ASTRAZENECA

Moderator: Pascal Soriot - CEO
April 29, 2016
12:00 p. m. GMT

Operator: This is conference #23032512.

Good afternoon. Welcome ladies and gentlemen, to AstraZeneca's Q1 results analyst conference call. Before I hand over the call to Pascal Soriot, AstraZeneca, I'd like to read the safe harbor statement. The company intends to utilise 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.

By their very nature, forward looking statements involve risk and uncertainty, and results may differ materially from those expressed or implied by these forward looking statements.

The company undertakes no obligation to update forward-looking statements. There will be an opportunity to ask questions after today's presentation. Please press star one to indicate that you wish to ask a question at any time during the call. We will now hand you over to AstraZeneca, where the call is about to start.

Pascal Soriot: Hello everyone, I'm Pascal Soriot, CEO of AstraZeneca. Welcome to the Q1 2016 results conference call for investors and analysts. The presentation is posted online for you to download, and there is also an audio player. I'm joined today by Luke Miels, Executive Vice President for Global Product and Portfolio Strategy, Global Medical Affairs, and Corporate Affairs, Mark

Dunoyer, CFO, and Sean Bohen, our CMO. We plan to spend 20 to 25 minutes on the presentation, and then leave ample time for Q&A. In total we have about one hour together, so please turn to slide two, where you'll see our forward-looking statements. Moving to slide 3, you will see there the agenda. The plan for today's forum is to provide a short overview and then I'll hand over to Luke for an update on our growth platforms, and ongoing launches of new medicines. As usual, Mark will cover the financials and our guidance, and then Sean will provide a pipeline update, and I will end up with concluding remarks before we take your questions. Moving to slide four, Q1 2016 was a good start to the year for AstraZeneca and we met expectations. We delivered five percent growth in our total revenue. Six percent growth in our growth platforms, and our focus on cost discipline continued as we reduced SG&A costs by six percent. In R&D costs, we saw a slowdown in growth despite taking on-board any costs related to the ZS pharma and Acerta Pharma deals

We received four regulatory approvals and four regulatory designations which underline the continued progress of the pipeline. Now taking a step back and looking at how we advanced our strategy. AstraZeneca continues to make significant progress towards the total revenue target that we communicated earlier for 2023. The company has increased pipeline productivity, we've built our therapy areas, our leadership, we've developed our growth platforms, and clearly we've transformed our culture as well. The shape of the business is evolving rapidly now with a growing number of specialty care medicines, in particular in oncology. In line with this strategy, designed to deliver benefits to patients, and value for shareholders, we today announced further focus on our main therapy areas to drive greater productivity across the organisation.

The growth of our pipeline is such that we have to further prioritise and further sharpen our focus, and we have to allocate additional investments to oncology. Alongside this, we'll continue to work with others in the opportunity led part of the portfolio, and accelerate the partnering in areas such as infection, neuroscience, and inflammatory diseases outside respiratory. This focus will also streamline the operations primarily in commercial and manufacturing. This, together with the drive for greater

efficiency, will deliver a material decline in our SG&A costs in 2016 and 2017, as we previously guided you we would be targeting. These changes will increase our operational effectiveness, and by the end of 2017 they are expected to generate net annualised benefits of about $1.1 billion, that will be reflected primarily in **our** SG&A costs. We expect to incur a $1.5 billion one-time restructuring charge, the majority of which will be cash.

Final estimates for programme cost, the benefit, and the impact will be subject to consultation. Mark will provide further details later on. Turning to slide 5 you see the five percent growth in total revenue here that was impacted by four percent hit from currency movements. The growth in total revenue was primarily driven by externalisation revenue from the new China partnership on Plendil, a medicine for hypertension. Our product sales grew by one percent. The growth platforms grew by six percent. As I said earlier, R&D cost growth slowed to 15%, the total cost broadly in line with last year. In fact, the growth in R&D would have been only 9% if we adjust for recent acquisitions.

We're on track to deliver what we communicated as far as R&D cost for the year. We continue to see a reduction in SG&A. We're also on track to achieve our goals for cost management for the year. And the core EPS decline of seven percent reflects the lower level of other operating income, and increased financing costs from the recent transactions.

Slide six, this is a very exciting slide that shows that we achieved four approvals in the first quarter, and four designations. So as you can see here we are pleased with the fact that the first medicine from our acquisition, of Pearl Therapeutics can soon benefit patients with the approval of *Bevespi*, previously known as PT003. With the triple combination of PT010 in phase III we are well positioned to offer the benefit of the unique co-suspension technology that allows multiple medicines in the same unique device. *Zurampic* and *Brilique* received approval in the EU for gout and post-MI, respectively. Very importantly, Tagrisso received Japanese approval in some forms of non-small cell lung cancer, and we consider this a true milestone. Not only is Japan the market with the most potential patients, but the timeline

for Japanese approval is a new record: only a few months after approval in the US and the EU. It reflects the quality of the product, of course, but the commitment and the dedication of our team as well, in Japan and globally. We look forward to publishing further data for Tagrisso as we see longer and longer progression free survival and also a large benefit to patients with brain metastases, a frequent site for disease progression in lung cancer patients. On top of the four approvals we received four regulatory designations that are detailed here on the page. We're excited with the external recognition of our advances in science and the patient benefit that this brings. With this I'll hand over to Luke who will take you through the growth platforms.

Luke Miels: Thanks Pascal. Hello everyone, so if we can just go to slide 8. So quarter one marked a good solid start to the year for growth platforms. Our growth rate slowed in some areas versus last quarter, however our performance remained in line with our long-term goal.

Despite a challenging external environment our performance was driven by our well-positioned geographic footprint, and diverse product offering focused within our key therapeutic areas.

If you'd move to slide 9 thanks. So if I start with respiratory this morning, we delivered two percent sales growth during the quarter which reflected a strong performance in emerging markets and the contribution from new products.

This was offset however, by *Symbicort* in the US and the EU. Total sales of *Symbicort* declined seven percent in the US specifically. Volume growth was partly offset by pricing as a result of new contracts.

Moving forward we do expect pricing to stabilize over the year as these new contracts settle in. Europe sales continue to be affected by slower in class market growth, and competitive pressure from both branded competition, and analogues. However, despite a highly competitive market environment in the EU, *Symbicort* maintained its market leadership in the class, and encouragingly Symbicort in the PMDI format was also approved in Europe.

Emerging markets respiratory sales grew 18 percent, now accounting for 14 percent of global product sales, and *Pulmicort* growth was largely driven by 24 percent increase in emerging markets, particularly in China which delivered a very pleasing 34 percent growth.

Pulmicort in China continues to grow from the expansion of treatment centres, and we believe that this growth is sustainable with additional initiatives in home nebulization, and link to this a change in the marketplace that should ultimately benefit Symbicort.

As for the new medicines in respiratory, *Duaklir* is achieving market share of 20 to 30 percent in our lead markets, and *Eklira* and *Tudorza* managed to grow ahead of the market in a decreasing LAMA class. In the US, Tudorza was impacted by tougher access and a voluntary recall.

We remain confident about the potential of the class, given that the treatment guidelines recommend the addition of a third bronchodilator to standard ICS/ LABA combination treatment for patients who are not control.

