

## **Half Year Results – July 2009**

### **Adners Ekblom script**

Thank you Simon.

I am very pleased to provide you with my first R&D half-year review especially in this exciting period of late-stage delivery for our R&D organisation. There has been a tremendous degree of change within the industry generally and with our R&D efforts specifically in AstraZeneca. We have seen our pipeline grow, mature and significantly expand into biologics. We now have an organisation that is more focused, cost-conscious and productive. We have seen a transformational change in our science and technology base as well as our partnering approach. This degree of change will become 'normal' as we continue to be passionate about science while at the same time ensuring we get an attractive return on the investment we make in R&D.

### **Slide 2**

During the first half of 2009, we've continued to strengthen the pipeline and have seen strong evidence of its growing maturity. Key accomplishments have been the approval and launch of Iressa in Europe, while Onglyza's registration is progressing strongly with a positive FDA adcom in the US and a CHMP approval recommendation in Europe. We had 3 other NCE submissions with Certriad, Vimovo and Zactima, and have made significant progress in our LCM activities, of which the delivery of the Crestor JUPITER sNDA and MAA was a particular

highlight. Brilinta has been another key accomplishment as the PLATO study achieved its primary endpoint.

In addition to the progress our projects are making, our productivity initiatives also continue to provide benefits. We are faster and leaner than ever before and are striving to continuously improve as we move forward managing our cost base.

### **Slide 3**

Let me turn now to our late stage portfolio, which I'll cover over the next few minutes in some depth. As you can see from this chart we are steadily transitioning our Phase III projects into the registration phase of their life-cycle. We filed 4 projects last year, 2 of which were biologics. We are also on track to deliver 4 this year as well as the projects due to be filed during 2010 and 2011. Of-course the ultimate result is not the filing, it's launching these medicines and making them available to patients. We are working very hard within R&D as well as with regulators and our marketing colleagues to do just that. As I mentioned already we have launched Iressa in Europe and hopefully next in line is.....

### **Slide 4**

.....our most mature Phase III project; our joint development with BMS of Onglyza, the DPP4 inhibitor for the treatment of Type II diabetes. There remains a very high unmet need in diabetes with significant morbidity and mortality. It currently affects 246 million people world-wide and is set to increase to 380 million patients by 2025. 50% of treated

patients do not reach glycemic control therefore it is clear that additional therapies, like the growing DPP4 class, are required.

Our discussions with the regulatory authorities are progressing well. In Europe we received a positive CHMP opinion, which is currently awaiting a decision by the European Parliament. In the US, as David mentioned earlier, the PDUFA date is today. Discussions with the FDA are progressing well and we remain confident in the comprehensiveness of the regulatory submission we made. I'm sure you'll also appreciate that there is little more that I can add at this point other than to say that we are hoping to have positive news soon. As you know, we intend to conduct a cardiovascular event study and planning is at an advanced stage, so that it can be initiated post approval.

## **Slide 5**

Another key filing is CERTRIAD, our investigational medicine developed with Abbott for the treatment of mixed dyslipidemia. It contains the active ingredients of our statin, Crestor and Trilipix (fenofibric acid). Certriad provides efficacy benefit by controlling the 3 primary lipid targets – LDL-C, HDL-C and triglycerides. As you can see from this chart it targets a distinct patient population currently uncontrolled by existing treatment alternatives. In the US there are currently 46 million patients on medication, 29 million of which remain uncontrolled. A significant segment of these patients could potentially benefit from CERTRIAD.

We have now submitted an NDA one quarter ahead of our previously communicated timelines.

## **Slide 6**

The next key filing delivered during the first half of 2009 is VIMOVO™. The NDA was filed with the FDA on June 30<sup>th</sup> and pending US regulatory approval, VIMOVO™ is the proposed trade name for PN400. It is a fixed dose combination of enteric-coated naproxen and immediate release esomeprazole in a sequential release formulation that we have developed with POZEN for the relief of signs and symptoms of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis in patients at risk of developing NSAID associated gastric ulcers. There are currently 140 million osteoarthritis patients world-wide. Up to 30% of these patients switch or augment their therapy in a year either because they do not get the pain relief that they seek or because of side effects and up to 50% of OA patients taking NSAIDs are at risk of developing NSAID associated gastric ulcers, representing a large unmet need for this patient population. The two pivotal registration studies, 301 and 302, demonstrated that the incidence of gastric ulcers was significantly lower in patients taking VIMOVO™ compared with enteric-coated naproxen through 6 months. Abstracts have been submitted to congresses including ACR and ACG. From a regulatory point of view, POZEN submitted an NDA to the FDA on June 30<sup>th</sup> and we are on track to submit an MAA during the 4<sup>th</sup> quarter this year.

