AstraZeneca

# news release

November 7, 2002

## ASTRAZENECA REPORTS SIGNIFICANT PROGRESS ACROSS ITS PROMISING RESEARCH AND DEVELOPMENT PORTFOLIO

AstraZeneca today updated analysts on the company's late stage development products and projects; the progress of earlier stage products, notably in the cardio-vascular and oncology therapeutic areas; and the improved productivity in drug discovery, at its annual business review meeting in Alderley Park, Cheshire, UK, a centre of excellence for Oncology Research and Development at AstraZeneca.

***Late Stage Development Progress and Product Line Extensions***

- **CRESTOR** has received its first approval in The Netherlands, and will enter European Mutual Recognition Procedure in December. The US NDA will be supplemented with a data package in 1Q 2003; the Japan NDA was submitted in 2Q 2002.
- **EXANTA** is set to be the first new oral anticoagulant for 50 years:
    - The first indication in prevention of venous thromboembolism (VTE) in patients undergoing orthopaedic surgery was filed in Europe in July 2002.
    - Positive top-line results in the EXULT A study (confirming EXANTA's efficacy in preventing VTE when compared to warfarin in US patients) announced today will support the US filing for prevention of VTE in orthopaedic surgery, scheduled for 4Q 2003.
    - The main chronic indication, the prevention of stroke in patients with atrial fibrillation, based on the SPORTIF trials, will be filed in the US and Europe in 4Q 2003.
    - Encouraging data from THRIVE III, the first study to report using EXANTA in a chronic indication, were announced today and showed a significant reduction in VTE events and no difference in bleeding when compared to placebo. The study used a fixed dose of EXANTA without the need for coagulation monitoring, which is normally required for warfarin. A further indication for the treatment of VTE, based on the THRIVE studies, will also be filed in Europe in 4Q 2003.
    - Full details of EXULT A and THRIVE III will be presented at the American Society of Hematology meeting in Philadelphia in December 2002.

- **IRESSA**, the first epidermal growth factor receptor inhibitor, is already approved in Japan. In the US, IRESSA is under active review by the FDA, following a positive US Oncology Drugs Advisory Committee (ODAC) recommendation. A further ODAC meeting is not anticipated. The European filing is now scheduled for 1Q 2003.

**AstraZeneca**
S-151 85 Södertälje
Sweden

**Tel** +46 8 553 260 00
**Fax** +46 8 553 290 00
www.astrazeneca.com
www.astrazeneca.se

Reg Office AstraZeneca AB (publ)
S-151 85 Södertälje Sweden
Reg No 556011-7482
VAT No SE556011748201

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- The completion of the EU Mutual Recognition Procedure for approval of **ARIMIDEX** in early breast cancer, a significant market opportunity, was announced today. An approval has been granted in the UK and other European approvals (Austria, Germany, Italy, Portugal and Spain) will follow. ARIMIDEX was approved for early breast cancer in 3Q 2002 in the US, and other reviews are ongoing in the rest of world.
- **CASODEX** is now approved for early prostate cancer (EPC) in 26 markets. An EPC indication for CASODEX in the US will be the subject of a US ODAC meeting scheduled for December 18th.
- **FASLODEX** has been approved for second-line treatment of breast cancer in the US. European submission for this indication is scheduled for 2003, while the Japanese submission is under consideration.
- **NEXIUM** is growing strongly with sales of $1.6 billion (MAT 3Q). New indications for treatment of NSAID GI side effects and a new parenteral formulation for the hospital setting will be submitted for approval in 2Q 2003.
- **SEROQUEL,** now a $1 billion brand, has demonstrated efficacy in treating bipolar disease (mania). Filing for this indication is scheduled for 1Q 2003 in the US and Europe.
- Promising results for **SYMBICORT** in the treatment of chronic obstructive pulmonary disease (COPD) (a $2.9 billion global market) were announced, supporting the filing submitted to the EU earlier in 2002.
- Additional significant line extensions are planned for **FASLODEX, IRESSA, EXANTA, ATACAND, SEROQUEL** and **CRESTOR.**

