

Annual Results – January 2009

Thank you /Simon

Today I'll be giving you our customary R&D Annual Review for 2008 and will then close with a brief review of the progress that we've made over the last four years. While we've achieved a lot in that time period, in this Industry, with long cycle times, it's worth noting that 4 years only amounts to one third of a 12 year Development cycle at our old speed and half an 8 year cycle for today's programmes.

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During the year, we've continued to strengthen the pipeline and, as evidence of its growing maturity, have completed 3 Phase III programmes and delivered 2 first NCE submissions. In addition, we've maintained the momentum in our life cycle management programmes

with 8 major new packages submitted and 3 approvals to date.

We started 18 Phase II programmes in the year – more than double the number of starts in 2007 and triple 2006.

Our productivity initiatives continue to deliver benefits and we are making good progress towards delivering an 8 year median cycle time by 2010 with a leaner and more cost efficient organisation, whilst delivering a larger portfolio. And 2009 could be an even better year with up to 4 new product submissions.

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Let me turn next to our Phase III portfolio, which I'll cover over the next few minutes in some depth.

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There are now 4 cardiovascular Phase III development projects. The most mature is our joint development with BMS for Onglyza, the DPP4 for the treatment of Type II diabetes. The NDA was submitted in America in June and the MAA accepted for review by the European Authorities in July, the European submission being 15 months ahead of previous schedule. This large clinical development programme involved over 5,000 individuals with a significant cohort, having had long-term follow-up, with no discernible cardiovascular or skin safety signal affecting tolerability across the dose range tested in Phase III. Those regulatory processes are ongoing and we are preparing for the scheduled PDUFA date at the end of April.

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The other BMS shared development in Type II diabetes is Dapagliflozin. Phase IIb data were presented at the major US and European diabetes conferences last year. The Phase III programme is now maturing with nine studies ongoing of which four are fully recruited. We will roll out the results at the major diabetes meetings. The programme is designed to meet the recently published FDA requirements on cardiovascular safety, much of which was already built into the planned database. Following our announcement that we have extended our BMS alliance to include Japan, studies there will start this year.

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Today we are announcing that AZD 6140 now has the trade name “BRILINTA”. The “PLATO” study has

completed its recruitment phase and data will be available around mid year following independent adjudication of over 9,000 events. I am looking forward to the results of this large study alongside the onset and offset trials that should show Brilinta to be a real improvement over current treatment.

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The approval of Abbott's Trilipix monotherapy in December has paved the way forward for the fixed dose combination treatment with Crestor, which is targeted at a third quarter 09 NDA. Trilipix is the first fibrate indicated for use in combination with a statin, making this fixed combination an obvious next step.

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The extended release formulation of AZD0837, the oral reversible thrombin inhibitor, completed Phase II but an

unexpected stability issue has delayed the start of Phase III dosing. We now believe we understand the problem and if the ongoing stability studies prove satisfactory, dosing will commence in second half of this year. In the meantime, for absolute transparency, we will place AZD0837 in the Phase II column of our pipeline table.

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PN400 is a fixed dose combination of naproxen and esomeprazole that we are developing with Pozen. The two pivotal ulcer risk reduction studies have now been completed and met their primary end-points. Two additional Phase III studies are still ongoing and the US NDA submission is planned for mid '09. The FDA have just confirmed the validity of the gastric ulcer end-point in these studies, so we can continue to plan for this NDA as one of our four potential filings in 2009.

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All the Zactima Phase III studies in lung and thyroid cancer completed recruitment on schedule. The slower than anticipated event rate in lung cancer has delayed the licensing submission by approximately 6 months. We released the headline results of Zodiac, the primary study, in combination with docetaxel, in November.

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The first Kaplan Meier curve shows a clear and statistically significant improvement in PFS, (the primary end-point agreed with FDA), as a result of giving Zactima in addition to optimal cytotoxic chemotherapy. as second line treatment. In addition, the second Kaplan-Meier curve shows that in the ZODIAC study, patients who received Zactima also had a significant improvement in their quality of life. No other oral

targeted agent to date has achieved significant clinical benefits when added to chemotherapy in 2nd line NSCLC. Furthermore, although only just over half the patients had died at the time of analysis, positive trends in prolongation of Overall Survival were seen, but did not reach statistical significance.

In the smaller pemetrexed combination study (ZEAL), although there is no significant difference, the Kaplan Meier curves for PFS and overall survival are virtually identical to those from the ZODIAC study. In both studies, the combination therapy was well tolerated, improved objective response rates and the symptoms of lung cancer.

