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# EDITED TRANSCRIPT

AZN.L - Full Year 2013 AstraZeneca PLC Earnings Conference Call

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## OVERVIEW:

AZN.L reported full-year 2013 revenues of \$25.7b, core operating profit of \$8.4b, and core EPS of \$5.05. 4Q13 core EPS was \$1.23. Expects 2017 revenue will be broadly in line with 2013. Expects full-year 2014 revenue to decline low-to-mid single digit on constant currency basis and core EPS to decline in teens.



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## PRESENTATION

**Pascal Soriot** - *AstraZeneca PLC - CEO*

All right. Let's get started. Good afternoon, everyone. And welcome to our full-year 2013 results presentation. It's really nice that so many of you could actually make it today despite the tube strike.

As you can see, I'm actually joined today on the platform by Marc Dunoyer for his first quarterly results as our new Chief Financial Officer. Welcome to you, Marc. Marc will take us through the business performance, the 2013 financials and then spell out how we will guide for 2014.

You'll also hear from Briggs Morrison and many of you know Briggs already. Briggs is our Executive Vice President for Global Development and our Chief Medical Officer. Briggs and his team will become more and more familiar to you, I'm sure, over the coming years as attention shifts to our growing pipeline. And it's a pipeline that is balanced with small and large molecules, but also primary care and special care products. So, we believe we have a well-balanced portfolio of products.

To help you keep track with our rapidly maturing pipeline, what we decided to do is that on moving forward we will provide you with an updated pipeline table every quarter, not just twice a year.

And maybe one more thing to point out before we get started. We've actually listened to your feedback and we'll try our best to get through the presentation today as quickly as we can so that we can address your questions and wrap up this session in the less than 90 minutes that we usually dedicate to this meeting.

So, if I had to choose two -- one word, actually, to describe 2013, I would use momentum because I think we've made good progress and we are on a good momentum. As some of you heard me say at last month's JPM conference in San Francisco, I believe we're on a journey and our journey



starts with we're building our pipeline. Looking back over the last 12 months it's clear that we have made progress in this area. We're building momentum. But there's still a lot of work ahead of us.

In 2014, we'll actually continue to advance the early stage pipeline. And we're focused on the three core therapy areas that we selected and we communicated last year to you.

Our goal is that by 2017, our revenues, as we said before, will be broadly in line with our 2013 revenues. And we actually believe we can return to growth faster than many people have been forecasting so far.

And finally, as this graph -- this chart shows you, our ultimate objective is to employ -- to leverage our science, the strength of our science to become a leader, a science leader, and, of course, a commercial leader, in each of our core therapy areas.

So, before we turn our attention to the future, I'd like to touch on 2013 performance.

The headline here is that despite having to navigate the anticipated loss, specifically on several brands, we actually delivered a set of financial results that were in line with our expectations.

Revenues were down 6% at CER to \$25.7b, as we continued -- as we continued to invest in our pipeline and in our growth platforms.

Core EPS declined by 23% at \$5.05.

And, our commitment to our progressive dividend policy is reinforced by the payment of the second interim dividend of \$1.90, which brings the total annual return to \$2.80 per share.

Now, if you look at our global revenues by region, the US and Europe are, of course, continuously impacted by the generic competition and the government interventions. Nothing new there.

The good news is that our emerging markets delivered growth in the high single digits, as we communicated early last year, and, importantly, on a steady basis quarter to quarter.

And Japan progressed by 4% at CER. This is underestimating a little bit our performance, our Group performance, in Japan, as I will show you later.

Now, we laid out three strategic priorities during our Investor Day in March last year. The first one was to achieve scientific leadership in our core TAs. The second was to return to growth as quickly as we could. And the last but important one was to keep building a great place to work.

AstraZeneca is a great company. And we want to keep building our culture, simplify how we operate and make decisions faster than we have in the past. A good example of this is how we've integrated the diabetes business. We've done that very, very quickly.

In 2013, we've made good progress against all those priorities. But I will focus today on the first two.

So, if I start with scientific leadership, we added six projects to our late stage pipeline, as you can see here and we built momentum in the area of scientific leadership.

We've nearly doubled the number of programs in Phase III, or registration, compared with the previous year. That's really a great achievement. And, importantly, those new projects strengthen each of our core TAs.

We've also identified 19 potential Phase III starts in 2014 and 2015 from our internal pipeline. As you can imagine, we'll have to be very selective. Very active also, but certainly very selective in terms of the projects we move forward out of our pipeline, but also on the business development



front. 2013 was very rich in terms of business development activities, as you can see here and we certainly strengthened, again, our core TA. 2014 we see ourselves focused more on execution and progressing what we have in our pipeline.

Targeted acquisitions and partnerships have clearly helped us, especially in oncology where our innovative immunotherapeutics portfolio is attracting more and more attention. We can talk more about this later. Briggs will highlight some of those projects later in this presentation.

And, of course, our biggest single transaction for the last 12 months is the acquisition of the other half of the Diabetes Alliance from our colleagues at BMS. And that gives us -- that gives us the opportunity to strengthen this franchise now that we have it completely in our hands.

And finally, importantly, we've made great progress transforming our R&D model to build this biotech-like culture, supporting smart decision-making, fast decision-making and innovation.

In March last year, if you remember, we announced plans to establish three global strategic centers, including an important one in Cambridge that we are going to build and that move will place our scientists at the heart of the world-leading biosciences hotspots. And, importantly, we're now waiting for the construction of this site. We've accelerated our relocation and, in fact, several hundred people will start moving to Cambridge to rented facilities this year. And we want to take advantage of the science environment in Cambridge as quickly as we can. So, we also made good progress against our goal of returning to growth.

And as you can see from this slide, each of our growth platforms played their part in the overall 10% increase in revenue. We added almost \$1.3b of sales out of these growth platforms from a base of \$12.5b. You see here the addition of those five growth platforms and I'll briefly touch on each of those in turn.

Now if you look at Brilinta, full-year revenues were \$283m. It is fair to say that we are doing very well in Europe and very well in countries like Australia, Canada. And, in some of those countries, we now have leadership position with Brilinta in the OAP market. So, this actually demonstrates the potential of this product and it demonstrates what it can do when marketed.

Of course, driving growth in the US remains our main priority. It's clear that we still have some challenges to overcome. In the United States we are not where we would have wanted to be. We actually, as this chart shows you, we were making some positive movement. Our plans -- the new plans we put in place in the US last year came in full force only by August last year and now we're starting to see some impact. But, unfortunately, the DOJ investigation suddenly impacted us negatively in the latter part of 2013.

We're still focused on this product. We still believe we can succeed. And our US team is very committed to returning to a growth trajectory for Brilinta. But, it's clear that the bottom line is we're doing very well ex-US. There's still more work to do in the US.

So, as we -- we are -- as we look at this product, we are continuing to invest to realize the significant potential that Brilinta offers. I think it is important to remember when we look at our penetration that we only accessed this 20% ACS segment that you see at the bottom here thanks to the PLATO study and the indication we have today. So, we need to remember that and we also need to remember the potential that will come from additional studies.

And, -- so, in addition to, of course, strengthening our commercial efforts, we are still working very intensively on our cycle management. In particular, the large 21,000 patient PEGASUS trial for post-MI is the first one that we will read out in Q1 2015. And then we have SOCRATES for stroke and EUCLID for PAD that will help us unlock more potential out of Brilinta.

If I turn my -- our attention to diabetes now, I guess we made a clear statement of our commitment to diabetes when we announced our plans to acquire the other half of the alliance. So, it's really nice to see that we've completed the transaction very quickly and we kicked off the integration process less than two months after the signing the deal.

The teams have already been meeting country by country and the feedback is incredibly good so far. We've got 4,000 people joining us from BMS who are very committed, very excited about building this unique franchise.



So, with the US launch of Forxiga that is scheduled for tomorrow actually, we have an early opportunity to demonstrate -- demonstrate the strengths of this -- this alliance. I think it is fair to say here that Onglyza was stable in 2013 and you know very well we faced a pretty challenging environment.

Exenatide, the franchise was certainly a bit challenged in the first half of the year, but in the latter part of the year we saw an improvement in the market share as I will show you in a minute.