***New Cancer Therapies***

- Further information was provided on new cancer therapies that target tumour growth mechanisms:
    - **ZD6474,** an anti-angiogenic, in phase II development, and **AZD2171,** another anti-angiogenic in phase I development, both target the growth of blood vessels of tumours.
    - **ZD6126,** a vascular targeting agent that will soon enter phase II development, targets and destroys the vasculature of tumours, working to destroy the tumour from within.
    - **AZD4054,** an endothelin antagonist in phase II development, works by inhibiting the $ET_A$ receptor, which is responsible for tumour cell proliferation.
    - **AZD0530**, an anti-invasive designed to prevent tumours from spreading, will enter clinical testing in 2Q 2003.
    - **AZD3409**, a prenylation inhibitor designed to inhibit proliferation of cancer cells, will enter clinical testing in 2Q 2003.

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***New Cardiovascular Therapies***

- Positive phase II data has been generated with **GALIDA (AZ242),** a new treatment for type II diabetes.
- **AZD6140,** an anti-platelet approach to prevent blood clots (which can lead to heart attacks and strokes) is currently in phase I development.
- **AZD7009,** a new treatment for atrial fibrillation, is also now in phase I development**.**

***New CNS/Pain Therapies***

- Phase III clinical trials for **NXY-059,** a novel neuroprotectant for acute stroke, will commence in early 2003.
- Encouraging clinical data was presented on **AZD3582**, the first Cox Inhibiting Nitric Oxide Donator (CINOD) for pain control, further demonstrating its attractive efficacy and side effect profile, versus COX-2 selective NSAID's.

***The full AstraZeneca development pipeline update is attached.***

***Drug Discovery Enhancements***

- **Candidate drug (CD)** delivery has increased by 20 per cent in the last three years--one quality CD is now entering preclinical development each month.
- The number of **CD's** that have progressed to clinical development has doubled this year.
- To increase the likelihood that CD's will progress through late-stage development to market, AstraZeneca is:
    - Bringing new aspects of **clinical medicine to the drug discovery process**—enabling better understanding of human diseases and how future drugs will work to prevent and treat those diseases.
    - **Front-loading risk** in clinical development by introducing more stringent safety and drug metabolism/pharmacokinetic (DMPK) testing earlier—allowing for early identification of CD's that will not succeed.
- **200 new collaborations** with leading academic centres and biotech companies have been initiated in 2002, supporting AstraZeneca's drug discovery strategy.

**Tom McKillop, Chief Executive, AstraZeneca, said:**

"The transformation of AstraZeneca's product portfolio continues apace with today's significant news of CRESTOR's first approval in Europe; progress with other late stage development projects; and the announcement of a raft of exciting new compounds in early development. A changing external environment and the rapid adoption of new technologies are combining to provide new challenges for the

pharmaceutical industry, but they will also bring new opportunities. We are driving productivity not only in R&D, but also in our overall business—bringing forward new indications for our key growth products and enhancing our sales forces effectiveness. By operating in a creative, fast and efficient manner, I am confident that AstraZeneca will continue to deliver important new medicines and deliver top-tier financial performance."

**Jan Lundberg, Executive Vice President, Head of Global Discovery Research, in an overview of the company's discovery strategy said:**

"With the research environment increasingly focused on finding disease relevant mechanisms combined with a plethora of fantastic new technologies, AstraZeneca is working as one global team to improve the predictability of drug discovery. We are introducing elements of clinical development in the earliest stages of our activities to make our research as relevant to man as possible, and using the latest technology for the early identification of projects unlikely to succeed in development. These actions will result in a much better ratio of CD's reaching the market. AstraZeneca has already been able to deliver a fruitful pipeline that is admired across the industry, and we will continue to populate that pipeline with novel quality compounds to provide added value and benefits to patients worldwide, faster than ever before."