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As a result, we are planning to file a regulatory package for Zactima in combination with chemotherapy in the second quarter of the year. The Zest monotherapy study, head to head with erlotinib, showed non inferiority but

did not achieve superiority in PFS or OS. A monotherapy claim will now have to wait for the ZEPHYR study in EGFR failure patients, which has completed recruitment and, subject to the event rate, will report in the second half of the year.

The medullary cancer thyroid study, ZETA, is also fully recruited and will be analysed when the number of progression events reaches target.

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Recentin met its efficacy and safety targets in first line colorectal cancer, triggering a continuation of the Horizon III study into Phase III. This study completed recruitment on schedule at the end of last year, the Phase III recurrent glioblastoma study is recruiting and a new lower dose combination study in first line non small cell lung cancer is about to start with the National Cancer Institute of Canada.

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Finally, in the cancer programme, the Endothelin A antagonist, AZD4054, is now recruiting well (and ahead of schedule) in the Phase III study in hormone resistant prostate cancer patients with metastatic disease. This study is very similar in design to the Phase II EPOC Study 6 published in December and shown on this chart. The 10 mg dose we are studying in Phase III gave a significant overall survival benefit in Phase II, something we don't see very often.

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The Motavizumab BLA was filed in the US in early February and received a complete response letter from the FDA late last year. Until we've met with the reviewing division, the timing of our response cannot be finalised. While we believe that no new studies will need to be performed, they have requested additional

clinical data from our completed study in infants born at term with congenital heart disease. This study remains code unbroken for efficacy and the RSV assays will only be performed after the code is broken following FDA discussions. Thus a late 2009 response is currently planned.

The large database on our nasal spray influenza vaccine was submitted in Europe on schedule in 4th quarter. Flumist, as it is known in the US, is now undergoing a European centralised registration process and has been accepted for submission by the EMEA.

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We've signed a deal for a new addition to our life cycle management portfolio, Unit Dose Budesonide, or UDB. In December 2008, we announced that we entered an exclusive worldwide agreement to develop and commercialise UDB with MAP Pharmaceuticals. It's being developed as a potential treatment for paediatric

asthma. UDB has the potential to be nebulised more quickly and at a lower nominal dose than the commercially available product and to be compatible with the new generation of nebulisers. The deal is subject to review under the Hart Scott Rodino Act.

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All four Crestor outcome studies reported to date have given strong support to the safety of Crestor at doses up to 20 mg and whilst Jupiter, Corona and Gissi have all been published, Aurora, a study in patients with end stage renal disease, is targeted for publication this spring.

The Jupiter study is a landmark study. Patients were selected with levels of LDL within normal limits but with an elevated HsCRP. This primary prevention study in men over 50 and women over 60 with a number of non lipid related risk factors demonstrated Crestor's unprecedented beneficial effects, irrespective of gender.

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In addition to the reduction of CRP, there was a very significant LDL lowering in spite of the low base line values. A regulatory package is under preparation for submission in the second quarter this year.

We shouldn't overlook the fact that we successfully concluded a repeat mutual recognition process in the EU last year gaining approval in 5 new markets, which means that we now have marketing authorisation in every EU market. This will allow us to gain an additional 6 months of market exclusivity in the EU upon approval of our agreed paediatric programme.

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Seroquel life cycle management has begun to repay the major investment we have made over the last few years with both the immediate release and the XR gaining new indication approvals in multiple jurisdictions throughout the year. The extended release FDA package for major

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depression generated a complete response letter at year-end. We don't anticipate the need to generate more efficacy data to gain approval but do recognise that there are bound to be questions to resolve with regulators as we move into this different patient population with Seroquel.

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Life cycle management continues for Symbicort with both the COPD and paediatric submission filed in the US, as well as the PMDI formulation in the UK. We launched our dose counter in the US but the Japanese NDA remains in a backlog of reviews at the regulatory agency.

We were pleased with the outcome of the triple FDA Advisory Committee on the benefits and risks of Long Acting Beta Agonists in Asthma. The panel voted unanimously to support the continued use of long acting

beta agonists in combination with steroid therapy in adults, in general and Symbicort in particular.

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The final life-cycle management project worthy of mention is for Iressa. In Asian patients pre-selected to have a high likelihood of EGFR mutation, Iressa proved superior to the standard first line treatment regime of carboplatin and paclitaxel. The progression free survival curves are shown on the graph. Taken together with a very favourable tolerability profile, these data will allow clinicians to deliver personalised healthcare with Iressa, or stratify their patients on clinical grounds and, where possible, on mutation status.

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The European Licence Application submitted in May is based on non-inferiority against docetaxel as a second

line treatment for non small cell lung cancer, a setting where, interestingly, clinical factors and mutation status did not appear to be a useful stratification tool. Both the INTEREST and IPASS studies are part of the ongoing regulatory review through the centralised procedure at the EMEA.

