1,100 patients. And in looking at MYSTIC, we are confident that we have the anticipated representation of PD-L1 expression across PD-L1 high, PD-L1 low, PD-L1 negative.

We also feel great confidence that with the increase in size, we have adequate power to detect the treatment effect, both in PD-L1 high patients with Durva as monotherapy, possibly Durva/Treme as combination if it's significantly better and then also with the combination in PD-L1 negatives.

You also asked a question about stratification. We have stratified for the meaningful known prognostic factors in non-small cell lung cancer within MYSTIC. So we're confident there that we've incorporated what we can anticipate into the trial.

With regard to anything we couldn't anticipate, I think the size of the trial and the randomization should give us confidence that we should get balance across the trial. There's nothing coming out of ESMO that really changes our interpretation of either of those particular questions or factors. I think now probably to Marc to answer the second question.

Marc Dunoyer - AstraZeneca PLC - CFO

So just on the externalization revenue, I think I can say that this is part of our business model and, therefore, we're expecting to continue the externalization revenue in 2017, 2018 and so on. So yes, we -- needs to continue. To the question, what is the impact on lost sales on the forward years, it's more difficult to answer your question.

Obviously, it depends on the ratio between external revenue and other income and also it depends on the deal structure, whether we are letting the older value go or not. It's a very difficult question to answer. We will try to next year, for the guidance, try to provide some help in projecting these two lines out of our P&L. But for the time being, what I can say, to continue at reasonable level for the years to come.

Pascal Soriot - AstraZeneca PLC - CEO

Thanks, Matt.

Operator

Simon Baker at Exane. Simon, go ahead.

Simon Baker - *Exane BNP Paribas - Analyst*

Firstly, just going back to the guidance, at first blush, looking at what you've now delivered for the first three quarters and the reiteration of the guidance, one might think that the guidance on revenues is a little too optimistic and the guidance on earnings is a little too pessimistic. So I was wondering if we were missing anything or anything else you'd like to highlight. I'm thinking particularly about SG&A and gross margin.

And then the second question for Sean. Going back to the DURATION-8 Farxiga/Bydureon in combination study, they look to be a good continuing trend on weight loss at 28 weeks rather than any plateauing, so I wonder if you have any plans to run longer studies or further follow-up for DURATION-8 is to see what full impact of weight loss from that combination is? Thank you.

Pascal Soriot - *AstraZeneca PLC - CEO*

Thanks, Simon. Sean, do you want to start with the DURATION-8 question?

Sean Bohan - *AstraZeneca PLC - EVP of Global Medicines Development and Chief Medical Officer*

Yes. Thank you, Simon, for the question. We didn't miss that shape of the curve either when we looked at DURATION-8 and what we're doing right now is we are looking at what would be the best options going forward for further study of the combination.

I alluded to that a little bit in describing the diabetes franchise and really looking at obesity, hypertension and hyperlipidemia and whether this combination has particular potential in those -- in people with those risk factors. But unfortunately, I don't have any more to update you on than what we have with the 28-week data, which we showed you for DURATION-8.

Pascal Soriot - *AstraZeneca PLC - CEO*

Thanks, Sean. Guidance, Mark, maybe you want to cover this element. As far as the top line, we see the business is totally on track. Of course, we've had some one-offs in the third quarter but if you look at the underlying growth rate of the so-called new AstraZeneca growth platforms overall, we have a good growth rate of 6%, including in the third quarter, and we see this continuing.

So we're very much on track. I don't think that there's any reason to change our guidance there as far as the top line and as far as the bottom line, I'll let Marc answer that one. Marc, go ahead.

Marc Dunoyer - *AstraZeneca PLC - CFO*

Thank you, Simon. So to the question whether our sales guidance for the year is optimistic, I remind you that our sales guidance for sales is low to mid-single digit decline and despite the one-off impact on the quarter three, we remain confident that we can achieve that guidance and, therefore, we believe that maintaining it is appropriate. On the bottom line, obviously, we have talked to you about the tax impact which is very significant.

But we also have another negative which needs to be considered and I will -- I don't know whether I can call it a negative but a negative as far as EPS impact and we are spending more R&D that we were expecting to do. We continue to invest behind our key molecules.