**Martin Nicklasson, Executive Vice President, Head of Clinical Development, in an overview of the AstraZeneca portfolio said:**

"AstraZeneca's key growth products have delivered strong business performances in the past year, and will continue to as their indications are broadened through aggressive life-cycle management programmes. Underpinning an already impressive portfolio of products in our key therapeutic areas, we are happy to announce the progression of several promising early-stage research projects including NXY-059, a novel neuroprotectant agent for stroke, GALIDA, a new treatment for type II diabetes and lipid disorders, and our CINOD, AZD3582, a new treatment for pain. These projects along with a score of others will ensure the future success of AstraZeneca as a global leader in pharmaceutical research and development."


| | | |
|---|---|---|
| Media Enquiries: | Steve Brown/Emily Denney (London) | +44 207 304 5033/5034 |
| | Staffan Ternby (Södertälje) | 08 553 26107 |
| | Rachel Bloom (Wilmington) | +1 302 886 7858 |
| Investor Relations: | Mina Blair-Robinson (London) | +44 207 304 5084 |
| | Jonathan Hunt (London) | +44 207 304 5087 |
| | Staffan Ternby (Södertälje) | 08 553 26107 |
| | Ed Seage (Wilmington) | +1 302 886 4065 |
| | Jörgen Winroth (New York) | +1 212 581 8720 |


For copies of the presentations from today's annual business review, please visit www.astrazeneca.com.

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This press release contains forward-looking statements with respect to AstraZeneca's business. By their nature, forward-looking statements and forecasts involve risks and uncertainties because they relate to events and depend on circumstances that will occur in the future. There are a number of factors that could cause actual results and developments to differ materially. For a discussion of those risks and uncertainties, please see the company's Annual Report/Form 20-F for 2001.

***TRADE MARKS***

**The following brand names are trade marks of the AstraZeneca group of companies:**

**ARIMIDEX, ATACAND, CASODEX, CRESTOR, EXANTA, FASLODEX, GALIDA, IRESSA, NEXIUM, SYMBICORT, SEROQUEL.**

**AstraZeneca Development Pipeline: NCEs and line extensions**
**7 November 2002**

## ***Gastrointestinal***

**NCE's**

| Compound | Mechanism | Areas under investigation | Phase | Estimated Filing | |
|---|---|---|---|---|---|
| | | | | MAA | NDA |
| AZD0865 (was AR-H044277) | Reversible acid pump inhibitor | Acid related GI disease | I | >2005 | >2005 |
| AZD3355 | Inhibitor of transient lower esophageal sphincter relaxations (TLESR ) | Gastroesophageal reflux disease (GERD) | I | >2005 | >2005 |

**Line Extensions**

| | | | | | |
|---|---|---|---|---|---|
| Nexium® | Proton pump inhibitor | Treatment of NSAID GI Side effects | III | 2Q 2003 | 2Q 2003 |
| Nexium® | Proton pump inhibitor | Parenteral formulation | III | 2Q 2003 | 2Q 2003 |
| Nexium® | Proton pump inhibitor | Prevention of NSAID GI Side effects | III | 1H 2004 | 1H 2004 |
| Nexium® | Proton pump inhibitor | Extraeosophageal reflux disease | II | >2005 | >2005 |

## ***Cardiovascular***

**NCE's**

| | | | | | |
|---|---|---|---|---|---|
| Crestor™ | Statin | Hyperlipidemia | III | Filed | Filed |
| Crestor™ | Statin | Atheroma | III | >2005 | >2005 |
| Crestor™ | Statin | Outcomes | III | >2005 | >2005 |
| Exanta™(melagatran) | Thrombin inhibitor (s.c) | Prevention of VTE | III | Filed | >2005 |
| Exanta™ (H376/95) | Thrombin inhibitor | Prevention of VTE | III | Filed | 4Q 2003 |
| Exanta™ (H376/95) | Thrombin inhibitor | Prevention of stroke in AF | III | 4Q 2003 | 4Q 2003 |
| Exanta™ (H376/95) | Thrombin inhibitor | Treatment of VTE | III | 4Q 2003 | >2005 |
| Exanta™ (H376/95) | Thrombin inhibitor | Arterial/Post MI | II | >2005 | >2005 |
| AZ242 | PPAR agonist | Diabetes /Metabolic Syndrome | II | >2005 | >2005 |
| AZD6140 | ADP antagonist | Arterial thrombosis | I | >2005 | >2005 |

| | | | | | |
|---|---|---|---|---|---|
| AZD7009 | Atrial Repolarisation Delaying Agent (ARDA) | Atrial Fibrillation | I | >2005 | >2005 |
| AZD9684 | CPU inhibitor | Thrombosis | PC | >2005 | >2005 |
| AZD0837 | Thrombin inhibitor | Thrombosis | PC | >2005 | >2005 |
| AZD7806 | IBAT inhibitor | Dyslipidaemia | PC | >2005 | >2005 |