Finally, we're very happy to receive the FDA approval for *Bevespi*, a LAMA/LABA, using our proprietary co-suspension technology. *Bevespi* is the first in class to be delivered in a PMDI. With this approval we are very pleased to offer a new treatment option to COPD patients and the approval of *Bevespi* represents a successful milestone for our respiratory franchise, which we expect to see further evolve later this year with benralizumab and tralokinomab data, and Sean will cover this shortly.

If you can just go to slide 10 thanks.

So for *Brilinta/Brilique* global product sales were robust, growing by 46 percent. In the US, *Brilinta* gained further total market share at the expense of generic Clopidogrel and our branded competitor. And if we look at new to brand prescriptions, Brilinta remained the branded market leader.

And we also had some good news on guidelines in March. So the updated ACC/AHA guidelines in the quarter now recommend *Brilinta* over clopidogrel in STEMI patients with the support for treatment beyond 12 months of dual antiplatelet treatment. These guidelines now support the long-term use of this therapy in patients beyond one year.

While the US sales are encouraging, we do need to keep patients on the medicine longer for them to fully benefit from the treatment, and this will be a focus for us, and the guidelines support this messaging.

In the EU, we had growth of 19 percent, with approval of *Brilique* in the post-MI indication in February. The launch of the 60 mg dose is now underway in Germany, the Nordic countries and the UK, and the Netherlands has already secured early reimbursement.

In emerging markets, consistent growth continued with particular strength in China, despite the fact that there is no price listing or reimbursement. We also saw encouraging growth in Russia.

Please turn to slide 11.

If we now look at diabetes, the strong performance in 2015 continued into the first quarter. We have a strong performance of 23 percent. Growth was visible across all the regions; you see this on the slide here in the middle in what remains a very competitive market.

I think we're well positioned in our broad portfolio exposure to all classes in the non-insulin market. If you look at the *Forxiga* family, it continued to lead the SGLT-2 class in volume share in the EU and international markets, and also lead the dynamic market share in Japan. In the US we'll see it gain share due to preferred status with one major health plan and outgrow the SGLT class, but I think it's fair to say the competition within the class is expected to remain very intense.

For *Bydureon*, the growth was supported by strong class growth of around 25 percent overall and the continued successful launch of the pen device help drive product sales across the globe.

Product sales in Europe and Japan continue to outpace the class and while the US also benefited from market growth, competitive pressure remained.

Next slide thanks.

If we look at emerging markets in aggregate during the quarter the overall emerging markets growth rate slowed, however we are on track with our long-term goals. Our established portfolio is well-positioned as the main near-term growth driver in emerging markets. Trends in better diagnoses, improved access and favourable patient dynamics all bode well for established products in respiratory, diabetes, and CV medicine. The slowdown in growth in the first quarter was mostly attributable to two factors: the macro economic situation in Venezuela, and a significant cut in government spending within Saudi Arabia. Looking at geographic performance: while growth in China slowed during the quarter, including some inventory reductions in the sales channel, we are growing faster than other multinational companies, and growing faster than the overall market.

Pulmicort Respules are now the top medicine in China amongst the multinational company medicines with *Nexium* and *Crestor* also in the top 15. Looking forward we expect to maintain the solid growth in China.

Brazil and Russia grew faster than the market at 19 and five percent respectively, and also the Middle East and Africa and most of Latin America outperformed the overall market growth.

Moving from geographic performance, just to give you a little bit of colour around product sales, emerging markets growth was supported across all of the main therapeutic areas. Respiratory sales were up by 20 percent. Brilinta was up 109 percent, diabetes was up 65 percent, and finally legacy - and I emphasize legacy - oncology was up 5 percent. As a reminder, and we've

placed this on the slide for you, the long-term target for emerging markets was mid to high single digit's percentage growth in product sales and we remain on track for this.

Next slide thanks.

Coming to Japan. In Japan product sales declined by 7 percent, driven by the mature portfolio which had a decline of 10 percent. However, the growth platforms grew by 8 percent. Specifically, our off patient oncology medicines continued to face strong generic competition and there was also some destocking in the quarter in advance of the biennial price cuts from 1 April, and these price cuts are at a similar level to those in 2014 with a total impact of about 6 percent. These were concentrated on the off patient oncology, and anaesthesia medicines, as well as our major revenue generating medicines *Crestor* and also *Nexium*. Specifically, for *Nexium*, the Q1 2015 comparison just to flag it to you, was high due to restocking, because we had a recall in 2014 Q4. During the quarter, key growth medicines in Japan *Symbicort*, *Crestor* and *Nexium* all maintain leading dynamic market share positions in the competitive market environment, and that's what we put there in the middle of the slide you see the bar charts. In addition to our established portfolio in Japan, we are also preparing for the next wave of product launches, and we are very excited about the recent regulatory approval for *Tagrisso* at the end of March of 2015, seven months after submission and a few months after approval in the US and EU. And we expect *Tagrisso* to benefit from our existing oncology presence and infrastructure as we outlined at the end year results, and it represents a significant opportunity to address a high unmet need in the population which is a high prevalence of the EGFR mutation. Please turn to slide 14.

So if we finish on some very exciting news. The two new oncology product launches. *Lynparza* continued its strong trajectory after one year of approval. Globally an estimated 2800 patients have now been treated with commercial supply of *Lynparza* despite the bulk of patients being fourth line. We continued to see encouraging signs of the durability of the response of

Lynparza, and interestingly we estimate around 20 percent of the patients remain on the medicine.

Lynparza has now been launched in 21 countries with reviews ongoing in 14. And as can be seen from the middle part of the slide, BRCA testing rates have again increased over the past 18 months to around 60 percent in the US, and around half the eligible patients in the EU, which is very encouraging. And as Sean will explain later, the extensive development programme is quickly advancing. 2016 will be an exciting year for Lynparza and also the promise in our commitment in the area of DNA damage response.

Turning to Tagrisso, again we've made very good progress just over a quarter after launch. We received approval in the EU in February in addition to the Japan approval I mentioned earlier, with multiple submissions and reviews ongoing.

In terms of patient numbers, just to provide a little bit of context for you, we currently have nearly 2000 patients in prelaunch access programmes, and as a leading indicator T790 mutation testing rates are on the rise. In the US the rate is around 40 percent up from 10 percent before launch. We think this is very interesting because unlike BRCA, prior to the availability of Tagrisso, there was no utility in testing these patients because there was no therapeutic option for them. On top of this we anticipate testing rates to increase further after the ctDNA diagnostic test is expected to become available in the US in the second quarter of this year. So in summary, reflecting on the growth drivers of performance in Q1, while the growth rates slowed in some areas, the resilience of the business was strong and in line with our expectations. I'll now hand over to Marc.

Marc Dunoyer: Thanks Luke, and now everyone I'm going to spend the next few minutes taking you through our performance in the first quarter and our guidance for the full year.

Please turn to slide 16. As Pascal mentioned earlier, total revenue grew by five percent at constant exchange rates. We continue to face currency

headwinds in the quarter, which impacted total revenue by four percent. Our growth platforms again performed well, and in line with our business model, we continue to generate value from externalisation. For example, through an agreement with CMS in China and an agreement with ProStrakan for Moventig in Europe.