As you can see here, we have a change in trend for this franchise towards the end of 2013 and we see a further acceleration in the early part of January. So, this February is certainly good news. We see a stabilization of Byetta, an increase in the share of Bydureon and total growth in the Exenatide franchise.

So, if I move to respiratory now, the news is very good here because respiratory did very well. Symbicort grew by 10% last year to \$3.5b.

And, in the US, we increased our share by 7 points, as this chart shows you.

We also saw very strong share growth in many markets around the world, in China in particular. In Japan also. So, very strong results around the world with Symbicort.

And, I think what is also nice to see is the progression of -- of our market share in the United States, as you see here. In the US, the sales reached about \$1.2b. They were up 23% with Symbicort and we grew 7 percentage points in terms of share. And, again, we see a further acceleration in the early part of 2014. So 2014 looks like a good year again for Symbicort in the US, but certainly around the world.

If I turn to the emerging markets now, what we can report here is despite rapidly changing economic circumstances, we actually achieved the growth rate that we guided for. We guided for high single digit growth rate in the emerging markets and we delivered 8% growth rate for the full year. What I think is really important to keep in mind is that it was a sustained growth rate quarter to quarter. And it's -- even the last quarter, we reported 6%. But if you adjust for the inventory decline in a couple of markets, in particular Mexico, in fact, our growth rate was again 8% in quarter four.

What I also wanted to attract your attention here is the success we are experiencing in China. We are now growing by 19% in China for the whole year. And, as the chart shows you, we outperformed the market, which is strengthening our position, number two position, amongst multinational companies. So, 19% growth rate here versus 14% for the market defined by multinationals or defined as total market, is really a very strong sign of our performance in China.

And, finally, I wanted to turn to Japan where again I think we achieved great performance there despite the negative impact of the yen, of course, which had a substantial negative effect on our top line in Japan, and globally, because it was very substantial. Our underlying performance in Japan is very strong.

The reported growth rate is 4% CER, but in-market growth rate is about 11%. And, in fact, in 2013, we gained three places. Our ranking moved from 12th to 9th in Japan in 2013. So, a very nice progression, supported by growth of our -- all our key products.

You can see here Nexium, of course, was in launch phase. We increased our share. But also, Crestor, 2.8 -- a bit more than 2 points of market share increase and Symbicort more than 4 points of market share increase.

So, across our entire portfolio in Japan, a very, very strong performance. That is a little bit unfortunately negatively impacted as we adjusted inventory with our distributors and our ex-factory sales are only reporting 4%.

So, that concludes my remarks. I will now hand over to Marc, who will take us through the financials in more detail before Briggs takes us through the update on the pipeline. Thank you.

**Marc Dunoyer** - AstraZeneca PLC - CFO

Thank you, Pascal. Good afternoon, everyone. Today is my first result presentation as the CFO of AstraZeneca. It's a great honor and a pleasure for me to be here.

Today I would like to focus you on the key priorities I see in our business. Our main strategic priorities are to achieve scientific leadership and return to growth. With this in mind, we need to invest in our improved pipeline and also support our commercial growth platforms.

As the CFO, I will focus our business on cash flow to sustain our ability to service our shareholders' distribution commitments and maintain a healthy balance sheet.

Today I will review the numbers for the fourth quarter and the full year, as well as discussing the key drivers of operating profit and margin. I will also update you of our announced productivity program, the stability of our cash generation as well as our decisions on shareholder distributions. Finally, I will close with a thought on guidance for 2014.

The revenue line for the fourth quarter is declining by 4% at constant exchange rate, with a 2% negative impact of ForEx. Compared to September year-to-date 2013, the rate of decline has been decelerating.

I don't intend to go into any detail on the fourth quarter accounts as the picture is similar to the full year.

Core EPS was \$1.23, in line with the expectations and declining at minus 25% at constant exchange rate.

Pascal covered the overview of the full year performance in his opening remarks. The impact of ForEx on the full-year revenues is negative 2%, leading to a sales decline of 6% at CER.

The core EPS was \$5.05. The currency headwind lowered our core EPS by \$0.17 in 2013.

I will now turn to the P&L for the full year and focus on core margins and profit.

The press release contains the statutory numbers and a detailed reconciliation of the core measures -- to the core measures.

When I refer to growth rates, they will all be at constant exchange rate. The core growth margin was 82% of revenue. This is down 50 basis points compared with last year, driven primarily by unfavorable product mix.

The core SG&A expense was up 7% compared with last year driven by investment in growth platforms as well as a full year of Amylin expenses.

Restructuring benefits and spending discipline did not sufficiently offset the increased investment in growth.

The excise fee imposed by the enactment of the US Healthcare Reform measures amounted to 2.7% of core SG&A expense for the year.

Core other operating income for the year declined by 30%, reflecting the \$250m milestone from the sale of Nexium OTC rights in the prior year.

For 2013, the pre-R&D operating margin was 49.2%, in the middle of the range we had indicated, namely 48% to 52%. However, core pre-R&D operating margin is not a metric that we will report on going forward as we progressively transition from a predominantly primary care company to a mix of primary care and specialty care.

The company will focus on managing its core operating expenses, including R&D, SG&A and other operating income.

Core R&D expenditures were up only 1% to nearly \$4.3b despite taking on additional costs associated with successful business development activity. This was possible due to strong cost control and flexibility in the reallocation of resources.



Core operating profit was \$8.4b, 22% lower than last year.

Core operating margin was 32.6% of revenue, 690 basis points lower than last year.

Turning to our productivity program for the full year, we have incurred \$1.4b of cost associated with the fourth phase of the restructuring, including the footprint and other changes that we announced back in March 2013.

The program as outlined last March would result in estimated headcount reduction of about 5,050 positions over the 2013-2016 period, with a \$2.3b of restructuring cost resulting in an estimation of \$800m of annual benefit by the end of 2016 when the program is completed.

It is now believed that previously announced restructuring activities will cost \$2.5b.

The program has been expanded to include additional activities to create further headroom for our investment activities and the total program cost will now be \$3.2b, of which \$2.4b will be cash cost.

These initiatives will result in annual benefit of \$1.1b of annual benefit by the end of 2016. In effect, 5,600 positions.

The impact of this new initiative has already been communicated internally. For the purpose of modeling, this cost and benefit will be predominately SG&A related.

As we stated in December last year, when we announced our plans to acquire BMS share of Diabetes Alliance, there will be opportunities for efficiencies that flow from combining the two diabetes teams under AZ's sole control. However, we only completed this transaction a few days ago, so we remain at an early stage in that process.

We will carefully assess resourcing needs for markets and country operation on a case-by-case basis, weighing up the potential for sales upside alongside the cost dimension. In that respect, our approach is the same as for the rest of our business.

Lower tax payments and positive movement in working capital offset the lower EBITDA for the year, resulting in cash generated from operating activities of \$7.4b for the year compared to \$6.9b in 2012.

It is worth noting that in 2011, when the business generated an EBITDA of over \$15m net cash from operations, -- sorry, the net cash from operations was \$7.8b. The strength of cash generation is an important feature of our business.

This stable cash generation from operating activities meant that despite cash outflows and business development and acquisition of about \$2.3b, we generated net cash flows after distribution of \$1.4b, so we ended up the year with a net cash position of \$39m.

The investment we have drawn -- we have done on business development have been in line with our three core therapeutic areas. The deals also address what we felt were gaps, either in our pipeline or in access to cutting-edge science.

We intend to continue this focused approach to business development in 2014, although we do not anticipate the deal flow continuing at the same rate.

Turning to cash distribution to shareholders, the second interim dividend is \$1.90 which brings the dividend for the full year to \$2.80, in line with our policy to maintain or grow the dividend over the investment cycle. It is a policy that we are committed to going forward.

The Board regularly reviews its distribution policy and its overall financial strategy to continue to strike a balance between the interests of the business, our financial creditors and our shareholders.



Having regard for business investment, funding the progressive dividend policy and meeting our debt service obligations, the Board currently believes it is appropriate to continue the suspension of the buyback which was announced in October 2012.

The financial performance for the full year 2013 was defined by the significant revenue decline associated with the loss of exclusivity for several products. Despite its revenue profile, investment to drive future growth and value remain necessary. Investment in both the pipeline and the growth platforms will continue in 2014.