That's one of them. We had some weakness in the emerging markets in the quarter three and also we had some true-up on Symbicort in the third quarter. So with all this together, the pluses and minus, we believe that it is appropriate for us to reconfirm our guidance on EPS for the year 2016. And again, it's low to mid-single digit decline.



Pascal Soriot - *AstraZeneca PLC - CEO*

Thanks, Marc. The key point here, Simon, is, really, we see the business totally on track from a top line viewpoint and we continue, of course, riding the growth of our growth platforms.

Operator

Sachin Jain, Bank of America. Sachin, go ahead.

Sachin Jain - *BofA Merrill Lynch - Analyst*

Affrication question to the last comment. Maybe just reframe it a little bit. So full-year guidance is unchanged. But it's -- versus sell side estimates, you have much greater one-off income now for the full year versus the start of year, roughly \$3 billion versus \$2 billion. Obviously, the \$450 million tax benefit totaling \$1.5 billion positive one-off delta versus the start of the year. Just to clarify, Marc, does the R&D EM weakness core account for all of that or are there other factors that we should be thinking about in terms of the base business.

then the two product questions. On MYSTIC, just a follow-on. Did the strength of PFS data through the [keynote] 24 provide you any color as to how you think about apportioning fiscal alpha between PFS and OS? And the background to that question is, you previously talked about PFS not being necessarily predictive to OS. How are you thinking about that?

And then secondly on acalabrutinib, Sean, I just wanted to check your confidence in the fast-to-market strategy there. There seem to be some emphasis on it being a Phase II study. So is there any change in your view of fast-to-market? Thank you

Pascal Soriot - *AstraZeneca PLC - CEO*

Sean, do you want to start with the two last questions and return to the guidance in a minute?

Sean Bohan - *AstraZeneca PLC - EVP of Global Medicines Development and Chief Medical Officer*

Sure. That sounds fine. So the first thing I want to do is I want to go back to Simon's question because we had a chance to look at the DURATION-8 details, didn't have them in my head. So Duration-8 follows patients for two years, Simon. So we'll be able to look at the weight loss curve over more time. But we just don't have anything to share at this time, so we'll get you updates in the future.

To Sachin's question about the true to data and what -- how it might relate to MYSTIC. So the first thing is that we view the Merck data as validating what I think we all felt was a pretty strong therapeutic hypothesis, which is that PD1 -- PD-L1 is a very effective treatment in first-line lung cancer. Albeit, in this case in a pretty highly selected group of PD-L1 positive patients.

And we definitely take all the data that we have seen from ESMO and the data that we have seen from some internal work that we're doing on other studies to inform our MYSTIC statistical analysis plan. And we are confident that MYSTIC is designed to show a clinically meaningful treatment benefit in PD-L1 positive patients, obviously, provided that the trial turns out to demonstrate that.

With regard to acalabrutinib, this initial filing in acalabrutinib was always an opportunistic fast-to-market opportunity based on non-randomized data with all of the caveats that come with an accelerated approval and an approval based on non-randomized data in terms of the magnitude of treatment effect that you have to demonstrate and having to demonstrate a clearly unmet medical need.

And so in that respect, nothing has changed with regard to the strategy. What has changed is that the data maturity we had previously expressed at end of this year and we're now saying it's going to be first half of next --

Pascal Soriot - *AstraZeneca PLC - CEO*

Thank you, Sean. Just the only thing I would add is just reinforce the point actually, Sachin, that the accelerated approval was always an upside, if you will. It was never based on our -- it was never a core strategy. We haven't changed our view as to the probability of this happening. There's no change of view at all. But it's just important to keep in mind, it was always an upside, not our base plan.

I'll ask Mark to cover the guidance. But again, in terms of this one-off, remember we have FluMist, that's a one-off that was not expected, of course. We have Venezuela. We have the Saudi Arabia situation and of course, the price effect for Symbicort in Q3. So those are to be all kept in mind as it relates to the top line.

As I said, the growth platforms, the underlying business, the new AstraZeneca is doing exactly as we expected. Just like to add on the Symbicort front, we need to recognize that there is a price pressure in the US. We just -- this is not something I would want to ignore or appear as we are underestimating.