**Line Extensions**

| | | | | | |
|---|---|---|---|---|---|
| Atacand® | Angiotensin II antagonist | Hypertension outcomes (SCOPE) | III | 4Q 2002* | 4Q 2002* |
| Atacand® | Angiotensin II antagonist | CHF outcomes (CHARM) | III | 4Q 2003 | 4Q 2003 |
| Atacand® | Angiotensin II antagonist | Diabetic retinopathy | III | >2005 | >2005 |
| Toprol-XL® | Beta-blocker | HCTZ combination | III | | >2005 |

*submission for variation to existing label.

## ***CNS***

**NCE's**

| Compound | Mechanism | Areas under investigation | Phase | Estimated Filing | |
|---|---|---|---|---|---|
| | | | | MAA | NDA |
| NXY-059 | Free radical trapping agent | Stroke | III | >2005 | >2005 |
| ZD 0947 | $K^+$ channel opener | Overactive bladder | II | >2005 | >2005 |
| AR-A2 | $5HT_{1\beta}$ antagonist | Anxiety/Depression | I | >2005 | >2005 |
| AZD1134 | $5HT_{1\beta}$ antagonist | Anxiety/Depression | PC | >2005 | >2005 |
| AZD5106 | NK-2 antagonist | Overactive bladder | PC | >2005 | >2005 |
| AZD4750 | Chemokine receptor antagonist | Multiple sclerosis | PC | >2005 | >2005 |

**Line Extensions**

| | | | | | |
|---|---|---|---|---|---|
| Seroquel® | $D_2/5HT_2$ antagonist | Granules | III | 2004 | 2004 |
| Seroquel® | $D_2/5HT_2$ antagonist | Sustained release | III | Under evaluation | Under evaluation |
| Seroquel® | $D_2/5HT_2$ antagonist | Mania | III | 1Q 2003 | 1Q 2003 |
| Zomig® | $5\text{-}HT_{1B/1D}$ receptor agonist | Nasal spray | III | Launched | Filed |

# ***Oncology***

## NCE's

| | | | | | |
|---|---|---|---|---|---|
| Faslodex® | Oestrogen Receptor Antagonist | 2nd line Advanced breast cancer | III | 1Q 2003 | Launched |
| Faslodex® | Oestrogen Receptor Antagonist | 1st line Advanced breast cancer | III | >2005 | >2005 |
| Iressa® | EGFR-TK inhibitor | NSCLC | III | 1Q 2003 | Filed |
| ZD6474 | Angiogenesis inhibitor (Vascular endothelial cell growth factor receptor tyrosine kinase inhibitor) | Solid tumours | II | >2005 | >2005 |
| ZD4054 | Endothelin A receptor antagonist | Solid tumours | II | >2005 | >2005 |
| ZD6126 | Vascular targeting agent | Solid tumours | I | >2005 | >2005 |
| AZD2171 | Angiogenesis inhibitor (Vascular endothelial cell growth factor receptor tyrosine kinase inhibitor) | Solid tumours and haematological malignancies | I | >2005 | >2005 |
| AZD3409 | Farnesyl-transferase inhibitor ( FAR ) | Solid tumours | PC | >2005 | >2005 |
| AZD0530 | Non-receptor tyrosine kinase inhibitor | Solid tumours | PC | >2005 | >2005 |
| AZD4440 | Vascular targeting agent | Solid tumours | PC | >2005 | >2005 |

## Line Extensions

| Compound | Mechanism | Areas under investigation | Phase | Estimated Filing | |
|---|---|---|---|---|---|
| | | | | MAA | NDA |
| Arimidex® | Aromatase inhibitor | Adjuvant Breast Cancer | III | Approved | Launched |
| Casodex® | Anti-androgen | Early Prostate Cancer | III | Launched | Filed |
| Zoladex® | LHRH agonist | Pre-menopausal Adjuvant Breast Cancer | III | Launched | |
| Iressa® | EGFR-TK inhibitor | Head & Neck cancer | III | >2005 | >2005 |
| Iressa® | EGFR-TK inhibitor | Breast cancer | II | >2005 | >2005 |
| Iressa® | EGFR-TK inhibitor | Colorectal cancer | II | >2005 | >2005 |