For 2014, challenging market conditions will persist, including continued government intervention in price.

The revenue impact from the loss of exclusivity will continue to affect our performance. For the full year 2014, the Company anticipates a low to mid-single digit decline in revenue on a constant currency basis. With continued investment in the pipeline and growth platform, we anticipate core EPS to decline in the teens.

We are also reconfirming our commitment to a progressive dividend policy.

The above guidance assumes the US Nexium generic entry end of May 2014.

Finally, I can reconfirm revenue guidance for 2017 which we expect to be broadly in line with 2013.

I believe that AstraZeneca is on track to return to growth and that we are gaining momentum on our turnaround journey. I will now hand over to Briggs.

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**Briggs Morrison** - AstraZeneca PLC - EVP Global Development and CMO

Thanks very much, Marc. It's really a pleasure to be here today to share with you our R&D progress for 2013 and a little bit of our aspirations for what we're going to do in 2014 and a bit in 2015 and 2016.

I think it's fair to say that 2013 was a very important year for AstraZeneca's R&D organization as we continue on our journey to be recognized as scientific leaders in the therapeutic areas in which we operate.

In 2013, while continuing to invest in our discovery and early portfolio, we've also rebuilt our Phase III portfolio through a combination of progressing our own molecules and supplemented that with some business development.

So, I showed you this slide when we met together in March. And what I said at the time was that we anticipated between five to seven new molecular entities would progress into Phase III over the 2013-2014 time period. I'm pleased to report that we are clearly on track for this goal. In fact, we believe we will be at the top end, if not higher, in terms of the number of new molecular entities that progress into Phase III over the 2013-2014 time period.

In 2013, there were four molecules that we hoped would progress into Phase III. All four molecules are now in Phase III and Phase III trials have begun.

If we look at the cohort that I showed you in 2014, not surprisingly there have been changes to these molecules because they were in Phase II and that cohort has evolved. So, the first thing to note is that 6765 has been terminated. We're not going to be progressing that one. And a number of molecules that we had hoped would get into Phase III in 2014 are now going to move over into our 2015 cohort.

Two of the molecules that we talked about when we talked in March are still in our cohort to go into Phase III in 2014 and have been supplemented by some additional molecules which I'll talk about in just a minute.



So this is an ugly and unreadable slide and Pascal has asked me to please stop showing ugly and unreadable slides. The only reason I show you this slide is because I showed it to you last year. And I wanted to show you that of the things we said we would do, in general, we've accomplished those things.

The things that were missed were, obviously, the Fostamatinib. Our team did a good job of getting us clear interpretable data, but we did not progress that to registration because of the profile.

CXL did not meet our criteria to move into Phase III and the psoriatic arthritis program for Brodalumab did not start in 2013. It will start in 2014.

But perhaps a better view of what we accomplished in 2013 is shown here. Since we spoke with you last year about this same time, we've had three additional approvals.

Dapagliflozin, referred to as Farxiga in the US, was approved. Xigduo, the combination of our SPL-2 inhibitor Dapagliflozin plus metformin, was approved in Europe. And the quadrivalent flu vaccine was approved in Europe as well.

We've had a number of regulatory submissions, including Olaparib being filed in Europe. We are on track to file Olaparib in the US as well this year. And these regulatory submissions will hopefully lead to some additional approvals this year and early into next year.

I've talked about the Phase III starts. And I'll say more about the early pipeline and some really promising data that's come from a couple of molecules in that pipeline in our lung -- in our oncology franchise in particular. And I'll talk about those in a moment.

So as the pipeline has progressed, we're clearly ahead of where we had hoped. So, again, this slide you saw when we spoke in March. The panel on the left shows, in the lighter color, what we anticipated our NME -- and the Phase III and our registration pipeline would look like. So we said at the end of 2012, we had six. We hoped by the time 2013 ended we would have eight and that by 2016 we'd be around 10 to 11. Because of the work we've done advancing our own internal molecules and supplementing that with BD, we're now at 11 molecules in Phase III or registration at the end of 2013, clearly exceeding what we had -- our goal was going to be. Great news for the R&D organization and great news for our pipeline.

This has put a bit of pressure on the R&D budget. So, what I show you on the right panel, remember when we met in March I said that we anticipated about 40% of our R&D dollars would be spent on late development, 60% on early. We had to redeploy resources in R&D to fund this growing late stage pipeline. And so as we close the books on 2013, we actually spent 45% of our R&D dollars on late development and 55% on early. And as we stand here today and look at our budgets for 2014, that's going to shift to about 50%, 50%. So it's about 10% of the R&D dollars have moved from discovery and early development into late development which, in round figures, is about \$400m. We've also, obviously, been working very hard to improve operational efficiencies so that we can handle this growing late stage pipeline with this R&D spend.

This is what the pipeline looks like today and I'm not going to go over it in detail. I'll just make a couple of key points.

Number one. I think it is pretty robust in Phase I, Phase II, and now in Phase III. A nice combination of both small molecules and biologics, adhering to our strategy of being excellent in both of those.

You'll see the color codings show our core therapeutic areas with predominant -- a lot of activity in oncology. The RIA portfolio has driven even distribution across the whole portfolio and cardiovascular metabolic is an area we're continuing to try to grow that part of our pipeline. And then you'll see a couple of other molecules in the areas that we're being more opportunistic.

14 new molecules have gone into Phase I since -- 2013. Eight molecules progressed into Phase II. So, although we're rebuilding the Phase III pipeline, I think it's important for people to understand the early pipeline is continuing to progress and continuing to grow as well.

Pascal mentioned the 19 possibilities we have to take molecules into Phase III over this year and next year. As you can imagine, we know more about the molecules that are in -- potentially will start Phase III in 2014 than we do about the ones in 2015. And I'm sure, as we come back here



next year, some of the molecules in 2015 will change, just as the cohort that I showed you for 2014 in March has changed. But we do feel comfortable knowing the 2014 cohort and we predict probably four or five of these will start Phase III this year.

So, again, if we go back to what I said in March, 2013 and 2014, five to seven. You can see we're clearly at the top end of that range because we put four in 2013. If we put another four in even this year, we'll be at eight. So, clearly, I think we're on track with that goal of what we said we would do in 2013 and 2014.

And I'll make a couple of comments about some of these key molecules that we have in our 2014 cohort.

So the first one is our anti-PD-L1 antibody. I think a molecule of great interest to many people. On the right-hand panel is some data that we had showed at a previous scientific conference. This molecule has -- is rapidly making its way through Phase I dose escalations. Pascal showed at JP Morgan all the cohort expansions and all the individual tumor types. And we're doing combinations, both with Tremelimumab and in a partnership with GSK with their BRAF and MEK inhibitor.

I think the key thing here is that at ASCO this year, we'll be giving a full update on where we are with this program and we do anticipate that this will start Phase III registration trials this year.

The second molecule in our oncology pipeline we're quite excited about is 9291 for a next generation molecule for the treatment of patients who have non-small-cell lung cancer driven by mutations in the EGFR receptor.

Again, on the right panel is some data that was presented at one of the lung cancer conferences showing some early efficacy data from 9291. We're continuing to see some very nice activity with this molecule. This molecule will also start Phase III registration trials this year. And, again, we'll give you a fuller update on this one at ASCO. There will be a full analysts' briefing at ASCO on our whole oncology portfolio by the leaders of our oncology franchise.

A molecule that we didn't talk about in March because it wasn't in our portfolio in March is Roxadustat. This is a molecule that we have -- are developing in partnership with FibroGen.

In simple terms, the way this molecule works, if you think about athletes like to go to high altitude to train. The reason they go to high altitude to train is that the low oxygen content at high altitudes triggers the body's normal physiological process to increase the number of red blood cells to increase your red blood cell mass.

What this molecule does is essentially mimic that physiologic process to increase red blood cell mass. And, therefore, it can be used to treat anemia.

The promise of this molecule is that it will be able to treat the anemia both of chronic kidney disease and the anemia of end stage renal disease with an oral agent. And, because you don't get these very, very high levels of erythropoietin that you get with the ESAs, potentially, that will have a much better cardiovascular safety profile. Remember that erythropoietins are associated with an increased cardiovascular risk. So, the potential here is for an oral molecule that doesn't have cardiovascular risk for both chronic kidney disease and end-stage renal disease and we think this is a very important area of unmet need.