There is a price pressure and it's on the -- will continue. But Q3 is not reflective of that price pressure. There's a one-off there that we should eliminate. Mark, go ahead.

Marc Dunoyer - *AstraZeneca PLC - CFO*

So first of all, let me emphasize, again, that obviously guidance is a range. Therefore, within that range, one needs to understand the positive and the negative factors. And to summarize the negative factors or the factors that have an impact negatively on the EPS, R&D is one of them.

The second, as Pascal just described, the quarter three true-up and that's predominantly Symbicort pricing true-up for previous quarters. We have [Imbrutinib] and Mark Mallon described them early on the emerging market one-off and that's Saudi, that is Latin America and as Pascal just reminded us, we also have the FluMist vaccine negative recommendation. Apart from these four main factors, there are none other.

Pascal Soriot - *AstraZeneca PLC - CEO*

Thank you, Marc.

Operator

Seamus Fernandez, Leerink.

Seamus Fernandez - *Leerink Partners - Analyst*

Thanks very much for the question. So just a couple here. There were some abstracts -- this is a question for Sean, some abstracts as ASH that have been published so far. Talking about acalabrutinib activity and efficacy in -- as well as safety in Imbruvica-intolerant patients. Just wondering if you could comment on that program.

It looked like the product was particularly well tolerated in this patient population. And as a follow-up to the acalabrutinib question, can you guys just update us on the intellectual property position for that product? And then just a quick separate question. I believe that we're going to see the SOLO-2 data presented at ECO or at least there's a placeholder abstract there in January.

Can you guys just give us a general sense of how competitive you feel Lynparza is with other PARP inhibitors and what your general view is on PARPs relative to PARP trapping capability and the efficacy in the class. Do you believe that there's meaningful differentiation in the class given what you've seen so far? Thanks.



Pascal Soriot - *AstraZeneca PLC - CEO*

I'll ask Sean if you want to cover those two points. Just on the Lynparza, we see it as very competitive in Japan. But we see it very competitive on the efficacy side and the differentiated on the safety front. So we believe this is a compound that has great potential. Sean, do you want to cover the ASH question, also [comment] on the Lynparza response?

Sean Bohan - *AstraZeneca PLC - EVP of Global Medicines Development and Chief Medical Officer*

Sure. I'm happy to. Thank you, Sheamus, for the questions. So the first question had to do with acalabrutinib and the Imbruvica-intolerant population. There have been several publications, mostly institutional experience retrospective publications, indicating that there is a significant fraction of patients on ibrutinib who discontinue the drug without having progressed.

That means that they're discontinuing for a reason other than resistance or disease progression. And most commonly, that's due to adverse events or intolerability. So what we've done is we're gaining some experience and these are really proof-of-concept abstracts with asking if patients seem to be benefiting from BTK inhibition but can't tolerate ibrutinib, will they be able to tolerate acalabrutinib?

As we say, the early data looks encouraging. But again, this is an emerging field and we're really trying to define what does ibrutinib-intolerant look like? So I will say it's encouraging. It's an interesting potential opportunity but it's evolving right now.

With regard to SOLO-2, just a clarification. We have said that the data, obviously, is positive top line progression-free survival with what we believe is a significant and competitive benefit. We did not indicate what meeting the data would be presented at. We just said an upcoming scientific meeting and when we get greater clarity on having it accepted and when we're actually going to be confirmed to present, we can provide more clarity on that.

With regard to competitiveness of the class, I think what Pascal said is exactly right. We believe from an efficacy standpoint, it is quite competitive and the trapping issue, it is true that there are different potencies in vitro for PARP trapping. We do believe PARP trapping is important.

The only point is that the doses of the different PARP inhibitors are different and we believe that all of them can be dosed well above the amount of PARP trapping that needs to be achieved in order to be efficacious. So it's actually not a clinically meaningful differentiation since many of them can achieve it.

One -- couple things I'll point out as you start to look at data in this field. In terms of tolerability, I think looking at dose reduction rates and as an AE thrombocytopenia in the class, we don't see much thrombocytopenia with Lynparza and we don't see many dose reductions.