In line with full-year guidance, SG&A costs reduced by 6 percent to 35 percent of total revenue. This was a significant improvement versus quarter one 2015.

Further down the P&L the rising financing charges reflected the dilutive effect arising from the ZS Pharma acquisition, and Acerta Pharma investment. The seven percent decline in core EPS at constant exchange rates to 95 cents, was also driven by the impact of the significant year on year decrease in other operating income.

The adverse impact of the currency headwinds on core EPS was 5 percent. Finally, as I mentioned at our last presentation we may well see greater fluctuations in the quarterly earnings performance this year as a result of the loss of Crestor which goes off patent next week.

Please turn to slide 17. Looking at other headlines in the P&L, product sales grew by 1 percent despite significant challenges, for example for Nexium. Given a 6 percent rise in the cost of sales, the gross margin on product sales fell by one percentage point to 83 percent.

The 15 percent increase in core R&D in the quarter, included the absorption of the R&D cost from acquisitions and investments. Excluding this absorption, core R&D cost would have grown by 9 percent, a significant slowdown.

Our core tax rate was 17 percent in the quarter, in line with the full-year comments I made in February of a16 to 20 percent range, which will depend on the eventual geographical mix of profits.

Please turn to slide 18. Core SG&A reduction continues to be a key focus for the business. We made good progress in the quarter. As I mentioned earlier, core SG&A cost declined by 6 percent in absolute value, and by over four percentage points relative to total revenue in quarter one 2015. As I stated in February, core R&D costs this year I expected to be at a similar level to full-year 2015. You can clearly see on the chart, the full year core R&D costs quarter four 2015 to quarter one 2016, despite the first-time absorption of the acquired R&D cost mentioned previously.

Please turn to slide 19. As we continue to maintain core discipline across the business, we have announced today actions to advance our strategy implementation by sharpening our focus on the three main therapy areas, enhancing operational effectiveness and adjusting cost structures.

We have made good progress, focusing on the main therapy areas. For instance, in RIA we have expanded the portfolio and are beginning to capture the benefits. In CVMD, we are broadening our portfolio recognizing the loss of Crestor. And in oncology we have one of the most exciting and balanced pipelines in the industry that we will further advance.

But we plan to go faster and further. In parallel to this focus and prioritisation, we will reduce costs at the global, regional, and country level, and make far greater use of shared services.

We plan to reshape our manufacturing base optimising our presence in key strategic sites, while taking into account the need to create capacity in our biologics supply chain.

As well as continue to focus on productivity and simplification, our R&D structure will benefit further from externalisation for example as we share R&D the costs with key partners.

These changes will enhance our overall effectiveness, and once implemented by the end of next year, I expect it to generate around 1.1 billion in annual net benefits versus full-year 2015. These benefits will fall mostly within the core

SG&A cost line. We expect to incur up to $1.5 billion in one-time restructuring charges, the majority of which are likely to be cash costs.

It is important to emphasize that these benefits are taken into account by our full-year guidance which remains unchanged today.

Please turn to slide 20. You may well be familiar with this slide that summarizes the challenges and opportunities we face this year.

We know that there are two clear pressures on the business. When we think about our 2016 guidance, namely the loss of exclusivity for Crestor in the United States, plus the dilutive effects of the recent acquisitions and investments.

But our growth platforms consistently perform well. We also have a very busy year for the pipeline and our launch programme. We will continue to pursue value creating externalisation and disposal opportunities.

As I just mentioned we will re-double our focus on cost discipline. All of these factors are within our control. This is why the adverse currency movement, that we now expect to impact total revenues by around two percent this year, and a similar percentage on core EPS, are not included within guidance.

Please turn to slide 21. To conclude, I want to reiterate the guidance for 2016 which is at constant exchange rates. We expect a low to mid-single-digit percentage decline in both total revenue and core EPS. Finally, I want to reconfirm our capital allocation priorities. We will continue to strike the balance between the interests of the business, our financial creditors and our shareholders. After providing for investments in business, supporting the progressive dividend policy, and maintaining our strong investment grade credit rating, we will keep under review any potential investment and value enhancing, and immediately earnings accretive opportunities. Thank you for listening and I will now hand over to Sean.

Sean Bohen: Thank you, Marc, and hello everyone.

Please turn to slide 23. I would like to start off by highlighting a few milestones achieved during the quarter.

We received US breakthrough therapy designation for durvalumab, for bladder cancer. In the EU, we received orphan drug designation for acalabrutinib, for a number of hematological cancers listed on this slide. Further, we received US orphan drug designation from MEDI-551 for neuromyelitis optica, an autoimmune disease of the central nervous system.

Finally, also in the US, fast track designation was received from MEDI8852 for hospitalised influenza A. These designations illustrated the quality of our pipeline, and also point to the evolution from primary care, to more specialty care programmes addressing unmet medical needs.

Please turn to slide 24. As Pascal and Marc mentioned previously, we have seen an acceleration of the pipeline. Nowhere is that more evident than in our milestones and upcoming news flow. First on Q1 milestones, I would like to review some late stage pipeline headlines since the last results announcement.

Starting with RIA, *Symbicort* in the pressurized metered dose inhaler device, was approved in the EU for COPD. And *Bevespi* or PT003 was approved in the US for COPD.

Zurampic received approval in the EU for gout. In CVMD, *Brilique* received approval in the EU for the post-MI indication. The SOCRATES trial for stroke also read out during the quarter, and though positive trends were detected, the trial missed its primary endpoint.

For oncology, starting with *Tagrisso* for lung cancer, we received approval in Japan at the end of March, just a few months following approvals in the US and EU. We also made the decision not to restart the CAURAL trial in combination with durvalumab. We are happy to report that the FLAURA first-line trial is now fully recruited. We expect data from the second line

confirmatory trial AURA3 in the second half of 2016, potentially already in Q3. Finally, after a successful phase II interim analysis, AZD3293, a BACE inhibitor in partnership with Eli Lilly for Alzheimer's disease, will continue into a phase III trial programme.

Please turn to slide 25. I wanted to highlight in particular the *Tagrisso* first-line AURA data, which were presented at the ELCC conference earlier this month. As an oncologist, I find this data particularly encouraging.

The AURA study is a phase I first-line trial in patients with EGFR mutated advanced non-small cell lung cancer.

Although in a small sample of patients, about 60, the results were encouraging. With a confirmed response rate of 77 percent and a median progression free survival of 19.3 months.

As a comparator, currently approved first line medicines for EGFR mutated non-small cell lung cancer patients typically provide less than one year of median progression free survival as per their approved labels.

This setting is being further evaluated in the ongoing FLAURA phase III trial.

Please turn to slide 26. We would like to update you on our durvalumab haematology IO collaboration with Celgene. As you can see, the development programme is extensive across disease types, with the first patient dosed in a phase I trial in relapsed refractory multiple myeloma. We're committed to advancing this programme, and also to the haematology space, which is an integral part of our overall oncology strategy.

Please turn to slide 27. Finally, we anticipate a very busy year ahead in terms of pipeline news flow.

We have previously communicated a PDUFA date for ZS-9 of 26 May 2016. In the second half of the year, we expect regulatory decision on saxa/dapa for type-2 diabetes, cediranib for ovarian cancer, and CAZ AVI, all in the EU. I

have in front of me here a note saying that we actually just got a CHMP "go" for CAZ AVI this morning.