The molecule has started Phase III in Europe. Astellas is running that part of the program. We intend to start the US and China studies this year with fillings potentially in 2016 in China and 2018 in the US.

And finally, I'll just make a comment about our BACE inhibitor. Again, very briefly, I think people know that Alzheimer's disease is believed to be caused by the deposition of beta amyloid in the CSF. That amyloid comes from a precursor protein that we all have endogenously. And one of the key steps in releasing amyloid from the precursor protein is an enzyme called BACE.

It turns out that there are certain families that have abnormalities, genetic inborn abnormalities of their precursor protein that makes them very susceptible to BACE cleavage. They get high levels of amyloid and they have rapid development of Alzheimer's disease.



There are other families where the precursor protein is resistant to the cleavage by BACE. They make less amyloid and they have a lower incidence of Alzheimer's disease.

So the genetics of validating BACE as part of the mechanism of Alzheimer's seems to be quite strong in humans.

What we're trying to do is to make a molecule that will mimic that protective effect, that protective mutation, inhibit BACE activity and, thereby slow the progression of either prodromal or early Alzheimer's disease.

On the right-hand panel is data that's been presented by our scientists showing that we get very profound diminution of Abeta in the CSF of patients.

This molecule will start registration trials. I want to be very clear that this is not -- I wouldn't necessarily call this a Phase III trial because we don't have the level of confidence that we would normally have to put something into Phase III. But the molecule seems very, very promising. And we think the right thing to do, given the public health need, is to move this molecule quickly into registration quality trials.

So, finally, of course, the goal of R&D is not simply to build a Phase III pipeline. The goal is to get that Phase III pipeline through Phase III, get the molecule submitted to regulators for regulatory approval, hopefully get those approvals with favorable labels, submit value dossiers to payers, so that they're willing to pay for it, and eventually have physicians write prescriptions so patients can take these medicines.

So the next major step, of course, as this pipeline progress are key submissions. And what I'm showing you here are anticipated or potential submissions 2014, 2015, 2016. Above the dateline are new molecular entities. And below the dateline are key lifecycle management opportunities. And I'll just call your attention to a couple.

Number one is 9291, the molecule I talked to you earlier about for patients who have EGFR mutation -- specific mutations in EGFR for lung cancer. That, if the program goes as we're seeing it progress right now, we think we can file that in 2016.

There's also the Brilinta PEGASUS program which we intend to file in 2015. That data should read out early next year and we should file in 2015.

Another important molecule or important combination molecule is our SGL-T2 inhibitor Dapagliflozin combined with our DPP-4 inhibitor Saxagliptin, the saxa-dapa combo. We hope to be able to file that at the end of this year. And there are a few others, but I'll take questions on those.

So, again, I think it's been a, I think, very good year for AstraZeneca's R&D organization. And hopefully you're getting the sense that we have a sustainable R&D model that can regularly, over time, continue to generate important innovative medicines. We put four molecules into Phase III last year. We think we'll put four or five into Phase III this year. And, as Pascal said, we're going to have to be picky, but it's possible we could put another four to five in next year as well.

So I'll stop there and turn things over to Pascal for the questions, or closing and then questions.

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**Pascal Soriot** - AstraZeneca PLC - CEO

Thanks, Briggs. So we'll now open the floor to questions.

Just because the entire MD team is very excited about the pipeline and they all want to talk to you about it, we, on top of Briggs today, we have Menelas Pangalos, who heads our AZ IMed Research and Early Development organization. And on the telephone we have Bahija Jallal, who leads MedImmune in Gettysburg together with Ed Bradley. Some of you may know Ed is in charge of our Immuno-Oncology pipeline.

And we also have here with us today in the room, Ruud Dobber, who is the Regional Vice President for Europe and also has kindly accepted to act -- to be the acting Head of our Global Product Strategy group.



## QUESTIONS AND ANSWERS

**Pascal Soriot** - AstraZeneca PLC - CEO

So with that, I'll now open the floor to questions. Who wants? Alexandra, do you want go ahead.

**Alexandra Hauber** - UBS - Analyst

Alexandra Hauber from UBS. I shall start with two non-pipeline questions and then it goes to the pipeline.

Just looking at your sales guidance for this year, the decline in sales of low to mid-single digit, I would have assumed that the consolidation of diabetes broadly cancels out the Nexium impact. So that means the rest of portfolio should still be down 2% to 4%. Can you just roughly tell us what the key moving parts in that thing -- in that Nexium ex-diabetes portfolios are that are declining?

Secondly, the 2017 outlook implies you have a gap of \$7b to fill from Nexium, Seroquel and Crestor, roughly. I would assume diabetes probably alone of that is about \$3b to \$4b including, obviously, the impact from consolidation. Now, in diabetes you have several tools to play. So, can you just give us roughly A, is the \$3b to \$4b incremental from the diabetes roughly the right ballpark or is there much larger coming from the pipeline?

And then within diabetes, really, what's going to be the key growth driver here?

And then finally moving to the pipeline. On your BACE inhibitor, a number of competitive molecules have had safety issues. How much patient exposure actually have you had? Do you know that this compound is reasonably safe?

And also if that is not a Phase III, what are you going to do instead, a very large Phase II and in which population?

**Pascal Soriot** - AstraZeneca PLC - CEO

Okay. So lots of great questions. Let me -- maybe, Mene, you want to take the BACE inhibitor question in a minute. Let me just comment on the guidance.

Starting with 2014, and Marc if you have anything to add, please jump in. But the big moving parts for 2014, they are, of course, Nexium. We still have a little bit of effect of Seroquel. But the big moving part is Nexium.

And, as you know, there is a certain level of uncertainty around Nexium in terms of the timing of entry of the generic, or generics, depending on what scenario plays out. And, so, as we communicated, the assumption we've used here is that we will see the first generic entry at the end of May this year. That's really the biggest moving part.

Then we also have -- sorry, Symbicort is growing around the world. But the assumption in our guidance was that we would have the impact of analogs in Europe. Whether they make it or not, we have to see. But certainly there is an impact from those in Europe.

What else to tell you?

As far as 2017 -- and, of course, diabetes will play a role.

As far as 2017, I can't give you specific numbers, as you will expect. The growth -- the drivers of diabetes for sure Brilinta. Symbicort is, we believe, a driver and again the emerging markets and Japan, there's no real great surprise there.



I think what I can tell you is that as far as diabetes, the growth drivers there really are Bydureon and Forxiga and the combination of SGL -- of dapa and Onglyza. I think this fixed combination product is really going to be a very valuable, very important growth driver in our diabetes portfolio. So, we have great expectations for that fixed combo which, as you know, not everybody has. So, certainly, it will be an important product.

Now the 2017 guidance we gave that sales will be broadly in line with 2015 relies on all of those growth drivers and some new product launches, of course, but it's essentially the platforms I've mentioned here.

Mene, do you want to cover the BACE question?

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**Menelas Pangalos** - AstraZeneca PLC - EVP Innovative Medicines & Early Development

So the first question, which is around the toxicity, the major toxicities that have been seen with BACE which are driven primarily by the chemotype are long-QT prolongation and hepatotoxicity which I think is actually specific to Lilly's molecule. So we've tested our molecule extensively pre-clinically. We have a very large margin because, actually, we have no evidence of any QT prolongation and from the hepatotoxicity perspective it's absolutely clean.

So, I think our molecule -- and in terms of the Abeta lowering, again our molecule is lowering Abeta levels by about 70%. We have a very, very potent molecule not dissimilar to Merck's molecule actually that's just entered Phase III.

Then the other molecule that is around is the ISA molecule, but we believe we're some way ahead of that as well.

In terms of the trial design, what we're doing is integrated Phase II/III trial. So we have interim looks at the data which that can be registered. It will be a pivotal trial if successful. But we'll take interim looks at which we will either kick off a second Phase III program or, depending on the data, file.

