

**Second Quarter & Half Year Results 2008, 31<sup>st</sup> July**  
**John Patterson script**

**Slide 1**

Thank you Simon. Over the past few years I've talked regularly about the four key components of the AstraZeneca R&D strategy. In the short term, we seek to maximise our marketed products through our life cycle management activities. Secondly, we're building our portfolio by increasing our discovery and development productivity. We've invested considerable time and effort improving the quality, speed and cost efficiency of our discovery and early development to bring more projects into Phase III, faster. Finally, in the medium and longer term, balancing our portfolio by complementing our internal efforts through externalisation as well as delivering an accelerated biologics strategy.

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This is an exciting time for R&D as we are now seeing concrete results from this strategy. We're delivering on our promise on all fronts. Over the next 20 minutes I plan to review the significant number of achievements in the first half of 2008, starting with an update of key developments in our Phase III and lifecycle management activities, followed by an overview of our pipeline.

So far this year we have delivered 12 Life Cycle Management regulatory submissions as well as 2 of the 3 new substance submissions we set out to deliver this year, namely Motavizumab and Onglyza<sup>TM</sup>. We're making considerable progress reducing our cycle times and our costs, without compromising the quality of our portfolio. We have increased our Phase III pipeline to 12 projects. This is a considerable increase from this time 2 years ago. Our externalisation efforts and the narrower focus of our disease area strategy are producing results. One clear example being in type 2 diabetes where our deal with BMS has delivered a submitted regulatory package as well as dapagliflozin in Phase III.

Finally our relationship with MedImmune is now 1 year old and we are on track to deliver a strong biologics portfolio.

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I would now like to take you through the key developments of the past 6 months starting with Motavizumab. Motavizumab, through its increased pre-clinical potency, could be a real step forward in Respiratory Syncytial Virus prevention. The BLA submission for premature infants and infants with Chronic Lung Disease was delivered in January 2008 and is currently under review. The Congenital Heart Disease study data is currently being analysed and we are on track for the US supplementary submission planned for the first half of next year as well as the EU submission for all high risk infants within the same timeframe. Finally the phase III Native American study accrual has now been completed.

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I am sure you realise that ONGLYZA is the trademark for the selective DPP-4 inhibitor with the generic name saxagliptin. The second key achievement of the first half of this year was the ONGLYZA<sup>TM</sup> announcement we made last Wednesday jointly with our partners, BMS. We delivered the regulatory submission to the FDA on June 30<sup>th</sup> and have recently received validation of the MAA from the European Medicines Agency, 15 months earlier than previously planned.

The submissions are based on data from a comprehensive Phase III program conducted in addition to standard therapies, as well as in treatment naïve patients as a monotherapy. The program included studies that evaluated the drug as 'well tolerated' at up to 80 times therapeutic clinical doses. The overall ONGLYZA dataset involved more than 4,000 patients.

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Data presented during June's ADA meeting showed significant reductions in all key measures of glucose control – HbA1c, Fasting and Post-Prandial Glucose. The remaining Phase III data is planned for disclosure at the European Diabetes Meeting in September. This is an important opportunity for us as type 2 diabetes is a growing, global problem. Its prevalence is expected to grow from 190 million to 330 million by the year 2030.

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2008 is also a key year for Zactima, a potential new medicine for non small cell lung cancer and medullary cancer of the thyroid. All 4 second line lung and thyroid registration studies; ZEST, ZODIAC, ZEAL and ZETA completed recruitment on schedule. These studies are powered to achieve benefits measured through Progression Free Survival as the primary outcome with Overall Survival as a secondary endpoint.

Event rates have slowed below predicted levels in the 3 lung studies, as you can see from this ZODIAC graph. The studies remain blinded and the code will only be broken after the completion of the studies. The results will consequently be delayed by one quarter, which means that data will still be available to us this year but the submission date has been revised to the first half of 2009. We still plan to submit the NSCLC and thyroid regulatory applications in parallel in the revised timeframe.

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Continuing with key developments in our Phase III programme, the PLATO outcomes study of AZD6140, a reversible platelet inhibitor in acute coronary syndrome, has completed recruitment and we have entered the 12 month follow-up window. Approximately 18,600 patients have been enrolled in the study. This is obviously a key milestone for this project as it means, subject to the event rate, we are on track for the EU and US submissions planned for the second half of next year.

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Moving on to Recentin, this oral VEGFR inhibitor, is currently being assessed in a wide range of solid tumours by ourselves as well as through a CRADA with the US National Cancer Institute.