We expect the resubmission of saxa/dapa in the US, during the second quarter and in the second half of 2016, *Bevespi* for COPD in the EU, benralizumab for severe asthma in the US and EU, the rolling submission for roxadustat in China, and potentially acalabrutinib for a blood cancer indication in the US. This potential regulatory submission for acalabrutinib would be for an accelerated approval.

Finally, we expect key data read outs for benralizumab for asthma and Lynparza for gastric cancer in the second quarter. And in the second half of the year, Brilinta for peripheral artery disease, Lynparza for breast and second line ovarian cancer, selumetinib for lung cancer, the durvalumab HAWK trial for head and neck cancer, and acalabrutinib for lung cancer.

We are advancing quickly in first line lung cancer with the MYSTIC trial which is enrolling well, with top line data on progression free survival expected in the first half of 2017. We're also advancing in first line bladder cancer, both in durvalumab monotherapy and in combination with tremelimumab in the DANUBE trial. We also have the only chemo free I/O combination for first-line head and neck cancer with the KESTREL trial.

A comprehensive registration programme is underway across multiple tumour types, stages of disease, and monotherapy, as well as combination therapy.

Additional combination studies of durvalumab with other immunotherapies and also chemotherapy are underway.

We're very pleased with the progression of our oncology portfolio and with the advancement of our broader pipeline in 2016 and into 2017. I will now hand back to Pascal.

Pascal Soriot: Thank you very much, Sean. We now open the floor for questions. Before we do that, let me just quickly summarize what we told you today, and ask if

you can move to slide 29. Essentially, we are – the message is we are very much on track, when we reflect on the progress we're making across the entire company. It also reflects the implementation of some of the commitments we gave you that included our reduction of SG&A cost, and it reflects the progress of our pipeline. The important point I would like to make to you is that we are really kind of still at a pivot point, if you will, we have actually rebuilt our pipeline with great success, in fact more than we expected to.

And we have now a tremendous number of exciting projects in oncology, in specialty care, but across the entire portfolio including respiratory and cardiovascular disease. And so, as a result of it, we really have to accelerate the shift to our specialty care, more balanced specialty care/primary care portfolio. So the programme we've announced today is really reflecting this pivot to a more balanced specialty care/primary care portfolio, and it's reflecting the strength of what we've seen in the pipeline, and the need for us to invest more in oncology, to invest more in preparing all those launches, and to invest in specialty care as we reduce costs in other parts of the business, reduce SG&A and facilitate that with deployment of resources. So all in all, we are very much on track with what we told you. Pipeline is coming online in effect faster than we thought, and we are starting to shift and prepare ourselves for the launch of these new products.

We reconfirm our guidance for the year, and we'll now stop here and I'll open the floor for questions with Tim Anderson at Bernstein. Tim, go ahead.

Tim Anderson: Thank you.

I'm trying to understand the comments about sharpening focus and what that means exactly. So you talk about that benefitting primarily SG&A, that would suggest that narrowing focus is not really on the R&D asset side but it's almost more on the in-line brand side.

My question is, does that narrowing focus imply that you're going to sell off or partner in-line brands, and if so is there any chance that these are wholesale divestures of entire therapeutic areas, or are these kind of items one at a time.

And then second question is on the MYSTIC trials as you know readout and first half of 2017, that's PFS. It's pretty clear there's a delayed response from I/O, with the CTLA reports specifically there is sometimes pseudo-progression before there's regression. So it seems that if PFS was the first readout that could embed some real risk: can you comment on that and then, will we see the LSD in 2017 or not or will that likely be a 2018 event?

Pascal Soriot: Right thanks very much Tim. So Sean if you want to answer in a minute, on the MYSTIC questions. The first question about narrowing the focus, thanks very much for this question because it really helps really sort of clarify the comments we made, and what we are trying to achieve here. Essentially focusing means we are going to really focus on oncology, cardiovascular disease, and we will continue in fact accelerate the partnering of assets in CNS, and infection, including autoimmune. Now we are going to invest more in oncology, and in other specialty care products. So as a result, certainly we will – this focusing has an impact on R&D, but a lot of what we said would be reinvested. And so we believe that this focusing here will help us maintain the R&D budget to deliver. We told you we would try to contain it, whilst investing more in oncology. On the savings side essentially we are continuing to reduce the SG&A cost, as we told you we would, and basically those savings will flow to the bottom line. In fact, the savings we've communicated of 1.1 billion are the net savings. We haven't communicated more details, but I can tell you in fact the savings are bigger than that, and we're making a big reinvestment in oncology and specialty care as a whole, and the $1.1 billion is the net of all of those movements.

Sean, do you want to cover the…?

Sean Bohen: Yes. So Tim, let me see if I answer this because arguably what I'm going to do is reiterate things that we said at the end of year, for 2015. Overall survival, I would say that the balance of the data that we are getting in immuno-oncology across companies, seems to indicate that overall survival is really necessary to capture the full benefit of immunotherapy for cancer.

Even recently at AACR we got more data, albeit in head and neck cancer, not non-small cell lung cancer, indicating that the overall survival benefit which was quite robust, was not very well captured in progression free survival. Or in response rate. So with regard to MYSTIC taking all of this into account, we were very fortunate to have the opportunity to elevate overall survival to a co-primary end point, and that does necessitate an increase in the size of the trial, the power for that end point. But our recruitment has been so robust that we've been able to do that without actually delaying our guidance that we should have data in the first half of next year.

Tim Anderson: I'm sorry I guess my question is on the PFS specifically. We get pseudo-progression with CTLA-4, and that kind of puts that end point at risk, and Pascal, my question on the narrowing focus is really does that involve out-licensing or sale of branded in-line products?

Pascal Soriot: Truly sorry, I should've been clearer there. No, I mean, certainly we will continue partnering in-line products just like we've done it with Plendil in China where we think we can generate additional sales by leveraging the capabilities and investment of partners, but there is no intent to out-license large products. Certainly we will continue partnering, but no, we might divest smaller products, but as we've done in the past but that's about it. So if we did it's going to be driven by the focusing on the core TAs for instance in infection we might look for partners for our new products in antibiotics.

Sean Bohen: Let me clarify Tim for CTLA-4 for are you referring to DETERMINE and the mesothelioma data?

Tim Anderson: No, no, there's been recognized a phenomenon when you give CTLA-4 that the tumour sometimes progresses before it regresses, so if the readout, so this is from prior data sets and tumours like melanoma, for example, that's led to mention that PFS is not a great end point. So if PFS is the first readout with MYSTIC and MYSTIC is looking at a CTLA-4 combo, doesn't that potentially put that readout at risk of being negative on the PFS, just the PFS side, I understand the O/S will capture the benefit, but my question is really on the PFS side.

Sean Bohen: Yes, so pseudo- progression phenomenon is what you're referring to. So, couple of things about MYSTIC. One, it does have a single agent durvalumab in both PD-L1 positive and PD-L1 negative patients, so we have an opportunity to look at the single agent durvalumab. Is there a risk to PFS? I think it's less from pseudo-progression and I think it's more from the possibility that PFS doesn't capture the benefit of immunotherapy completely. We've seen that in other trials not just with CTLA-4, but also with PD-1/ PD-L1 agents, and I think most recently the checkmate 141 data that was presented at AACR, with head and neck cancer, had what looked like a pretty nice overall survival benefit, but no PFS benefit. And a very modest non-significant difference in overall response rate. So we have accounted for that risk in the prioritisation of endpoints and the change in size from MYSTIC.