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**Sachin Jain** - BofA Merrill Lynch - Analyst

Sachin Jain, Bank of America. Two financials and then a couple of product questions please. Firstly, on SG&A. You saw a 7% CER increase in full year 2013. Can you give us any color on what level of increase we're looking at for 2014, particularly given the consolidation of the diabetes cost base which I'm guessing is at between \$750m to \$900m additional consolidation? And given that, through December I think you were commenting you expected SG&A to be flat as a percentage of sales. Does that statement still stand?

The second question is related to your comments that you're moving away from the pre-R&D margin target longer term. Any color on margin progression out to full year 2017 related -- relative to the flat sales outlook and what cost flex you have if the sales are below your expectations as they sit?

And then a couple of product questions. Firstly, on Lesinurad. You've commented in the headline press releases on renal toxicity. Do you still view that as a significant asset in light of that toxicity? Any color you can give?

Secondly on 9291. I see it listed as a 2016 filing. Any comments on breakthrough status and fast-to-market strategies?

And then the last one is on Brodalumab. I understand you've got a head-to-head study versus Stelara due late this year. Just any color on why you believe you can show superiority versus Stelara and some color from the Phase II data given that nobody else ran those studies initially? Thanks.

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**Pascal Soriot** - AstraZeneca PLC - CEO

Good. So quite a number of great questions too. Where do we start? Do you want to cover, Briggs, the question around Lesinurad and Brodalumab versus Stelara and also 9291 even though you will understand, Sachin, that as far as we do have fast-to-market strategies, we can't be very specific as to what they are for obviously reasons. But Briggs, go ahead.

**Briggs Morrison** - AstraZeneca PLC - EVP Global Development and CMO

Lesinurad, we do still remain excited about the molecule. The study that read out was monotherapy in patients who can't tolerate xanthine oxidase inhibitors. So, it's a small, very refractory population of patients who clearly need therapies and there with monotherapy we did see some renal toxicity.

In the Phase II trials, the combination where you add Lesinurad to Allopurinol looked much less toxic to the kidney than the monotherapy. So we're not -- we don't think the monotherapy informs what we're going to see from a safety profile from the combination and we'll get that data later this year.

**Sachin Jain** - BofA Merrill Lynch - Analyst

(Inaudible - microphone inaccessible).

**Briggs Morrison** - AstraZeneca PLC - EVP Global Development and CMO

We can cover with you the pharmacology of why that is, but there is a scientific reason why we believe it will be less and we did see less of it in the Phase II.

For 9291, we don't really comment on our regulatory strategies. But, all I can say is we have met with regulators and we think the plan that we have of moving that rapidly through to potential registration in 2016 is something that is quite viable.

And then the last one, Brodalumab. The reason we went head-to-head against Stelara is that Stelara seems to be the emerging best biologic in psoriasis and we, in collaboration with Amgen, felt that to really show that you have a significant advance in this area you have to be able to show that you're better than Stelara. To show that you're better than a TNF inhibitor we think is too low of a bar.

If you look at Amgen's Phase II data, it is quite impressive, particularly when you look at the PASI 100. And, so we did some modeling of the data they had and the data Stelara had and the data that Amgen had and we have a reasonable degree of confidence that we'll beat Stelara.

**Pascal Soriot** - AstraZeneca PLC - CEO

As far as Lesinurad, it's clear though that the combination data we'll get this year are going to be very pivotal because if we see the same renal -- same rate of renal adverse events then we're certainly not -- do not have a viable product. But, as Briggs said, there is a good reason to believe the combination will be -- will not see the same rate of adverse events and the Phase II data have confirmed this.

Marc, do you want to cover maybe the financial questions, SG&A and pre-R&D margin?

**Marc Dunoyer** - AstraZeneca PLC - CFO

I'm not going to give you any indication on the line by line R&D or SG&A and so on, but I have explained in my talk that we will continue to invest behind our growth platforms. So, this will be one factor. And the other is basically the mechanistic impact of the sales reduction. So, if you look at the margin, if we were keeping the same level obviously it would have a slight increase in the SG&A cost on the year. But, I won't give you more precision than this.

What we are going to look at is basically the operating expense as a whole, R&D, SG&A and other operating income. This will be a key metric we are going to watch very carefully within our redeployment of expenses.



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**Pascal Soriot** - *AstraZeneca PLC - CEO*

You can draw up your own estimate, Sachin, based on our guidance on the top line and the core EPS.

Maybe the one thing that I could add as far as guidance is, which we have said, is our commitment to the dividend itself and certainly the dividend policy. As you know, the dividend policy includes a dividend and a dividend cover and I think this is a very important part of our strategy and our commitment to shareholders. And, as many of you know, we have certainly good reasons to support that and stick to this. So with all these elements I'm sure you can model the cost evolution.

The key here is we're going to manage those expenses as a whole because the changing nature of our portfolio of specialty care, primary care, means that there may be, over time, over the next three years, changes in how we split SG&A and R&D expenses. As you know very well, when you have a specialty care business you tend to spend more doing lifecycle management, new indications, and certainly less in SG&A. So that mix is going to change.

Should I move maybe to one question online? Andrew Baum from Citi. Andrew, do you want to go ahead?

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**Andrew Baum** - *Citigroup - Analyst*

A couple of questions. So first, you're developing Treme for mesothelioma and there was some pretty exciting although small Phase I data. Given the outlook for these second and third line patients, have you sought a breakthrough status for Treme mesothelioma and should we assume potential commercialization as early as 2015 given the ongoing Phase III and the survival times of these patients?

Secondly, if you could comment what news flow on the immuno-oncology portfolio we're actually going to get at ASCO this year?

And then finally, I didn't hear anything in relation to Cediranib in ovarian cancer. Have you decided whether to file on the back of that positive Phase III data yet for ovarian? Thank you.

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**Pascal Soriot** - *AstraZeneca PLC - CEO*

The Ranbaxy assumption and Symbicort analog assumption in Europe.

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**Marc Dunoyer** - *AstraZeneca PLC - CFO*

As I mentioned during my presentation, the assumption that we have taken for the year 2014 is an introduction of a single generic on May -- the end of May 2014. We're aware that there are various scenarios possible playing out during the course of the year, but we have constructed our plan and, therefore, provided you guidance on our EPS based on that assumption.

And you also asked us a question I think on Symbicort analog?

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**Andrew Baum** - *Citigroup - Analyst*

That's right.

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**Marc Dunoyer** - *AstraZeneca PLC - CFO*

Andrew.

**Andrew Baum** - Citigroup - Analyst

Yes, in terms of generics, the timing.

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**Marc Dunoyer** - AstraZeneca PLC - CFO

We do not expect the introduction of Symbicort analog in the course of 2014.

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**Pascal Soriot** - AstraZeneca PLC - CEO

As you can imagine, Andrew, there are always moving parts in a budget or in a guidance, some upsides and downsides, and certainly the biggest moving part is next year, the timing of the generic entry. So you can, from what we tell you, you can model a variety of scenarios of course. And then Symbicort analog is also a scenario you can model.

But you have to look at a -- that's why we give you a range of forecasts. You have upsides and downsides in a budget.

Briggs, do you want to cover the ---

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**Briggs Morrison** - AstraZeneca PLC - EVP Global Development and CMO

I'll take two of the questions and then we have Ed Bradley on the line. Maybe he can tell you specifically about the news flow at ASCO.

So for Tremelimumab, we do have a randomized Phase II trial ongoing in mesothelioma. And, as you say, there have been publications on single-arm trials and, of course, we monitor the patients that are in our randomized trial and there is an opportunity there for that to be a registration opportunity. We're not projecting yet just when we think we might be able to file that. We're still estimating sample sizes and what the treatment effect would need to be. So I can't give you a firm answer on when we think we'll file that one.

In terms of Cediranib, you've seen the data from the MRC trial. What we're doing is working very closely with the MRC investigators to recapitulate the analysis to make sure that in our hands, with the data they have, we get the same answer they got essentially. Once that work is completed, and so far, as we've been doing that work, it seems to be a very nice study with very nice data, we will -- in parallel are discussing with regulators filing that both in the US and Europe. If all goes well, that could happen this year but we still need to dig through the data and make sure that we feel it's of regulatory quality.

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**Pascal Soriot** - AstraZeneca PLC - CEO

News flow at ASCO.