## **Slide 7**

Turning now to oncology; ZACTIMA is the first oral targeted therapy to show evidence of clinical benefits when added to chemotherapy in Phase III studies in 2<sup>nd</sup> line NSCLC. We recently filed submissions in the US and Europe for the use of ZACTIMA 100mg in combination with

chemotherapy for this patient group. Results from ZEPHYR – the 300mg monotherapy study in EGFR failures in advanced NSCLC and ZETA - the 300mg monotherapy in advanced medullary thyroid cancer, will be presented during the first half of 2010.

## **Slide 8**

That concludes the update on our recent approvals and submissions and I would now like to provide you with a status of our other Phase III projects starting with Brilinta. This is our investigational oral antiplatelet treatment for acute coronary syndromes (ACS). It is estimated that 1 in 3 ACS patients will die, have a recurrent heart attack or be re-admitted to hospital within 6 months of their first CV event. This points to a continuing need for more effective, safe ACS treatment options. Earlier this year we announced that PLATO, our large 18,000 patient trial, demonstrated that BRILINTA achieved a statistically significant primary efficacy endpoint versus clopidogrel. The primary efficacy measure was time to first occurrence of any event from the composite of myocardial infarction, stroke and CV death. The overall safety profile of BRILINTA was in line with the safety data observed in the Phase II studies. Given the size of the study, further analysis of the database, secondary variables and subgroups is ongoing. I understand there is considerable interest in the PLATO results, but as you would expect, details will have to wait until we present the results at the European Society of Cardiology annual meeting on the 30<sup>th</sup> August. We also aim to submit the data to a peer-reviewed medical journal. The submission to regulatory authorities remains on schedule for the 4<sup>th</sup> quarter of 2009.

## **Slide 9**

Our Recentin programme is progressing well and we are on track to deliver the colorectal cancer and recurrent glioblastoma submissions in the 2<sup>nd</sup> half of 2010. In CRC, the HORIZON II and III studies have now fully recruited, while in recurrent glioblastoma, recruitment of the Phase III REGAL programme is on schedule. The broad signal search programme continues to reinforce activity of this molecule with efficacy signals seen in a range of tumours. Posters were presented at ASCO on the findings earlier this year.

## **Slide 10**

Earlier I talked about Onglyza. The other compound in our joint development alliance with BMS is dapagliflozin, a potential 1st in class SGLT2 inhibitor for the treatment of patients with type 2 diabetes. The Phase III programme is progressing well, with 11 studies ongoing, 8 of which are fully recruited, and 2 having completed their initial 6 month treatment period. We presented further Phase IIb data at the ADA earlier this year showing that in a 12-week study, dapagliflozin improved glycemic control in type 2 diabetes patients who were inadequately controlled despite high doses of insulin and common oral anti-diabetic medicines. Six-month results from 2 Phase III studies will be presented at the EASD and IDF congresses in October this year. We are on track to make our first submission during the 2nd half of 2010.

## **Build**

The next compound I would like to update you on is ZD4054; this is the potential first in class Endothelin A antagonist in hormone resistant

prostate cancer patients with metastatic and non-metastatic disease. We are making significant progress with our Phase III ENTHUSE programme as the launch indication M1 study has fully recruited and the follow up indication studies, M1 combination and M0, are actively recruiting.

## **Slide 11**

Moving on to the biologics side of our business and the final Phase III project presented today; motavizumab. We continue to work on the CRL for motavizumab and are expecting to submit our response to the FDA in the second half of the year. MedImmune has completed the second season study in congestive heart disease (CHD) and will include the CHD data as part of its CRL response. Our rest of world partner for Synagis/motavizumab is Abbott International, and they plan to wait until we have incorporated the CHD data into the file before submitting in Europe.

## **Build**

Our seasonal live attenuated influenza vaccine continues to make progress as well, with several regulatory filings now completed. The review of our MAA filed late last year continues as expected. Our application in Hong Kong was submitted in the first half of 2009, while AZ Canada submitted a New Drug Submission (NDS) for FluMist to Health Canada on July 20.

Finally on the pandemic side, David has already covered the significant progress we are making on producing a candidate for a Novel Influenza A (H1N1) vaccine.

## **Slide 12**

Continuing with the LCM update, another key accomplishment is the progress that has been made with Iressa. Building on the success in Asia, Iressa is developing into a significant brand for AZ. It is the first and only targeted therapy to show superior efficacy to doublet chemotherapy in the 1<sup>st</sup> line treatment of advanced NSCLC. Data shown on this chart from the pan-Asian IPASS study shows superior progression-free survival for Iressa compared to doublet chemotherapy in EGFR mutation positive patients. EGFR mutation status was a strong predictive biomarker providing a truly personalised healthcare approach. EU approval was achieved across all lines of therapy for EGFR mutation positive NSCLC patients based on the INTEREST and IPASS studies as well as a full data review.