The last thing that I will say about SOLO-2 is SOLO-2 also enables a formulation which reduces the pill burden of patients quite considerably. So we're not only excited about filing the data to get the approval but also to be able to convert to the new dose formulation.

Pascal Soriot - *AstraZeneca PLC - CEO*

Thank you, Sean. On the active front on the finance -- the accountability of the patent expiries in 2032.

Operator

Tim Anderson, Bernstein.

Tim Anderson - *Sanford C. Bernstein & Co. - Analyst*

Thank you. Can I go back to MYSTIC, please? There's discussion about biomarkers and cut-off levels, but that's -- if I'm understanding right it's really only relevant to secondary endpoints and not the primary end point. And if you don't hit the primary then the value of those secondaries is questionable what the value is.

So are you comfortable leaving that primary end point as an all comers population, again, where I guess we don't really care what the biomarker cut-off is because it's all comers or is there potential that you change. If you change it to just a expresser population, would the timing of readout be the same?

Then a second question on MYSTIC. If you don't hit PFS on this first readout in the first half, is it possible we may not see you present any data until you have the OS data. I'm wondering if it could be a [vacuum] event formation under this scenario where maybe you don't hit PFS. Then last question on KESTREL and EAGLE and head and neck.

Squamous morphology. I'm wondering if that raises the risk that in something like squamous non-small cell lung, there could also be a potential bleeding issue with the CTLA-4 combo?

Pascal Soriot - *AstraZeneca PLC - CEO*

Thank you, Tim. Sean, over to you again.

Sean Bohan - *AstraZeneca PLC - EVP of Global Medicines Development and Chief Medical Officer*

Yes, okay. Thanks, Tim, for the question. So first of all with regard to MYSTIC and the cut-off, it's a good question. There -- it is true that if you don't hit primary end point, you don't have a positive trial. So that secondary endpoints aren't really very important in an overall negative trial.

We have the opportunity to revise our fiscal analysis plan and we've talked to everyone about that before, before we do our analysis. And so we can look at both external and internal data and decide how we want to fit cut-off and positive versus all comers into the analysis plan for the primary endpoints. So I won't guide anymore on that right now, just recognizing that, that's an opportunity.

You had another question, which is about progression-free survival and then going on to overall survival. So the change in the analysis plan doesn't change our guidance as to when we will see a progression-free survival readout. It is, however, true that if we don't hit progression-free survival, and again, I think as we've discussed before, we believe that overall survival really is much more meaningful in capturing the full benefit of immunotherapy for cancer.

I think the data in the field, as a whole, is really supporting that as it matures. If we don't hit the progression-free survival, it is true that we can still have a positive trial for overall survival subsequently. So we would wait for formal presentation of the trial data until we've completed the analysis of the trial.

The last one was about head and neck cancer and squamous cell carcinoma. So we -- as you know, there is a background rate of bleeding that occurs with squamous cell carcinoma of the head and neck and is distinctive from lung cancer, squamous or non-squamous. So a couple of things about that; first of all, we have placed on partial clinical hold because of a signal, a potential signal seen in a normal safety review of our head and neck program with IO.

And what we did is we first went on voluntary hold and then we were able to do a much more detailed analysis of the imbalance that we saw there. And we've now submitted that to the FDA and proposed how we would move forward. We feel very confident we will move forward in head and neck cancer, okay, and we have not revised our time line.



We don't think at this point, we need to. We'll still be able to achieve it. The hold was specific for squamous cell carcinoma of the head and neck. It did not apply to any other tumor type in the program, including MYSTIC, DANUBE, NEPTUNE, all of those trials. So those are ongoing, without change. They have normal safety monitoring that we do in all our trials and no such signal has been identified. So that's --

Tim Anderson - *Sanford C. Bernstein & Co. - Analyst*

I'm sorry, can I just ask a clarifying question? So if you were to change the primary on MYSTIC just to an expresser population, not all comers, is your timing of readout still likely to be first half of 2017? And then again, I'm not sure, maybe you answered it. Maybe I heard it incorrectly. But if you don't hit PFS on that readout, are you still -- are you saying you won't likely have any data then in that scenario until you have the mature OS data readout?