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**Briggs Morrison** - AstraZeneca PLC - EVP Global Development and CMO

So, I think maybe Ed should take that.

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**Pascal Soriot** - AstraZeneca PLC - CEO

Ed, are you on the line? Do you want to cover this question about the news flow at the ASCO as it relates to the immunotherapy portfolio?

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**Ed Bradley** - AstraZeneca PLC - SVP and Head Innovative Medicines

(Inaudible - microphone inaccessible)

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**Pascal Soriot** - AstraZeneca PLC - CEO

Thanks very much Ed.

Should I -- maybe there is another question on the line from Seamus Fernandez at Leerink. Seamus, do you want to go ahead and then we'll return to the room?

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**Seamus Fernandez** - Leerink Partners LLC - Analyst

Sure. Thanks very much. So a quick question on -- just again can you just clarify a little bit how we should be thinking about SG&A? It sounds like we should be thinking about SG&A being roughly flat and possibly increasing.

And then I have a couple of questions on the pipeline. Ed, it was a little bit difficult to hear you on that update from the line, so, maybe if somebody in the room could maybe clarify what Ed was saying in that regard. But in terms of the potential updates that we might see on the PDL1 and Tremelimumab combination, it would just be helpful to know the timeframe within which we could see that?

And also, Ed, if you could give us a little bit of color on your views as to the potential differentiation of your PDL1, specifically as it relates to the prospect of either the antidrug antibodies really not showing up and potentially having a better efficacy profile or if you really view the potential of this product as most enticing or exciting in combination with other therapies?

And then the last question. The respiratory biologic portfolio. I know that's something that nobody's really asked about at this point but my understanding is you have some potential data coming on Benralizumab at ATS, possibly. That study -- that product is in Phase III.

Also you had Tralokinumab. My understanding is that you were going to have some important Phase II data to make a decision on a go-forward basis. Just wondering if you can update us on both of those programs? Thanks a lot.

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**Pascal Soriot** - AstraZeneca PLC - CEO

Briggs, that's for you.

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**Briggs Morrison** - AstraZeneca PLC - EVP Global Development and CMO

Sure. So what Ed was saying about what you'll see at ASCO, Seamus, is that the dose escalation of PDL1 as monotherapy, the cohort expansion both in terms of safety and preliminary anti-tumor activity and some data on the PDL1 Treme combination.

In terms of the differentiation, I think it's perhaps a little early at this point for our molecules to be able to say on some of the parameters you asked about in terms of the antidrug antibodies, or efficacy, or safety that will evolve. But, I do think we do see the potential of the molecule in combination as well as in monotherapy and again the oncology group will give a full update on that at ASCO.

In terms of the respiratory biologics, yes, Benralizumab, our antibody against the IL-5 receptor has started Phase III and you'll see on the slide we tentatively think that as long as that enrolment goes as planned we'll be able to file that in 2016 and the Phase II data will be at ATS.

Tralokinumab, the Phase II data will also be at ATS and you're correct that we are -- it was on my list of things to potentially start Phase III this year. So, we're going through that data and going through our internal assessment to decide if we want to move that into Phase III.

**Pascal Soriot** - *AstraZeneca PLC - CEO*

There was a question again on SG&A. Just kind of repeat, what we decided we would do is guide you on revenue and EPS, core EPS, and again reconfirm -- because it's really important, reconfirm our commitment to the dividend. And, finally, to manage the expenses as a total core operating expense base but not give specific numbers line by line.

I think the one thing that I can probably say that we've said before is that, as Sachin identified earlier, taking on board the Diabetes Alliance, of course, the other half of the alliance means taking on board revenue but also cost. And what we are doing is looking for synergies across the entire portfolio and the entire sales force which we can manage now in a much more cost effective manner, not only in the US but elsewhere around the world. So, certainly, we are hoping to generate cost savings out of this better sales force management.

Shall we return to the room?

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**James Gordon** - *JPMorgan - Analyst*

James Gordon from JPMorgan. I have a couple of financial questions, one product one and one pipeline question.

On the financial, I understand you don't want to give exact line by line numbers but can you say beyond 2014, just in terms of general trends, where R&D spend could go because you talked about increased investment? Should we think of that as increased investment on an absolute basis? So that will be the first question.

One other financial question was just about the tax rate which looked low this quarter, what the tax rate might do beyond Q4 and then for 2014?

In terms of product questions, I was looking at the filings and there isn't anything for Bydureon monthly and that's out to 2016. So, can you give us an update on where we are on Bydureon monthly and when could that potentially file if it does work?

And then just one pipeline question. On the BACE, can you say -- have you seen any increased incidence of patients falling over because I think that was an issue for some other BACE inhibitors?

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**Pascal Soriot** - *AstraZeneca PLC - CEO*

Okay, thanks James. Shall we start with the last one? Maybe Mene, the BACE question.

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**Menelas Pangalos** - *AstraZeneca PLC - EVP Innovative Medicines & Early Development*

No.

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**Pascal Soriot** - *AstraZeneca PLC - CEO*

Okay, good. Bydureon. Maybe, Briggs, you can cover this in a minute and Marc, you could cover the tax rate if it's okay.

One thing as far as expenses, I think one thing we could also have said as it relates to the period of 2014-2017 is you have to think of our portfolio as 2014 is really sort of a launch/relaunch year. We're investing a lot in diabetes. We're investing a lot still in Brilinta. We're boosting the growth of Symbicort around the world, in the US, China, everywhere and we're also boosting our growth in the emerging markets. So, it's really kind of a heavy investment year in many ways to boost our growth. And I think as you look from there onward, you have to think of we have a relatively substantial expense base that we can manage over time. So you should not always think that this -- we're going to be in investment mode forever. That's also, I think, important to keep in mind.



Marc, do you want to cover the two?

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**Marc Dunoyer** - *AstraZeneca PLC - CFO*

I would caution you not to use the data from the fourth quarter and trying to extrapolate them going forward. I would rather recommend that you look at the guidance we have provided about a year ago on the overall tax rate for the year 2013 and going forward the tax rate should be broadly in line, or there should be no material change with what we had provided to you one year ago.

But, do not use the quarter by quarter because, as you may have noticed, there was a distortion due to the Amylin impairment on the fourth quarter.

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**Pascal Soriot** - *AstraZeneca PLC - CEO*

Taxes, quarter by quarter it's really hard to interpret.

Briggs, do you want to cover the Bydureon question?

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**Briggs Morrison** - *AstraZeneca PLC - EVP Global Development and CMO*

Obviously the Bydureon franchise starts with the dual chamber pen which has been filed. You saw on the slide that next year we anticipate filing the auto injector and then we're still working on the monthly to make sure that the formulation actually works. So, we don't have it -- I can't give you a firm date on when we think that's going to get filed.

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**Keyur Parekh** - *Goldman Sachs - Analyst*

Good afternoon. It's Keyur Parekh from Goldman Sachs and I have four questions please. Two for Marc, one for Pascal and then a product question please.

Marc, I found it very curious that all of your commentary was about focus on the cash flow from an internal management perspective and yet when I look out the next five years, the discrepancy between your cash flow and core earnings just keeps on increasing. So, can you help us think about why that's the case?

Secondly, as you look at the guidance for the tax rate going forward you said not to expect meaningful change. I think at the start of the year the guidance was to about 23%. You've come in at 21%. Was there anything exceptional about 2013 that wouldn't repeat in 2014 from a full year perspective?

From a product perspective, Pascal, you highlighted in March that Brilinta was one of the areas where you thought there was upside relative to consensus expectations going into 2017/2018. Given what we've seen year to date, do you still see that as the case? And if so, what will it take for you to achieve that?

And then lastly, as I look at your R&D budget, and if I look at companies who are playing in the immunotherapy space, so Roche, Merck, both have an R&D budget that is roughly twice your R&D budget. Bristol is broadly similar but their concentration on immunotherapy is quite high. So, given your R&D budget, how should we think about the choices you will make between your metabolic portfolio, your respiratory portfolio and your immunotherapy portfolio, or are we missing something that you are doing completely differently from the rest of the industry?