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Moving now from the late phase projects to the ongoing and continuous improvement process, 2008 was the year in which a number of our efforts in this field have started to bear fruit. We promised you \$100 million of R&D synergies following the Medimmune acquisition and these were delivered during 2008, ahead of schedule, using both the Disease Area Strategy to focus our activities and operational efficiencies, such as Clinical Data and other process outsourcing. In 2008, these changes allowed us to invest for the future through the expansion of our Medimmune Biologicals organisation,

whilst delivering an essentially flat year on year budget and supporting a much bigger development portfolio.

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We are making good progress towards delivering an 8 year median development time in 2010, as previously promised, and as the bow wave of clinical projects goes through Phases I and II, we're able to generate meaningful statistics to show that we're meeting our intermediate time targets, as shown for Phase I in the bar chart. Our focus in 2009 will be on improving the speed through Phase II in particular.

We undertook to develop all our new projects, where possible, with an element of personalised healthcare and we now have evaluated every project in the portfolio against this challenge and have 10 projects in Phase I and II today where we're testing an element of personalised healthcare.

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In a portfolio as large as ours,

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there will inevitably be a significant number of projects that fail or are stopped for a number of different reasons.

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However, in 2008 these were more than matched

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By projects that have progressed to the next step or to a regulatory filing. The Green boxes represent the projects that progressed to the next phase while the amber ones are those that have been filed with the registration authorities.

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And, of course, we have continued to introduce new molecules shown here in red.. We have entered 32 new compounds into formal development, of which 8 are biologics and taken 17 into Phase I human testing, of which 2 have already progressed to patient studies.

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This final slide of the sequence shows the pipeline today and its composition based on all of the changes in the year. As always, it is quite a dynamic picture.

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Looking at the pipeline, of particular note are the 18 products that had their first patient exposures in the year – double the number from 2007 and further evidence of the continuing progress with the portfolio. We said that we had a significant number of proof of concept and

proof of principle decisions during the course of 2008 and, of those, 6 proved positive and have entered Phase IIb dose finding studies during the course of the year, in addition to the 3 that were ongoing from 2007.

Overall, the pipeline has grown in the course of the year from 137 to 144 projects and whilst the preclinical programme has remained relatively flat, as expected, the growth in Phase II from 20 to 31 represents excellent progress, as is the very significant increase across the whole portfolio from 2004 with a much better balance across the phases.

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Four years ago I said to you that we had to take a number of actions to strengthen the AstraZeneca pipeline. In the short term, we wanted to optimise our marketed products through life-cycle activities, we needed to increase the

Discovery output and speed up our Development processes, improve the quality of our molecules and reduce our attrition rates, especially in the later phases and to strengthen the short and medium term through in-licensing acquisitions and deal making.

We also set out to move from a small molecules focussed organisation to one with a significant biologics presence. How have we done?

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Overall, there has been an 86% growth in NME's over that period. We've delivered 33 significant life cycle management approvals, altered the risk portfolio through both first and best in class approaches, more than doubled our research output and doubled every clinical phase of the portfolio. We delivered 2 licence applications in 2008 with 4 further first potential submissions in 2009. We've also taken steps

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To improve our strategic position for the long term
Through our Disease Area Strategy, we've focussed our
research and spun out or closed some areas such as
Albireo and osteoarthritis.

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In a stepwise fashion, we've created and acquired a
biologics portfolio and gained a foothold in Vaccines.
Biologics make up approximately one quarter of the
portfolio today.

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We've stepped up our licensing activities to bring in
significant numbers of new molecules and technologies
to close the late phase gap and build for the future.

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I believe that, however you look at it, AstraZeneca has created a much more attractive portfolio of products and projects from Discovery through to the market place.

Our pipeline is bigger and more mature and has a better balance of high and low risk projects. We set ourselves some challenging time targets for 2010 and we're on track to meet them. In 2004 we were slow in comparison with our peers. Today we are amongst the best in the discovery and early phases of development having already taken 2 years out of the overall process with more to come. And we've done it while increasing our overall efficiency and productivity.

We undertook some major outcomes studies in life cycle and Phase III. Jupiter is a prime example.

Perhaps the most important step that we've taken over this time period has been to establish a strong culture of continuous improvement across the whole of R&D with

lean 6 sigma at its core. We've delivered a lot but, as ever, there is still more to come.

This is my last Annual Results presentation and as I hand over to my successor, Anders Ekblom, I will be watching from the sidelines, as both a shareholder and a pensioner. I have every confidence in Anders, Jan and the team and I wish them every success in realising our dream of turning molecules into medicines.

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