## **Slide 13**

Moving on to Crestor. I will outline our LCM activities that will fully maximise this product's potential; mainly JUPITER, SATURN and PLUTO. Starting with JUPITER, we followed up our presentation of the initial results at AHA at the end of last year, with a presentation of equally impressive results on stroke and VTE from the trial during the first half of this year. As a reminder of the profound impact rosuvastatin 20mg demonstrated in this trial, the graph presented shows the primary endpoint data with the 44% relative risk reduction. No other statin has demonstrated this magnitude of risk reduction in a placebo-controlled trial. The JUPITER sNDA and MAAs in the US, EU and other major markets are under active review.

SATURN is a follow up to our successful ASTEROID IVUS trial where regression of coronary atherosclerosis was demonstrated for the first time in a major clinical trial with a statin. SATURN is a head to head IVUS trial comparing Crestor and atorvastatin and is on track to deliver results in 2011. In April, we submitted PLUTO in both the US as well as the EU seeking a paediatric indication.

Based on the PLUTO submission, we can now announce that we have successfully fulfilled our US paediatric exclusivity requirements for Crestor and we were informed earlier this month that as a result we have been granted an additional 6 months of market exclusivity in the US.

#### **Slide 14**

Our Seroquel immediate release bipolar and XR bipolar, MDD and GAD life cycle management program is moving forward. In the US, the FDA issued CRLs for both MDD and GAD sNDAs requiring additional information. We have prioritised the re-submission of MDD over GAD, have issued a response and we expect a decision during the 4<sup>th</sup> quarter of this year. For GAD we are in ongoing discussions with the FDA.

In Europe we have referred our application for XR for patients with MDD to the CHMP and expect an opinion during the last quarter of this year.

For the European GAD application we expect a read-out from the Mutual Recognition procedure also by the 4<sup>th</sup> quarter.

In other markets, Seroquel XR for MDD, has been approved in Canada and Australia.

Finally our bipolar suite of indications is progressing to plan across all key markets.

#### **Slide 15**

Life cycle management also continues strongly for Symbicort. In the US we have received approval and launched the COPD indication. Our paediatrics sNDA received a CRL in April. We are working on our response, which we will provide to the FDA during the 2<sup>nd</sup> half of this year and it is likely to require new clinical studies.

In Japan, although we initially had a delay due to a backlog of reviews at the regulatory agency, we now expect to receive an approval of the asthma indication during the 4<sup>th</sup> quarter of this year. At the same time we are making progress on the COPD and asthma Symbicort SMART programmes in Japan.

In other markets; we launched Symbicort SMART in China during the 1<sup>st</sup> quarter and are on track to launch a COPD indication in China, Australia and Canada during the second half of 09.

## **Build**

Finally, Faslodex. This is a product whose LCM activities have not featured in our R&D updates for some time. Following a positive outcome in the Faslodex CONFIRM Phase III trial, which compares the efficacy of the currently licensed 250mg with the 500mg dose, we are exploring with a number of Health Authorities, the possibility of a label change in order to bring the benefit of the higher dose to patients. We plan to present the results of this study at the San Antonio Breast Cancer conference in December.

## **Slide 16**

I would now like to provide you with an overview of our pipeline. On the next few slides I will focus on the clinical component of our pipeline.

Back in January 2009 we had 98 projects in clinical development. In a portfolio of this size, .....

### **Slide 17**

.....there will inevitably be a significant number of projects that fail or are stopped for a number of different reasons. In the first half of this year we had 9 withdrawals overall.

### **Slide 18**

However, these were more than matched.....

### **Slide 19 and Slide 20**

.....by projects that have progressed to the next step or to a regulatory filing. The Green boxes represent the 11 projects that progressed to the next phase while the 5 amber ones are those that have been filed with the registration authorities. As late-stage projects are launched we can expect them to come off the LCM section of this table.

### **Slide 21**

And, of course, we have continued to introduce new molecules shown here in red. So across the clinical portfolio we had 12 new projects added since January.

### **Slide 22**

Looking at the pipeline overall, we are seeing strong evidence of its maturity. We are delivering the late stage projects while at the same time Discovery and early phase productivity has been maintained at the steady state levels we require in order to meet our overall targets. We now have a balanced portfolio representative of the investment we have made in alliances and biologics over the past few years.

### **Slide 23**

So in conclusion I believe that we are at an exciting period of late-stage delivery. We are moving key Phase III projects into the registration stage of their life-cycle while our LCM activities are maximising the potential of marketed products such as Crestor and Iressa.

All in all at this half-year point we are confident that we will meet the targets we set ourselves for this year. We have already delivered 3 out of the 4 submissions we expected for 2009 and the 4<sup>th</sup>, Brilinta, is on track for the 4<sup>th</sup> quarter.

We've delivered a lot but, as ever, there is still a lot more to do. As a scientist and a clinician I am passionate about continuously improving the science and innovation that underpins our portfolio. At the same time as a business leader I will ensure that we manage the cost base within R&D in the most efficient way possible.

And now I'd like to hand you back to David.