Back in February of this year we announced progression of this project into Phase III for 1<sup>st</sup> line Colo-Rectal Cancer. We are on track for the EU and US submissions in colon and recurrent Glioblastoma, which are planned for 2010. In addition, there have been a number of external presentations showing encouraging data in other tumours including renal, prostate and ovarian cancers. With regards to lung; we are reviewing our strategy in this indication and plan to share the final data from the Phase II/III BR24 study at a meeting before the end of the year.

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All of our other Phase III projects are making good progress and are on track for their previously announced milestones.

ZD4054, our Endothelin A receptor antagonist, is being developed in M1 and Mo hormone resistant prostate cancer. We plan to publish the Phase II data during the fourth quarter of this year.

PN400, the project we are running with Pozen using a fixed combination of Enteric Coated Naproxen and immediate release es-omeprazole in patients who would receive an NSAID for pain relief in arthritis, is on track for its NDA submission scheduled for the first half of 2009 as all Phase III pivotal trials have now fully enrolled.

The Phase III program of Dapagliflozin, a potential first in class agent for type 2 diabetes, is progressing well with 7 studies currently ongoing. The Phase IIb data presented at the ADA this year demonstrated that dapagliflozin induced glucosuria consistent with its mechanism of action, improved glycemic control, lowered weight from the baseline, showed little propensity to cause hypoglycaemia and was well tolerated over a 12 week period.

Finally Crestor/TriLipix, a combination of Crestor with Abbott's TriLipix, previously Abbott 335, is on target for its NDA during the second half of next year.

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In the past 6 months we have had 2 additions to our Phase III portfolio.

Firstly, MEDI 561, a potential first in class inhibitor of Heat shock protein 90, being developed with Infinity, is planned to commence a Phase III registration trial in refractory gastrointestinal stromal tumours (GIST) this quarter. In addition to this orphan indication, a program of Phase II trials in a number of tumours is ongoing. And finally, the latest small molecule entry to our Phase III pipeline, AZD0837.

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AZD0837 is a once daily, oral anticoagulant. It's a selective and reversible direct thrombin inhibitor. AZD0837 is being investigated for the prevention of stroke and systemic embolic events in patients with atrial fibrillation. Atrial fibrillation is the most common sustained cardiac arrhythmia with approximately 7 million patients worldwide diagnosed today while its prevalence is increasing with an estimated 12 million patients expected by the year 2020. AF patients have a 5-fold increased risk of stroke.

Anticoagulation is effective but Warfarin, as shown in the graph, is hard to control and has serious limitations such as; an increased risk of bleeding, a narrow therapeutic window and numerous food and drug interactions such that many patients who should be anticoagulated today are not.

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So what do we know about AZD0837? It has been intensively investigated in pre-clinical and clinical trials, details of which are on the slide. More than 900 Atrial Fibrillation patients have been dosed to date with the longest exposure being 16 months so far. We have demonstrated a positive overall benefit risk profile for AZD0837 when compared with a vitamin K antagonist, such as warfarin, in the prevention of stroke in patients with AF. As you might expect from our Exanta experience, we have scrutinised the tolerability in general and the liver effects in particular. In our comparative Phase II study, AZD0837 was well tolerated and no excess liver risk was seen.

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We are confident that there is a considerable opportunity for AZD0837. It could be a highly effective medicine that strikes the right balance between preventing stroke and risk of bleeding because there is a predictable relationship between dosage and blood levels while at the same time it has low PK variability. Our Exanta experience as well as our biomarker capability and the extensive modelling conducted have proved very useful in selecting the proposed dose in AF patients. The ER formulation is once daily with no relevant food, and low to moderate drug interactions. Most importantly, it reduces the plasma peak: trough variation which we see as a key to safe, predictable anticoagulation. We plan to start recruitment into Phase III this year and we expect to present Phase IIb data next year.

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Although we support all of our marketed products I would now like to highlight just 4 of the most important lifecycle management programs starting with Seroquel. This is a large and comprehensive clinical development program that has delivered differentiated data providing a strong platform for Seroquel XR growth. As you can see from this slide there has been tremendous progress in our regulatory activities since I last presented at the beginning of the year.

The list of submissions delivered is extensive. The two remaining submissions to be delivered are Seroquel XR for Bipolar Maintenance in the US and Generalised Anxiety Disorder in Europe. They are both on track to meet our fourth quarter 2008 timeline.

The slide lists approvals and PDUFA dates. Approvals are beginning to come through and as the claims breadth increases beyond Schizophrenia, we can further establish XR in the market place.