## ***Respiratory and Inflammation***

**NCE's**

| | | | | | |
|---|---|---|---|---|---|
| AZD2315 | Immuno modulator | Rheumatoid Arthritis* | II | >2005 | >2005 |
| AZD4407 | 5-lipoxygenase inhibitor | COPD | I | >2005 | >2005 |
| AZD9056 | Ion channel blocker | Rheumatoid Arthritis* | I | >2005 | >2005 |
| AZD8309 | Chemokine receptor antagonist | Rheumatoid Arthritis* | PC | >2005 | >2005 |
| AZD7140 | Chemokine receptor antagonist | Rheumatoid Arthritis* | PC | >2005 | >2005 |
| AZD3342 | Protease Inhibitor | COPD | PC | >2005 | >2005 |
| AZD0275 | Chemokine receptor antagonist | COPD | PC | >2005 | >2005 |
| AZD0902 | Ion channel blocker | COPD | PC | >2005 | >2005 |
| AZD8955 | Collagenase inhibitor | Osteoarthritis | PC | >2005 | >2005 |

*First indication; use in other diseases eg. COPD under consideration.

**Line Extensions**

| | | | | | |
|---|---|---|---|---|---|
| Symbicort®Turbuhaler® | Inhaled steroid/fast onset, long-acting ß$_2$ agonist | COPD | III | Filed | |
| Symbicort®Turbuhaler® | Inhaled steroid/fast onset, long-acting ß$_2$ agonist | Single therapy for asthma | III | 3Q 2003 | |
| Symbicort® pMDI | Inhaled steroid/fast onset, long-acting ß$_2$ agonist | Asthma | III | 4Q 2003 | 1H 2004 |
| Oxis® Turbuhaler® | Long-acting $\beta_2$ agonist | COPD | III | Filed | |
| Oxis® pMDI | Long-acting $\beta_2$ agonist | Asthma | III | 3Q 2003 | |

## ***Pain Control***

**NCE's**

| Compound | Mechanism | Areas under investigation | Phase | Estimated Filing | |
|---|---|---|---|---|---|
| | | | | MAA | NDA |
| AZD3582 | COX inhibiting nitric oxide donator | Acute /chronic nociceptive pain | II | >2005 | >2005 |
| AZD4282 | NMDA Antagonist | Neuropathic pain | PC | >2005 | >2005 |
| AZD 4717 | COX inhibiting nitric oxide donator | Acute /chronic nociceptive pain | PC | >2005 | >2005 |

**Line Extensions**

| | | | | | |
|---|---|---|---|---|---|
| Naropin® | Sodium channel blocker | Spinal anaesthesia | III | Filed | |

## *Infection*

**Line Extensions**

| | | | | | |
|---|---|---|---|---|---|
| Merrem® | Carbapenem antibiotic | Skin and soft tissue infections | III | | 4Q 2003 |

## AstraZeneca Development Pipeline: Discontinued Projects

**GI**

| Compound | Mechanism |
|---|---|
| Rofleponide | Oral steroid |

**CV**

| Compound | Mechanism |
|---|---|
| AZD7545 | PDK Inhibitor |

**Respiratory and Inflammation**

| Compound | Mechanism |
|---|---|
| Rofleponide palmitate | Intranasal steroid |

**Infection**

| Compound | Mechanism |
|---|---|
| Merrem® for use in neutropenics | Carbapenem antibiotic |

**Comments**
As disclosure of compound information is balanced by the business need to maintain competitive advantage, some compound information has not been disclosed at this time.

Compounds in development are displayed by phase.

Abbreviations:

PC – Pre-clinical: Candidate Drug accepted for development but not yet administered to man.
MAA - Marketing Authorisation Application (Europe)
NDA – New Drug Application (USA)

7 November 2002