Tim Anderson: Thank you.

Pascal Soriot: Thanks Tim and so moving to Simon Baker from BNP Paribas, Simon, go ahead.

(Simon Baker): Thanks a lot for taking my questions. Firstly, and continuing on from Tim's question on sharpening focus, what one way presumably accelerating the sharpening of focus would be to move from doing product by product deals, to larger partnering's or divestments or carve outs of products: is that something that you would consider doing either en masse or via therapeutic area rather than the single product deals?

And then secondly a question for Luke on China. Your performance in China in Q1 was very solid, there's been very divergent performance across your peer group. I just wondered if you could share your thoughts on the market dynamics in China at the moment, and why you seem to be significantly outperforming some of your competitors. And then finally a question on medi-4166, the PCSK9 GLP-1 combo, I wondered if you could now that that's moved into phase 2, give us an update on your development plans for that molecule? Thanks so much.

Pascal Soriot: So you want to start with China?

Luke Miels: It's a combination. We have a very good commercial organisation in China. We are investing extensively in R&D and we've had announcements with WuXi, and we also have a discovery unit in Shanghai. But also we are benefiting from a very attractive combination of products for China right now. I think if we looked in 10 years' time, that collection of products may not be as competitive, but right now it's extremely competitive. So we've got a good sequence here. We got products like Pulmicort, if we look at Pulmicort around half our sales of Pulmicort come from the top 1000 nebulizing centres.

The next bracket, the other half, is around 6000 other centres. And that expansion continues. So there are lots of opportunities with products like that, or for some of the other products such as mepo continue to grow. So it's a good mix of products. Then if we look into the medium to longer term, a product like Tagrisso is extremely exciting in terms of the value that it could add to treatment for patients in China.

Pascal Soriot: I think in China, Simon, you have to consider a few things. First of all, we have a tremendous pipeline portfolio that really fits the needs of China at this point in time too -- we have a tremendous team, a really fantastic team of people there. And certainly we've invested and will continue to invest as Luke was saying, and so this combination is leading to, we believe, the great results we see and we believe they're sustainable. By the way in Q1, just for you to consider, is that last year, the first quarter we had an increase in inventory in China, this quarter we had a decrease. So the inventory movement played against us in the quarter this year, when you compare to last year, so our market sales are even better than what you see in the reported sales in China.

Very strong performance far above the market growth rate. As far as the focus, you know, I don't think I can comment more specifically and give you a lot more than what we have said so far, but the focus you know, we are considering all sorts of options but essentially it's really continuing to sharpen the focus in the core areas we have communicated before: the place where we

could potentially partner more broadly is antibiotics for instance, where we have a couple of very interesting products, I mean, CAZ AVI for instance just got approval in Europe. But it is not an area where we want to focus and we may partner that, CNS is another area of course.

So it's essentially going to be, autoimmune is an area where we also look for partners except for anifrolumab, which we decided to make an exception of and keep to ourselves, that will enable us to invest more. With CAZ AVI, by the way, just a clarification, when I say 'approval' it's actually the CHMP positive recommendation, of course, we still have to have final approval but it's a very nice signal for this product.

So that's really what it is we are doing, and in fact we've communicated that before, but we're doing it in accelerated manner. And we also are including the autoimmune assets which we had not made clear – we had not made clearly candidates for partnering in the past.

PCSK9 GLP-1, Sean, you want to cover that?

Sean Bohen: Thank you, Simon for asking a question about a Phase I-II molecule. That's fun. So MEDI4166, if you look at our full Q1 results, you'll see that it moved into phase II, it did that in Q1 of 2016. So our Medimmune group is moving that forward very quickly.

Pascal Soriot: So you have to wait a little bit longer to get more information…

Sean Bohen: I'm not going tell you more!

Pascal Soriot: We also have a glucagon in early development by the way, which is also moving quite nicely, but we need more data before we can give you an update. Let me just go back, by the way, to the externalisation to be totally 100% clear: in many of those areas, like autoimmune, for instance, we have tremendous antibodies for infections, we have a tremendous team of scientists and they're doing a fantastic job. Our intent there is to continue doing research and early development in those areas and retain the teams we had because

they're doing a fantastic job. So when we talk about partnering, we talk about partnering at the development stage for development and commercialisation of those assets but we certainly will continue doing some research in those areas.

So next question is from Diana Nah with JPMorgan

Diana Nah: Hello, thanks for taking my question. I have three questions, please.

So first, what key data will you be presenting at ASCO and what updates will you be providing at your ASCO meeting please? And then secondly, so Merck has filed already for their PD1 in head and neck cancer and I'm wondering where this leaves you in terms of the HAWK study and the potential for fast-track filing for development, please?

And then thirdly, despite the addition of the PEGASUS data onto the label, *Brilinta* sales trajectory hasn't changed very much. Should we expect an inflexion or a continuation of the current trend, please? Thank you.

Pascal Soriot: Thank you, Diana. So one question, by the way with PEGASUS, I assume you are talking about the US, because in Europe we're still in the process of getting reimbursement, we're only launching in Germany and the UK so it's very early days. So maybe, Luke, you could start with the PEGASUS question and then Sean cover the other two…

(Multiple Speakers)

Sean Bohen: So the trend, it's a positive trend so at the end of last year around eight percent of Pegasus scripts were with 60 and we're up to around 14 percent now and actually it's even trending higher than that, but I would say if we look at the number of people being prescribed 60, the bulk of them are coming off the 90, so very much in line with the label. The other thing is, if we look at the guidelines, we have class I recommendation for treatment up to and beyond 12 months anticipated treatments. We also have a class II recommendation supporting *Brilinta* over and above clopidogrel, so these are things which are

positive, and actually if we look at the weeklies that we just got in now overall they've moved up to 12 percent which is the new high. So it is a build.

I think the key thing is if you look at the trends, when people are discharged from the hospital, and this is true for clopidogrel, it's true for Effient as well, we lose a lot of people in that first couple of months.

And so that's a big focus for us is to make sure that they're discharged, then what we can see is if they go out to 12 months then they have a higher chance of being switched to 60 so this collection of positives hopefully should further drive growth.

Sean Bohen: All right. So I'll give a few highlights for ASCO first and then I'll get onto HAWK. What we're talking about here is submissions of abstract, so not everything is finalized, I want to be careful to qualify that. So with regard to our DNA damage response portfolio, we have *Lynparza* monotherapy, in ovarian cancer, we also have early trials, both monotherapy and combination, that we will present and also updates on the WEE-1Inhibitor AZD1775; for *Tagrisso*, I alluded to this a little bit, we are going to present some brain metastasis data from the BLOOM trial for immuno-oncology, we're going to talk about durvalumab in bladder cancer.

And as I mentioned, that's the indication that has breakthrough designation, recently granted breakthrough designation from the FDA. We will see the DETERMINE data obviously the trial was negative top line. We announced that before but we will get a detailed look at the data and some early combination data in I/O and then acalabrutinib as well will have a couple of abstract updates and there's the potential for FALCON results as well.

