

**Slide 1 – Title slide**

Thank you David and good afternoon.

**Slide 2 – Agenda**

Today, I am going to give a brief update on where we are with the R&D strategy and our transformation goals.

I will talk about portfolio performance in 2010, and finish with a review of a selection of late stage projects.

**Slide 3 – How are we addressing the R&D productivity challenge**

Our strategy recognized that we need a dramatic change in R&D performance. Last year we decided to address this with a leadership and operating model transformation. In terms of the portfolio we conducted a root-and-branch attrition analysis to learn from our failures and we reviewed every R&D programme.

We decided to invest in a number of key capabilities and also set out to access the very best of external science.

Lastly, we made hard decisions to close some of our sites and reduce our internal headcount.

I will show some examples on the next slides.

**Slide 4 – Leadership**

I would not normally show a slide of leaders to this audience but I thought it was the best way to illustrate the extent of change we've seen this year with a few examples.

We conducted an extensive review across the R&D organization and this resulted in a large-scale change in 'who leads R&D'. We've attracted talented people from across the industry and globe as well as appointing great talent from within AstraZeneca. In fact over half of the senior leadership changed.

I believe that the changes were necessary. And now it's about pipeline delivery.

**Slide 5 – One R&D organisation**

My second focus was to set clear accountabilities for leaders. We constructed a simple operating model with Mene Pangalos and Bahija Jallal leading our small molecule and large molecule research engines, respectively. At proof-of-concept Anders Ekblom and a very experienced team of drug developers take ownership of the programs.

The model has single points of accountability, with fewer but higher hurdles.

**Slide 6 – Criteria used for portfolio review**

We also conducted a root-and-branch review of our portfolio to learn from our failures and there were some clear issues that came to light.

We asked a number of questions:

Did we have the right target engagement – were we confident in efficacy based on the level of understanding of human disease biology?

Did we have the right tissue exposure and duration suitable to deliver clinical efficacy?

Was pre-clinical and clinical safety supported by knowledge of on- and off-target toxicity?

Did we have the evidence and ability to identify patients most likely to respond?

And did we have a differentiated value proposition against current and future standard of care?

Successes across the industry invariably scored highly against these criteria while failures scored poorly.

We have applied this framework to our portfolio.

If we turn now to the latest update on the R&D pipeline you can see an early impact.

### **Slide 7 – Significant changes to the pipeline**

We've made tough decisions in terms of terminating programs as well as progressing those considered with the highest potential. For the first time since 2004, we see a reduction in the total size of our pipeline.

In addition and not shown on this slide, the portfolio review has reduced the number of compounds in the preclinical phase. In fact approximately 30% of programs were stopped.

In the long term, we believe that a smaller pipeline which is more carefully scrutinized for quality and value will serve us well. I will not be seduced by the vanity of large numbers but rather we will be careful stewards of the money invested in us.

### **Slide 8 – Investing in capabilities to drive productivity**

We believe that building the capabilities shown here will be essential to improve future R&D productivity:

The R&D and Commercial organizations are working together on an integrated payer strategy to deliver the best reimbursement dossier.

Personalised healthcare aims to deliver the right treatment, to the right patient, at the right dose, at the right time. This enables us to focus our discovery and translational efforts to the right disease segment.

In terms of clinical trial design and interpretation we are identifying best practices to improve the overall effectiveness and speed of clinical decisions.

And for predictive sciences we are using translational medicine to better link pre-clinical and clinical data helping us take earlier decisions.

### **Slide 9 – Portfolio highlights 2010**

How is our core business doing in the meantime?

2010 was a year of some good successes tempered by a number of clear disappointments. We have seen approval for Brilique, and Vimovo.

Together with BMS we have a new once daily fixed dose combination of Onglyza/Metformin called Kombiglyze XR, which we recently launched in the US. We have also submitted Onglyza/Metformin IR fixed dose combination in the EU.

David talked about Brilinta and I will speak about the CRL in a moment.

We have also made submissions in the EU and US for Dapagliflozin, and Vandetanib. And we submitted our antibiotic Ceftaroline, now branded Zinforo, and Axanum in the EU.

At the same time, lifecycle management continues to add value.

We have new indications for Crestor in the US and the EU based on data from the landmark JUPITER trial and for Seroquel XR in the EU as add-on treatment in MDD.

We have started phase 3 programmes for TC5214 and fostamatinib.

However, our internal performance has been disappointing in terms of securing approval for late stage projects, and we have had CRL's for motavizumab, and Certriad which we have since discontinued. As David also mentioned, we had disappointing trial results for Recentin and Zibotentan.

Now let me turn to our late stage assets where I am going to highlight 5 of our projects.