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**Pascal Soriot** - *AstraZeneca PLC - CEO*

Let me start maybe with the last question and Marc, if you want to think about the guidance, tax, and the cash flow questions.



First of all Brilinta. You know, I still believe that there is upside to this product versus what is forecasted and the one question you ask here is really what needs to happen. And what needs to happen is we need to see an acceleration in the US, very simple, because in Europe and in a variety of countries around the world, we are doing very well.

I think first of all we always need to ground ourselves in the fact that we only have an indication for 20% of the volume. And I think it's really important because gone are the days when, like 10 years ago, physicians were kind of allowed to do what they wanted and prescribe products even in indications that were not approved. Today, of course, as a company, we focus on the indications we have approval for, but even the physicians can't really have much flexibility because it's only reimbursed for certain indications. So, that's what we have access to and it's kind of limited. That's important.

But in Europe, we're doing very well and in some countries we are leader. Brilinta has leadership position in terms of discharged patients after ICS and so I think here we show the potential of this product and it's doing very well.

The other thing you have to keep in mind is this -- the material uses this pool of prescriptions and that is made of patients who have had -- who have been on say Plavix and other products for a long, long time and so the total prescriptions pool is very large. But, you only have a small number of new prescriptions and with a product like Brilinta, we only access the new prescriptions and we fill the pool over time so it takes a long time in terms of seeing the total impact. But, I would say in Europe we're in a good place.

The question is the US really and we felt we are moving in the right direction, actually. We saw some nice feedback, nice movement until the DOJ investigation impacted us and we hope -- so far we feel confident that we'll resolve this investigation positively. We've answered all the questions that were asked of us and it's been done very quickly. So, if we resolve it, we'll return to growth. We're certainly very committed. We keep focusing on it.

Our plans, basically, have been in place only since August last year in the United States. And, I think we have to wait until we can actually clear this phase of the DOJ investigation and see whether we can grow. If we can't, then we'll have to accept we cannot grow. But I still remain confident that we have a chance to succeed, even in the US.

And then the PEGASUS data also will be very critical because they will potentially reinforce the value of this product and allow treatment beyond 12 months. So then you get access to another part of the total prescription pool and then, of course, the other indications. So the jury is still out in the US. We need a bit more time.

Your other question is an important one is how do we fund the IMTs. First of all, we're in the process of looking at the plans and the costs of developing those products, but we certainly are looking at options for it. Certainly, the anti-infectives is an option. We've decided that it's an opportunistic area and certainly we could look at alternative options there. We can also partner some of our products in development. Not the IMTs, but some other projects we have in our portfolio. We've been approached by other companies to partner some of the products we have in the portfolio, so we can look at a variety of options.

And, as Briggs showed you, we've been shifting resources also to the late stage pipeline and we will keep doing this. And if at some point we found that we do not have enough resources to maximize the value of this IMT portfolio, we certainly would look at alternative solutions; further partnering of parts of our portfolio. But we're not at this stage yet. So far, from what we have in our hands, we can manage.

We have a very productive actually -- it's not because Briggs is here in the room, but we have a very cost-effective, very productive clinical development group at AstraZeneca and we are able to run clinical studies very effectively, fast, and at relatively low cost, actually.

Marc, do you want to cover the guidance and cash flow?



**Marc Dunoyer** - AstraZeneca PLC - CFO

I'll first talk about the tax rate and then I'll say a few words about the cash flow. So, first of all, the tax rate that you are referring to, 23% was the guidance we provided last year on the reported tax rate and it finished -- the year finished at 21.3% because some settlements went one side rather than the other side. So, 21.3% versus 23%, this is basically \$50m or \$60m difference. This is basically the precision, or the accuracy, of our forecasting in terms of settlement and tax settlement.

So for 2014 we believe there will be no material change in the reported tax rate. But, of course, with the same caveat on the accuracy of our projection on tax settlements.

We see no major trends of change of the corporate tax rate. So, again, it depends on how we finalize our negotiations with various tax authorities around the world.

Turning to cash flow, if you remember the slide I presented on the cash generation, in 2013 we have a net cash flow from operations of \$7.4b. If you just do a simple ratio of this cash flow on sales, this is close to 30%. It's a very high cash flow on sales. Higher than many other companies. And if you also look at the cash conversion cycle, we also -- the company has posted very good results. So, we are not providing you any projections or guidance on the cash flow, but just to point on the results of 2013, these are two very strong measures in terms of cash flow.

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**Amy Walker** - Morgan Stanley - Analyst

Thanks. It's Amy Walker at Morgan Stanley. I have three questions if I may, please.

The first one, I know you don't want to guide line by line, gentlemen, but just around the gross margin evolution, that was weaker than we'd expected in the fourth quarter and presumably Nexium's gross margin should be high and is going off patent so that will have negative implications. Should we, therefore, expect gross margin to decline in 2014 just directionally because consensus seems to be looking for a flat evolution at the moment?

The second question on respiratory. Symbicort in the US did some great growth in the fourth quarter. I think you mentioned something about a 4% share gain. So that would imply that you took some good pricing in the US perhaps. Can you just talk about what's driving that and how you expect that to evolve going forward?

And the last question Pascal, forgive me if I'm misquoting you here, but I think when I asked you at Q3 about the potential impact of the DOJ investigation on your ramp in the US for Brilinta, you said you didn't expect any limitation. Has anything changed and do you have any visibility on when all of this might be concluded? Thanks very much.

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**Pascal Soriot** - AstraZeneca PLC - CEO

Yes, as for the DOJ investigation, of course, we can't predict this. It's out of our hands. The only thing we can do -- that we can influence is how quickly we answer the questions that are asked of us and here, as you can imagine, we've answered the questions as quickly as we could. We've provided all the data that we were asked. We understand that we've answered the questions so far and they need to process the information and come to a conclusion and they may come back to us. But, so far, the investigation seems to be going as positively as possible.

The problem is we don't know. Basically, we don't influence the decision-making process, of course, and we don't influence the timing of it either. Certainly we've alerted the DOJ to the importance of this medicine to patients because the more confusion you create the less likely patients are to take a medicine that saves lives. It's pretty simple; when challenging players like NICE and IQWiG and others reimburse a product like this, it's basically because they've been convinced of the clinical value. So, there is clinical value. We want to make sure patients get the drug.

So everybody is aware of this, but beyond this, there's not much we can do but wait until the outcome.

As far as respiratory, what I think I mentioned -- what I know I mentioned earlier is that we gained 7 points of market share. So it has nothing to do with our pricing because I was actually talking about our prescription share. So, I don't know if I understood your question very well here but what I was talking about is prescription share, new prescription share, and that's the growth we saw.

And, of course, that again takes time in translating into total prescription share because it's only new patients. But it's a very substantial lift in our new prescription share that will over time lead to increased share in sales. And, in fact, we grew by 26% in the United States last year. Some of it is price, but not much. Most of it is really share increase.

And gross margin, again we don't -- I don't know if you want to comment on 2013 specifically Marc, but again we don't guide on specific line items.

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**Marc Dunoyer** - AstraZeneca PLC - CFO

I think obviously the timing which Nexium or Nexium generic will be during the course of the year 2014 would influence the gross margins. That's one factor.

The other factor that you need to take into account is the integration of the diabetes 50% alliance with BMS as we were booking the revenues, alliance revenues, directly on the gross margin. Now we are going to book it, I would say, normally from sales, gross margin and so on. So this will have also a slight mechanistic impact on the gross margin.

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**Jo Walton** - Credit Suisse - Analyst

Jo Walton from Credit Suisse. Three questions please. Firstly, a product related question, and it goes back to Symbicort. You've had a fabulous increase in market share. Glaxo pointed yesterday to the fact that a number of formularies, or one big formulary kicked in February 1 and that reversed some of the formulary element so that the loss of Advair and the growth of Symbicort should reverse. So, just from your perspective, have any major formulary changes kicking in in February that would at least reverse some of that?

And I wonder if you could also, while talking about that, just generally comment on the gross to net and rebate pressures in the US. Whether you had to give significantly higher rebates, this was something you specifically decided to do to get both Symbicort and also to get Byetta Bydureon on. I guess it wasn't you that necessarily made that decision. It was still in the JV. Now you are going to have to live with whatever price that JV put. But, on that formulary aspect, you could perhaps also tell us a little bit about your initial expectations for Forxiga? You've talked about the challenging formulary environment in Europe. We will no doubt be looking at prescriptions. Do you think we should look for the same sort of rate of growth for Forxiga as we saw for Invokana which -- can you give us some help on your initial expectations?