And then the next question was HAWK, given the Merck filing: the HAWK data we expect in the second half of 2016, has fast-track designation from the FDA and should the data support it obviously, we can still file the data.

Again, accelerated approval of an agent in an indication doesn't close out further submission in that indication. So our hope is that if HAWK's positive,

the FDA will have both filings in front of them simultaneously and can evaluate and make their own decisions.

Pascal Soriot: Thank you. Next question from Sachin at Bank of America. Go ahead

Sachin: Hi, a couple of questions please, first on the durva treme combo, you're not citing next presentation of data. So I wonder if you could just clarify when you'd have the next update for the phase I lung and when we could expect PFS from that, and then data for the combination in tumours beyond lung, the reason for question is Bristol is alluding to both sets of data at ASCO; secondly on CAURAL, you've outlined you've stopped recruitment of the *Tagrisso* durva combo, it sounds like more of a trial design issue, so are you considering *Tagrisso* durva with a new trial design, any colour you can give around that?

And just one financial, you've clearly outlined continued appetite for earnings accretive bolt-on on deals but I wonder if you can just clarify that statement in light of the fact you did two deals last year and the need for an earnings accretive deal given that by the time you announced it today and it closed, you were basically sitting close to an earnings inflexion anyway, so maybe just outline your thoughts around that? Thank you.

Pascal Soriot: Yes, thanks, Sachin, so maybe let me cover the last one and then, Sean, if you want to cover the other two, the other first on data and then *Tagrisso*.

So on the earnings question is, you know, what we want to signal is that in the last 2 to 3 years we have worked very hard to rebuild our pipeline both internally but also externally and we've had a number of acquisitions. If you look to those acquisitions they all fit in the pipeline in our main areas and by now we have a full pipeline getting stronger day after day.

I mean *Tagrisso* is a good example. The product is making incredible progress. A year ago people didn't think we had a product and today we have a product that is really making enormous progress. But as a result, we have to

put more money into developing and preparing for the launch of such products.

So essentially we said we're going to focus now on execution, turning this pipeline into reality for our patients and our shareholders, and any acquisitions we would consider would still reflect the criteria we had before but on top of it we have this criteria of the fact that it should be earnings accretive. Now do we need an acquisition to be successful? We believe we don't. But if we find an acquisition that would be earnings accretive and continue to strengthen our strategy and our pipeline and our portfolio, we would certainly do it, beyond that I cannot say much more.

Sean, do you want to cover the other two?

Sean Bohen: Sure. let me start with CAURAL, so as we have communicated late last year, we saw an interstitial lung disease signal in the CAURAL trial in the combination of durvalumab with *Tagrisso* and further analysis of that, as I said, we decided not to restart enrolment of the trial and we do not have intention for further study that combination.

With regard to 006, the phase I trial we continue to expand the trial. We do not currently have a particular date for when we will announce or share the data from that expansion.

And then I think I went through pretty extensively what we intend to have at ASCO specifically.

Pascal Soriot: Excellent. Andrew at Citi will go ahead.

Andrew: Three questions please. I am not quite sure – Astra's been linked to Medivation in press articles. I wonder if you care to comment on the appetite for engaging in a very competitive bidding process for this asset, given the earnings accretion which is more the focus now than the state of pipeline that you outlined.

Second there's been some notable departures from Medimmune and Astra on the R&D side; Ed Bradley retired and your Head of Development and your I/O Head of Research have gone to competitors: could you outline replacements for those positions and the impact, if any, on the organisation and then finally with regards to the shaping focus initiative it does mention R&D productivity as well as SG&A and marketing.

So how should we think about any change in the current relationship between AstraZeneca and the Medimmune organisation, either as a function of that initiative expressly or other factors there that may be going on concurrently?

Pascal Soriot: Thanks, Andrew, a few great questions, I mean… Medivation, it's a good question, but I'm sure you don't expect me to really answer that question.

So, apart from what I've just said in answer to Sachin's question, I really want to comment more than that.

I guess you have to see what we do, but I have to say we're very committed. We are very focused on delivering our pipeline. That's really our number one priority and we'll do nothing that would distract us from this because we are at a very important turning point, I mean, look at *Tagrisso* again, I don't want to be repetitive but I mean, this agent is so exciting. The I/O study we can't share this data because those are commercially sensitive but in terms of recruitment, I mean this study, the recruitment of the studies is going gangbusters – I mean, it's really going very well and we really want to stay very focused on turning this into a reality.

The other question, R&D productivity, there is no intent to challenge the model at all, we think we have a great model, but there is no perfect model of course. And a model is usually an assumption of what you think, what you believe in, but also what is right for your organisation and so different companies will cover with different responses depending on their own culture, their own people, their own history, and a variety of all those things but that model we think works for us and I guess hopefully the pipeline is there to support that statement.

So there's no intent to change that – the question about changing, losing a few people. First of all, we lost a couple of people, and they were certainly regretted losses, because they were good people but they got great jobs.

And I'm a believer that people have to of course grow and develop and so disappointed in one hand but on the other hand happy for people when they take a great job. It also shows that we have great people and it also shows that all the companies are looking at our people so it's really a great reflection of the strength of our organisation, the strength of our people.

And the final comment I would make here is that we talk about people departing, we never talk about people joining us and I can tell you we've had, like, so many great people joining us and I've got one sitting next to me on my left in our new CMO.

But we had also many other tremendous talented people joining us. So always sort of sorry to see someone good leaving even though you are happy for them to see their career develop, and on the other hand we welcome new people and we always try to recruit very talented individuals who will strengthen our organisation.

So I think that maybe covers this and we'll move to Nicolas Guyon-Gellin Morgan Stanley. Go ahead.

Nicolas Guyon-Gellin: Hi. Thanks for taking my questions. I have three actually the first one was on the SG&A standing and the volatility in the last three years. So you increased G&A by more than a billion in 2014 then you reduced it by about 1 billion last year with others cuts to come in 16 and 17. Not sure I understand what makes your promotional spending so easy to switch on and off, and isn't there any risk to underinvest behind your brands, notably with all the new launches that you have?

Second, in the U.S., correct me if I'm wrong, but it seems to me that you only communicate on filing when it has been accepted so could you please confirm that you have not yet filed saxa/dapa in the U.S.? And finally on MYSTIC, I'm sorry to come back, just a clarification on Sean's previous comments, you do expect PFS data in H1 17 but do you also expect OS data in 17? Thank you.

Pascal Soriot: Thanks Nicolas. So where do we start, MYSTIC? Sean, do you want to cover that?

Sean Bohen: Sure I can cover that, yeah so I confirm for you that we confirm filing when the filing is accepted. And we haven't mentioned it because the filing has not yet been accepted. With regard to MYSTIC PFS data first half of 17, that is correct.

Obviously these analyses are event driven and in first-line non-small cell lung cancer the survival events or deaths are considerably delayed from progression so it will be further out before we have overall survival data. There will be some events but it will not be mature or powered in the first half of 2017.

Pascal Soriot: Thanks Sean. Also SG&A question you have to think about what has happened over the last couple of years because first of all we acquired the BMS franchise. Secondly we acquired the portfolio of products and each time we welcome new people with, so that drove an increase.