#### **Slide 23**

IRESSA is the first and only EGF targeted therapy to demonstrate survival as good as single agent chemotherapy in pre-treated advanced NSCLC with better tolerability and superior QoL. In May 2008 an MAA was submitted to the European Medicines Agency seeking approval for Iressa as a treatment for locally advanced or metastatic non-small cell lung cancer in patients who have been pre-treated with platinum-containing chemotherapy. If approved this will offer these patients another much needed treatment option.

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The other key recent study of IRESSA is IPASS (Iressa Pan-Asia Study) in Japan and Asia. IPASS exceeded its primary objective and demonstrated superior progression-free survival for IRESSA compared to intravenous carboplatin/paclitaxel doublet chemotherapy. In addition, IRESSA again demonstrated a more favourable tolerability profile and superior quality of life. IPASS is an open-label, randomized parallel-group study which enrolled 1,217 clinically selected Asian patients with advanced NSCLC who had not received prior chemotherapy, whose tumours were adenocarcinomas and who had either never smoked, or were long-term ex-light smokers. The full data are still being analysed and detailed results of this exciting study will be presented at a forthcoming medical congress.

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Supplemental NDA's were submitted in the US for Symbicort use in COPD and for paediatric asthma, specifically 6 to 11 year olds, in April and June, respectively. We're also on track to file supplemental data for the pMDI formulation in Europe for asthma/COPD later this quarter.

Last, but by no means least, of the life cycle programs I want to cover today is Crestor. Back in March we announced the early closure of JUPITER due to unequivocal evidence of efficacy. We aim to present the results of the study at the AHA this coming November. You will also hear the results of the GISSI-HF study, the independent outcomes study of Crestor in unselected HF patients, at the ESC meeting in September.

Finally the SATURN study, a direct head to head comparison between Crestor and atorvastatin which is looking at plaque progression and regression is ongoing and actively recruiting.

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Let me focus-in now on our R&D productivity and the overall pipeline picture. During the first half of the year we have continued our efforts to improve our speed, quality and cost efficiency. This is paying off as we are seeing clear evidence of a stronger portfolio, which is progressing faster without cost increases. In January, we guided you towards a high single digit year on year R&D increase. Our improving productivity and efficiency, together with portfolio changes such as an early end to Jupiter and Recentin lung cancer, lead me to lower that guidance to the low to mid single digit range increase this year. We're doing more and moving faster while controlling the cost base.

Focusing our attention on Phase I as an example; we've reduced our cycle times considerably since 2006, as you can see from the graph, and are already close to achieving our 2010 Phase I target of 10 months. This is coupled with a significant reduction in our project costs as we are stopping failing projects earlier and for those that do progress we are seeing a reduction of approximately 33% versus 2006 figures. It is these efficiency benefits, coupled with our restructuring efforts and portfolio changes that have led to the revised 2008 guidance.

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So looking at our pipeline today it now includes 143 projects, including 100 projects in the clinical phase of development. Since the last update on 31 January 2008, 20 projects have progressed to their next phase (including 7 molecules entering first human testing), 15 compounds have been added from Discovery Research while 3 compounds have been withdrawn. It is worth noting that Discovery is playing a very active role in improving the productivity and speed of the whole R&D process.

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So in summary, as you can see from this bar-chart, we have built a stronger and more balanced pipeline. We are seeing clear evidence of delivery of the strategy we announced 2 years ago and we are on track to deliver our 2010 targets. We have achieved the portfolio breadth we require to launch on average 2 NCEs per year from 2010 onwards. We've more than doubled our Phase III pipeline since 2006 and we're building our Phase II portfolio. The flow of projects from Phase I to Phase II is clearly visible and indicates a dynamic shift in the composition of our pipeline. At the same time our Discovery and early development productivity has increased in order to sustain our future portfolio growth. We can still get better. In particular, we need to continue to build our mid-phase portfolio through progressions and in-licensing. At the end of last year we mentioned an unprecedented level of Phase IIb decisions that will occur this year. So far we've had 3 positive progressions and are expecting 10 other project decisions before the end of 2008. By this time next year that bow wave of projects should have led to a considerable strengthening of Phase IIb as the current Phase III projects move into registration.

We've demonstrated real progress and evidence of improvement on many fronts. However we can't afford to stand still and we will seek continuous improvement with the same vigour and intensity until we have met and exceeded all expectations.

Thank you. I'd now like to hand back to David Brennan.