#### **Slide 10 – Brilinta CRL status**

In December last year the FDA issued a Complete Response Letter for Brilinta. This is our top priority in R&D. The additional analysis requested were produced by the team and last week we announced that we had replied.

The additional analyses of the PLATO trial requested in the CRL focused on interactions between ticagrelor and high dose aspirin. We believe these supplementary analyses support the hypothesis that the apparent difference in treatment effect observed in the US and non-US patient subsets in PLATO is most likely a reflection of an underlying interaction between ticagrelor and higher doses of aspirin.

We remain of the view that either the play of chance or this interaction are viable explanations for the efficacy differences observed in a subset of US patients in the PLATO trial.

The CRL did not request that additional studies be conducted as a prerequisite for approval of the NDA. We remain confident in the submission and are now waiting to hear if we can expect a 2 month or 6 month review time.

#### **Slide 11 – Fostamatinib oral spleen tyrosine kinase inhibitor**

The next programme I will update you on is fostamatinib that we in-licensed from Rigel last year. It is the first oral spleen tyrosine kinase, or SYK inhibitor, in development as a novel approach for RA in adults who have failed to respond adequately to therapy.

We commenced our Phase 3 programme, called OSKIRA, in September last year and this was only 6 months after the deal was signed.

Recruitment is progressing in line with expectations to meet 2013 regulatory filing dates assuming positive results.

We intend to commence a Phase 2b study that explores fostamatinib as a monotherapy in RA and this will provide information in the absence of DMARDs.

#### **Slide 12 – TC-5214 an exciting opportunity in MDD**

In the neuroscience area our most advanced programme is TC-5214 which we have licensed from Targacept. It is a neuronal nicotinic receptor modulator, a novel mechanism of action relative to standard antidepressant agents and is initially being developed as for MDD in patients with inadequate response to first line SSRIs or SNRIs.

More than 50% of MDD patients currently don't achieve remission after initial antidepressant therapy.

The key Phase 2b results are shown on the right. All patients received citalopram during the first eight weeks and were then randomised to TC-5214 or placebo. All patients continued to receive citalopram throughout the study. The placebo group is denoted in red and the TC-5214 group in blue.

Dosing in the Phase 3 Renaissance programme commenced last summer and the programme is progressing to schedule. In addition, a long term safety study has completed enrolment.

We anticipate a US NDA submission in the second half of 2012, and EU filing in 2015.

In addition, a Phase 2 study to assess TC-5214 as a switch monotherapy treatment for MDD is targeted to start in the first quarter of 2011.

### **Slide 13 – Zinforo next generation cephalosporin antibiotic**

Let me now turn to our next generation cephalosporin antibiotic Zinforo, which forms part of our collaboration with Forest laboratories. We have the responsibility for the development, regulatory approval and commercialization of Zinforo in all markets outside the US, Canada and Japan.

Zinforo is a new extended spectrum and well-tolerated antibiotic which has shown good activity in two important types of hospital infections, namely complicated skin and soft tissue infections and community acquired pneumonia.

The key clinical data supporting our Zinforo filing in Europe is depicted on the right of this slide. There were four pivotal phase 3 studies: two CANVAS studies in cSSTi and two FOCUS studies in CAP. All four studies were non-inferiority designs versus active comparators and met their primary endpoints, demonstrating a good efficacy and tolerability profile, including MRSA activity in the skin trials.

Our EU regulatory filing was submitted in December last year and today I can confirm the EMA has accepted our filing earlier this week.

### **Slide 14 – Dapagliflozin an exciting new approach to diabetes**

One of the most exciting projects in our late stage portfolio is the first-in-class SGLT2 inhibitor dapagliflozin, which we are co-developing with Bristol Myers Squibb.

On the right hand side of this slide you can see a depiction of the mechanism of action of dapagliflozin, which is novel for antidiabetic drugs and works independently of insulin, resulting in excretion of glucose and associated calories in the urine.

Data from five pivotal phase 3 studies are now in the public domain and suggest a product profile that is encouraging with differentiated patient benefits. This includes the potential benefit in uncontrolled patients with type 2 diabetes who require HbA1c reduction and the additional benefit of weight loss.

In the phase 3 studies, genital infections and urinary tract infections were generally higher in the dapagliflozin group but mild or moderate, generally responded to an initial course of standard treatment and rarely led to discontinuation.

Further data from the phase 3 programme will be presented later this year.

Together with BMS we filed, in December 2010, for regulatory approvals in the US and in EU.

### **Slide 15 - Summary**

2010 was a year of significant change for AstraZeneca R&D. We made hard decisions around people, our portfolio and the way that we work.

I came to AstraZeneca to lead a successful R&D organization, one that will create value for our shareholders, help patients and be admired by colleagues. I believe that we have set a clear path and now we must focus on delivery of our portfolio.

I would now like to hand over to our CFO, Simon Lowth.