And each time we decided to focus the organization, we continued to keep the focus on the launch and the promotion. But we always said over time we would gain productivity improvements across this entire commercial organisation. This is basically what we are doing now.

So we always sort of fine tune it so we remain competitive but certainly we are looking for improvement across the entire commercial organisation so we can deploy resources and invest more in oncology but at the same time of

course protect our profitability and the delivery of our dividend which is an important part of our commitment.

So maybe we can move to Matt Weston with Credit Suisse. Go ahead.

Matt: Thank you for taking my questions, three if I can.

The first on the new focus on SG&A costs. It is a topic that management has been talking about for some time.

And if I look at consensus estimates is already a substantial saving in SG&A baked into consensus assumptions.

Can I just check that -- are you indicating that this is the way management is actually going to deliver something that's been talked about for some time or are you indicating that there's an incremental $1 billion on top of what consensus already has baked in that we should consider from a cost base?

Secondly, clearly strong success in China, a number of your competitors are highlighting a risk in the second half of the year as reimbursement for some drugs goes from federal to provincial governments. How do you feel about that, given it's such a substantial business to you?

And then finally on MYSTIC, Sean, I assume you're going to be relying on the contribution of component's pathway to file the combo if neither of the drugs has received accelerated approval before the MYSTIC results are out.

Have you actually had interactions with the regulators that suggests this is acceptable because, by my read of the rules, you could argue, and particularly given that you're doing treme mono arms in a number of other studies, you could argue you really should have a treme mono arm in MYSTIC if you're relying on it for the approval of two novel drugs simultaneously? I'd love your feedback on that.

Pascal Soriot: So I can cover first question that SG&A essentially it is implementation of the commitment that we made that we will reduce SG&A over time, starting this year and showing that we continue reducing SG&A in the next couple of years.

And essentially it's reflecting the shift of our pipeline and portfolio to a more balanced specialty care/primary care mix, and we are re-deploying our resources and our efforts to this future portfolio. As to your specific question relating to 2017 and whether it's additional to the consensus forecast. I will not answer this because if I did, I would give you a guidance for 2017 which we haven't done so I'm sorry, I cannot answer it. We'll give you guidance for 2017 in the early phase of 2017 as we always do. Suffice to say we just kind of continue doing what we said we would do: we said we would reduce SG&A, we're doing this, we said we'd build a pipeline, we're doing this and essentially despite quite a number of sceptics we continue doing what we said we would do and continuing to prepare to bridge to 2018. And then maybe one point about 2018 is to think about how the pipeline is shifting to specialty care.

And with the addition of the acquisitions we made last year we should consider this and think that as we kind of rebalance we should have leveraged growth in 2018 and beyond and therefore quite a profitability rise because of the changing mix and the shape of our pipeline; as far as China goes, maybe Luke, you want to add something here, but we are – we believe we continue to grow very rapidly in China.

And we continue to believe we can outpace the market in China and just want to highlight we believe we have critical mass in China: it's really an important point and we have a tremendous team we think it is going to be a tremendous business for us in the years to come.

And today we are relying on the portfolio we have which is really exactly what the Chinese patients need today, specifically in the areas of vascular and diabetes. I mean, diabetes, everybody talks about diabetes being a difficult market in the U.S. and it's true, but we need to keep in mind it is a really

important growth driver for emerging market businesses, in particular in China, it's going to have an important part to play.

So that's where we focus on today but also we're starting to prepare the launch of our new oncology drugs. Luke, do you have anything to add now?

Luke: I'd just add, we have a third of the patients on DPP4s in China and if you look at *Brilinta* alone it's not reimbursed and we only have one percent so not all our portfolio is exposed to reimbursement.

So I agree.

Pascal Soriot: *Brilinta's* not even reimbursed yet China, we're doing tremendously well already in the first few months…

(Multiple Speakers)

Sean Bohen: …Yeah, the contribution of component.

So I guess a simple answer to the question is that we are confident in our strategy around contribution of components, particularly the data that we will have for tremelimumab, that is based on interaction with regulators.

So the fact that it doesn't occur in the same trial within MYSTIC we do not view as a challenge.

Pascal Soriot: Richard Parks with Deutsche Bank. Go ahead.

Richard: Thank for taking my questions.

Firstly, on saxa/dapa, updates: Heart failure signal- are you assuming you have also this label? Could one of you could update us on that work and whether that level is likely to impact your expectations for the saxa/dapa product?

Secondly just a couple of product ones really, Bydureon in the U.S. is flattening, just wondered if you could update us on any plans that you've got that might help to reinvigorate that, I know you've been working on some different pens in development devices. And then finally, on ZS-9, I wanted to get an update on your interactions with the FDA and how confident you are about achieving a label without the disadvantage of drug to drug interactions. Thanks.

Pascal Soriot: Thanks, Richard. Should we start with Luke, then Sean if you could cover the ZS-9, US and also the saxa/dapa label question?

Luke: Yes so you're right. It is very competitive meaning we're holding share because we have a very focused effort. It's interesting, there's a pull of physicians that have a lot of confidence in *Bydureon* and have a very favourable view towards the pen and you can see that in the numbers.

I think it continues to be… I mean it's a very attractive area to operate in and I think the recent outcome studies just reinforce that, I mean many of us have been following this class for a long time. I think a couple years ago if you had to pick a class that would have a positive outcome study, then the GLP1s would be the ones you'd put at the top of the list. And I think again recent years we've now got two outcome studies which are favourable for the class and we have ours ongoing.

In terms of life cycle, we have a number of things that we're looking at that we will update you on in the future. If we look outside the US, and I think sometimes we forget that sticking with the diabetes portfolio, we are really in good shape in Europe as well as emerging markets with *Bydureon*, *Onglyza* and *Forxiga*.

Pascal Soriot: Thanks Luke. So Sean, the ZS-9 question was about FDA interaction and then, Richard, apologies but on saxa/dapa, we were not so sure we got the question, so if you don't mind, we'll ask you to repeat it.

Sean Bohen: I'll do the ZS-9, then we'll try and get a clarification. So the answer to the ZS-9 is the due date as we have communicated, is the 26th of May and we have had relatively typical interaction to date with regard to approaching that due date and obviously when we have more definitive details, we'll communicate it but that's all we have right now.

And then again, as Pascal said, clarify a little bit what you're looking for around saxa/dapa?

Richard: Yes, on saxa/dapa, with two components firstly, what impact does the label update have on your expectations for the combination product and then secondly it's obviously still not 100 percent clear whether the heart failure signal is a drug specific or a class specific effect. I know there's been some work exploring the mechanism there so just wondering if there's anything that might come out that might help us delineate whether it is a saxa specific or a class specific issue.

Pascal Soriot: OK, Richard, so there are two parts to your question, I guess one part is for you, Sean, with heart failure and we do anything to understand that data. Our focus now is really very much on *Farxiga*. But some questions for you here and then the next question Luke, is probably for you Sean: I mean, we are looking at data to try to investigate DPP4 for heart failure, there's not much I can communicate until we actually have the data and see what we find. We do think that the label will be for our class so not specific to particular agents in the class. So I'll let Luke Miels talk about the impact…

Luke Miels: I mean it's interesting. I think it's around 100 million now so it's not insignificant and it's clearly an unmet need if we look at the combinations that we have with metformin is a sizable part of the business. I think we also need to balance that with exactly what you commented on which is the presence of a device and a combination.