Sean Bohan - *AstraZeneca PLC - EVP of Global Medicines Development and Chief Medical Officer*

So the answer is that our PFS readout will be in the first half of 2017. And if we do not hit for PFS, we have the opportunity to wait for the maturation of the OS data, at which time, we will analyze the OS data and report whether we have hit for that endpoint or not. And we anticipate that in 2018, I should say.

Tim Anderson - *Sanford C. Bernstein & Co. - Analyst*

Okay. Maybe if you change the primary end point, the timing of readout, is it still first half? If you were to change the primary --

Pascal Soriot - *AstraZeneca PLC - CEO*

The answer is yes, Tim. We have a reading in the first half of 2017 and then second reading early -- the first of half of 2018. Before we go to the last question, I'd just like to reiterate what Sean said a minute ago as far as head and neck. We are confident to be able to resume enrollment. To the extent that we are not changing the dates for the readout of those head and neck studies.

Operator

So I'll move to Vincent Meunier from Morgan Stanley. Go ahead.

Vincent Meunier - *Morgan Stanley - Analyst*

The first one is, again, on the guidance with a focus of -- on SG&A savings. The savings are, again, being very important and higher than expected. Could you elaborate on the sources for the savings you are able to extract now and more importantly, the potential for further savings?

Second question is on respiratory. You talk about preparing a platform for Bevespi and Benra. Does it mean more SG&A business? Will this (inaudible) be only in-house or does that include external contribution in [Almirall]?

Pascal Soriot - *AstraZeneca PLC - CEO*

Vincent, just want to be sure I understood the second question. In terms of respiratory and Bevespi, can you repeat the question?

Vincent Meunier - *Morgan Stanley - Analyst*

You say that you are preparing a platform for Bevespi and Benra. So does that mean that you will increase your SG&A investment in respiratory or would you like to improve the existing platform with acquisitions or maybe in-licensing or partnerships?

Pascal Soriot - *AstraZeneca PLC - CEO*

Sorry. You got it. Thank you so much. At this point the plan is to launch Bevespi on our own and to certainly look for synergies in our respiratory team across Symbicort and later on, of course, Benralizumab. But we don't intend to partner on Bevespi. We are planning to -- preparing, I should say, to launch it next year. Mark, anything you want to add to this?

Mark Mallon - *AstraZeneca PLC - EVP of Global Product and Portfolio Strategy, Medical Affairs and Corporate Affairs*

No. We've got I think a top notch respiratory sales team, market access team, medical teams. They're very excited about this product. It's going to make a big difference for patients with COPD. We're confident that they will do a good job. We're preparing to do the same thing for Benralizumab.

Pascal Soriot - *AstraZeneca PLC - CEO*

Marc? The other Marc, on SG&A?

Marc Dunoyer - *AstraZeneca PLC - CFO*

So as far as SG&A savings, you have seen that we had -- we made a commitment in 2015. We are, in a good way, to meet also our commitments and even exceed them for 2016 in terms of SG&A cost reductions. Whether this comes from, as your well aware, that we have initiated a new footprint initiative, we have also started three years ago a large program of IT cost reduction. These are well on their way.

And earlier this year, we have also started another initiative to increase our SG&A, as in medical and marketing productivity. So I think it's a combination of various productivity initiatives which are being started at different times in the last two or three years. But we are determined to maintain the core discipline and to make sure that our SG&A ratio comes more in line with the rest of our peers.

Pascal Soriot - *AstraZeneca PLC - CEO*

Thank you, Marc. So we'll close here and thank you again for your participation, your great questions, and in closing, let me just reiterate that what I said earlier, we are completely on track, from our viewpoint, in terms of implementation of our strategy. We are ahead of plan as far as pipeline in total oncology.

There's great news flow coming over the next 12 months. From a financial viewpoint, we believe we're on track and importantly, the new AstraZeneca is really starting to emerge and over the next 12 months, we expect to make more progress on this. Again, thank you so much and have a great rest of the day.

Operator

Ladies and gentlemen, that will conclude today's conference. We thank you very much for your participation. You may now disconnect. Thank you.



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