And my other question would be about 2017. Your IR department does a fabulous job of collecting every excruciating number we could ever think of so, you have a very good view of what we're forecasting out there. And you know that the aggregate numbers aren't anywhere near your expectations for 2017. So, I wonder if you could tell us where you think collectively we're missing it? Is it we haven't forecast businesses you haven't yet bought, or we really haven't understood emerging markets, or we just haven't got the patents right and really you're going to be able to keep some of your older products going for much longer? So just give us some help in generality there please.

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**Pascal Soriot** - AstraZeneca PLC - CEO

All right. Thanks, Jo. I thought you were going to ask another question, but probably kept that one, the traditional accounting question.

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**Jo Walton** - Credit Suisse - Analyst

Oh, I've got several of those.

**Pascal Soriot** - *AstraZeneca PLC - CEO*

So the formularies. Apart from the ESI change I'm not aware of any material change. I don't know if you've heard anything on your front. I'm not aware of any material -- there are changes, constant changes, of course, as you can imagine, but I'm not aware of any material change in formulary status in the US that would affect Symbicort negatively on a material basis. The only one I'm aware of is ESI. That is of course an important one because it affects 20% -- a bit less than 20% of commercial, so-called commercial lives in the US marketplace.

Now, that sort of brings me to your second question which is the gross to net. How to answer that? The first thing is that on an overall basis across the portfolio we have indeed seen increased rebates and the gross to net has been reducing. But it's not new. It's been happening over the last few years. It's the evolution of the US marketplace. But it is not actually necessarily coming from Symbicort or Bydureon. This ESI listing, they don't result from very substantial price reductions at all.

The total gross to net reduction really is driven very much by Crestor where, of course, as you can imagine, we've seen pretty substantial pressure there. But I would say for Bydureon or Symbicort I would not see -- I can't report a very substantial increase in rebates and a reduction in gross to net.

Forxiga, maybe, Ruud, you want to say a few words about Europe. But, in particular, Germany and as far as the US, we certainly have very ambitious plans, as you can imagine. But, of course, you also have to factor in that we launched the second product in the marketplace. We're not the first with SGLT2. We're second, and there will be competition. But, we certainly have very ambitious plans and very substantial focus and resource allocation behind this product.

Beyond this, I don't know that I can tell you a lot more. But, in Europe, we can certainly comment on it and particularly in Germany.

**Ruud Dobber** - *AstraZeneca PLC - EVP Europe & EVP Global Portfolio and Product Strategy*

Yes. So the situation in Germany is a little bit volatile. You all know that we launched the product early last year. I dare to say a highly successful launch having the trajectory line of Januvia moving extremely quickly. Then, unfortunately, the GDA decision came out with no additional benefit. So, currently, we are in arbitration in order to secure a reimbursement price. The chance is we will see whether we are able to convince the Arbitration Board in Germany. So, as a result of the mismatch between our expectation and the expectation of the German authorities, we stopped supplying the market mid-December.

The positive piece is that we are in the process of launching Xigduo, so the fixed dose combination of Dapagliflozin with metformin and, thereby, offering patients, as well as physicians, an alternative for those patients who were on the mono component.

We are in full swing in a couple of other European markets, UK, the Nordics, the Netherlands where we have full reimbursement, and we are still working through the reimbursement situation in big other European countries like Italy and France. But, the response of the physicians, as well as the patients is very positive.

**Pascal Soriot** - *AstraZeneca PLC - CEO*

It's an important point because nobody, or almost nobody, gets an SGLT2 first line. They always -- patients always get metformin. So when they get SGLT2 Forxiga, it's on top of metformin. So, having the fixed dose combination to launch will enable us to shift -- to move all those patients to the fixed combo and keep growing Forxiga in Germany.

2017, I think really it's again hard to answer specifically. We see potential in diabetes with the upside still in products like Brilinta, Symbicort, the emerging markets, all of the above, and some of our pipeline products, of course. But, the guidance we gave doesn't rely on us acquiring new business. This is organic growth coming out of our portfolio of existing and new products.

Should I take maybe the last question from Tim Anderson on the phone? Tim, do you want to go ahead?

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**Tim Anderson** - *Sanford Bernstein - Analyst*

(Technical difficulty) melanoma and lung.

And then slide 44, you talk about filing timelines through 2016 with various products. Your PL1 is not on there. So, I just want to confirm that the earliest you could file that would be something like 2017 or beyond, or could it be filed earlier on the back of Phase II trials? This is not clear to me if you're going from the Phase I programs you're running now straight to Phase III.

Second question related to this is will any of those pivotals be using biomarker-enriched patient populations? I haven't yet heard Astra articulate any use or views on biomarkers.

And then last question, a quick one. On the Amplimmune product, I'm trying to understand your rationale for advancing the PD1 into human development when you already have a PDL1 further along in development.

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**Pascal Soriot** - *AstraZeneca PLC - CEO*

Thanks Tim. Maybe Briggs, you could share these questions with Ed. Those are important questions. Maybe just before you do that let me just say that the plans we share are our best plans and for a number of products -- we talked about 9297 a bit earlier -- we also have alternative plans and looking at whether we can fast-track some of those activities. But, what we share with you is what we think is reasonable and a higher likelihood of achieving so that we -- then from there we can model upside and downside to those plans. But it's really high probability of success plans that we present.

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**Briggs Morrison** - *AstraZeneca PLC - EVP Global Development and CMO*

Do you want to let Ed go first?

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**Pascal Soriot** - *AstraZeneca PLC - CEO*

Yes, Ed, do you want to start maybe with -- well you could cover the PD1 question. Why do we have a PD1 -- why do we move it into the clinic when we have a PDL1? And you could also cover the biomarker question maybe if you wish?

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**Ed Bradley** - *AstraZeneca PLC - SVP and Head Innovative Medicines*

Yes, PD1 and PD (Inaudible) monotherapy but also in terms of accommodating and we are actually working each of them as monotherapy and (inaudible) and in a variety of combinations. (Inaudible) exactly where, over time, these fall out in terms of best combinations, best patient population to use. So, (inaudible) gives us the opportunity to create combinations that I think time will help tell (inaudible) time will tell exactly which of these are best in which particular clinical setting.

(Inaudible). So, we're aware of the bio-marker data that has been published. All those protocols include a very [British] translational platform PDL1 versus the major bio-markers also and exactly how that is going to be used in registration collection (inaudible).

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**Pascal Soriot** - *AstraZeneca PLC - CEO*

Thanks Ed. I think it's important to remember that our strategy as far as IMTs is a combination-based strategy and we have reasons to believe a combination of PDL1 and PD1 is a possibility. They are all our combinations and, as Ed was saying, it's going to be data-driven and we'll explore the variety of alternatives to find the best possible combination.

And maybe Briggs, do you want to cover the 2014 IMT tumor types?

**Briggs Morrison** - *AstraZeneca PLC - EVP Global Development and CMO*

So Tim, I think it is fair that it'll be one of the tumor types that you described, and the filing timeline, as Pascal said, in part will be driven by data. So, obviously, there are faster routes to approval or filing and approval with certain levels of activity and then there are the longer ones. So, what we're giving you as our base case is the longer one assuming that what we've seen from our competitors makes it a little harder to go on some of those faster timelines. But again, it will be data-driven.

**Pascal Soriot** - *AstraZeneca PLC - CEO*

Good. Thank you so much. I think Carl is reminding me we should close. So, I just wanted to thank you very much and hopefully you had a chance to look at our news flow slide. If not, you can look at it in the deck we presented to you. As you will see, it's a very rich news flow this year.

I'd just like to conclude quickly by reminding you that we're making progress with strong momentum. ASCO and ESMO this year will be very critical for us with our oncology portfolio and we have 19 candidates over the next two years for Phase III starts. So we certainly have to be very focused and very selective in those. But the good news is we have a lot to choose from.

So with this, thank you so much for your participation.

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