So I think it's hard to say at this point. We need to look at the ultimate label that we get feeding into that as well as look at it from the portfolio level.

I think with regard to our outcomes study, we hope we have some positive news ourselves. It has raised expectations for the sub-class in the medium to long-term including a very competitive participant there and also again, if I look at the overall diabetes portfolio, it just reinforces that we've got more positive news and right now we're competitive in that segment so it is like anything in R&D, the puts and takes and depends on which label we get with saxa/dapa.

Pascal Soriot: (Simon) go ahead.

(Simon Baker): Thanks can you hear me. OK great appreciate the opportunity for the questions.

Just a few here. First off can you talk a little bit about your continued emphasis of the $45 billion target and progressing towards it? Just seems in the context of slow primary care launches and some of the dynamics there that data almost works against the goal of the business which seems to be shifting much more towards a specialty space and opportunity towards much greater profitability. So just wondering why you guys haven't moved away from that, particularly as greater externalisation continues.

Second question is on the opportunity for Lynparza. Historically guys of talk about *Lynparza* in the PARP class as a $1 billion sort of blockbuster opportunity. How has that been evolving particularly in the context of the information that you're gaining the I/O combination and also from studies like TOPARP?

And then my last question really is just a clarification or just trying to get a better understanding, Sean Bohen, you specifically said that you've increased the size of the MYSTIC study to capture the benefits of overall survival I'm a little confused by that.

Because I would think that you need the power of the study to be more for (PFS) rather than overall survival because it seems like smaller studies within the oncology products tend to need to be run longer rather than be larger.

So I'm just trying to get a better understanding of the comment? Thanks.

Pascal Soriot: So few good questions here. MYSTIC and Sean Bohen, if you want to answer the first question I think there are two parts within it. Luke Miels do you want to talk about potential of *Lynparza* and then I'll cover the $45 billion general question. Sean, do want to start first?

Sean Bohen: Sure let's talk about MYSTIC first. Yes, so the issue of overall survival versus PFS, your point is that there's a trade-off between time and power.

So it's an event driven trial so you do the analysis based on the number of events you need. The issue about the size of the trial is obvious if you have more patients you get the number more quickly.

So I would say that we have taken advantage of our robust enrolment to make the trial larger.

And to also be able to accumulate those events in a way that we can keep our PSF in the first half of 2017. The other part of it is you have to power for both primary end points.

So when you do that you then have to power for both endpoints and so when you make two primary endpoints you do have to make a larger trial.

With regard to *Lynparza* we started with sort of the purest, easiest to define patient population which is the BRCA patient population.

But as we said many times there are multiple ways that DNA damage repair can cause effect, I think the data from prostate cancer really illustrates this, because there was a way to select patients based on a panel of different mutations and defects that can lead to DNA damage repair problems and the data has been quite interesting.

So we see the potential of *Lynparza* as being able to expand quite a bit beyond where we started with mutation ovarian cancer. And then the other thing I would add is that we do have a whole portfolio behind that I mentioned (AZD 1775) WEE-1 inhibitor and we are starting the drugs in combination as well. So you can see this as really extraordinary potential portfolio for treatment cancer.

Pascal Soriot: Thanks Luke. And I'll just add a comment to the point earlier. DNA damage response is a core component of some of the R&D we are redirecting and we believe we are in the lead. Obviously oncology has been focused for some time on something that could continue to give positive trends of data. We have got data at ASCO with quite good responses and the number of patients continuing on treatment is a little bit higher than we originally modelled.

When we see the data emerging, we're certainly encouraged by the early *Lynparza* level of prescriptions and testing when talking in the community about it.

Pascal Soriot: Thanks. So to answer your general $45 billion question: I would note that given currency fluctuations, I think you will be more around north of $41billion.

Just to add a quick reminder the currency pressure cost us about one dollar in EPS term. So if you calculate EPS in 2013 rates it is kind of the same. But when looking to 2023, at our long-range plans, we will get there.
There is downside and upside in that plan. Some products are being a little bit less valuable and others will be more valuable in that estimate. And some products we will divest or not count because they are because they are launching in 2020 or beyond.

But on the other side we have the upside progress -- *Lynparza* was recently adjusted because initially we didn't necessarily think that *Lynparza* would have the potential we think it will have now.

So you know, as Luke said, puts and takes and the plan number and upsides and downsides are important pieces. One other shift in the plan we had developed and communicated two years ago is that the plan is more likely to have a larger proportion of oncology and more specialty care Products.

So we will maybe finish with one last question from (Ryan). Go ahead.

(Ryan): Yes. Good afternoon.

Three short ones. First in Japan, if you talk about the potential of *Tagrisso* in Japan can you approximate more precisely how big you see this drug in Japan including how we should think about price versus US and about the ramp-up maybe for the drug in Japan?

Second Nexium revenues in Q1. Just to be clear about what you call revenue from Pfizer. Is that a one off? Does that include also royalties? How should we see the specific agreement across the year and maybe across the years to come?

And lastly very short one about brodalumab. Looks like you are now expecting the final approval and the launch in 17. Does that mean that there won't be any further milestone from 16? And by the way did you get any reassurance of their commitment to the drug from Valeant in the recent past?

Pascal Soriot: Thanks. So maybe Luke you could take the Japan ones?

Luke Miels: Yes, sure. If you look at patient numbers in Japan, it's around 8000 and it's not 80,000. And then if you look at second line T790M mutation rates, it gets to around 70 percent of 8000 patients for the mutation rate is actually higher incident in Japanese patients -- the key thing here is ultimately looking at second line and get very interested in the potential to challenge first-generation TKIs in the first line in Japan is a very encouraging marginal opportunity.

Pascal Soriot: On the Nexium milestone, this is the second milestone we received from Pfizer. This is a sales milestone. Other milestones are related to approval dates and we have to work with Valeant to get approval. We are also working on Europe and Japan-based milestones that are defined by timing of our -- at this stage, I mean – Luke do you want to comment on that?

Luke Miels: It just -- what we've done is made the calculation based on when the filing was accepted and then we look at when to predict the approval would be. That's why you have that date there.

Obviously it's a regulators discretion when the actually act, but the way we do this is perhaps the conservative we and that is to use the filing submission as the basis for calculating the launch date and that's what you're looking at there.

Again, when the milestone is triggered depends upon the regulators actual approval so we're forecasting 16.

(Off mic)

(Ryan): So the launch would be in 16 probably?

Pascal Soriot: I think you have to just do the math for yourself. It would be defined by the approval date as Sean said, and really have to make a judgement call at this stage. And there's also the question of the timing approval in Europe, we don't have at this stage more data to kind of give you indication one way or another.

As far as the timing dates, we just we keep working on this with our partners and also the regulators to see what is the best way to get approval. We really don't have much more we can share compared to what we really told you before.

(Ryan): OK. Thank you

Pascal Soriot: Thank you so much. So maybe we will close here and again we would like to thank you very much for your interest in AstraZeneca. And we would like to wish you a good day. Bye-bye.

END