

ASTRAZENECA PLC  
Form 6-K  
January 23, 2004

**FORM 6-K**

SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549  
Report of Foreign Issuer

Pursuant to Rule 13a-16 or 15d-16 of  
the Securities Exchange Act of 1934  
For December 2003

Commission File Number: 001-11960

**AstraZeneca PLC**

15 Stanhope Gate, London W1K 1LN, England

Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40-F.

Form 20-F

Form 40-F

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(1): \_\_\_\_\_

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(7): \_\_\_\_\_

Indicate by check mark whether the registrant by furnishing the information contained in this Form is also thereby furnishing the information to the Commission pursuant to Rule 12g3-2(b) under the Securities Exchange Act of 1934.

Yes

No

If "Yes" is marked, indicate below the file number assigned to the Registrant in connection with Rule 12g3-2(b):  
82-\_\_\_\_\_

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**AstraZeneca PLC**

**INDEX TO EXHIBITS**

1. Press release entitled, "Repurchase of Shares in AstraZeneca PLC", dated 1 December 2003.

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2. Press release entitled, "Repurchase of Shares in AstraZeneca PLC", dated 2 December 2003.
3. Press release entitled, "Repurchase of Shares in AstraZeneca PLC", dated 4 December 2003.
4. Press release entitled, "Repurchase of Shares in AstraZeneca PLC", dated 8 December 2003.
5. Press release entitled, "Further data supports safety and efficacy of oral direct thrombin inhibitor, Exanta™ (ximelagatran) in prevention of venous thromboembolism", dated 8 December 2003.
6. Press release entitled, "Repurchase of Shares in AstraZeneca PLC", dated 9 December 2003.
7. Press release entitled, "Repurchase of Shares in AstraZeneca PLC", dated 10 December 2003.
8. Press release entitled, "Repurchase of Shares in AstraZeneca PLC", dated 12 December 2003.
9. Press release entitled, "AstraZeneca Prilosec® Patents Upheld by Federal Appeals Court", dated 12 December 2003.
10. Press release entitled, "Repurchase of Shares in AstraZeneca PLC", dated 15 December 2003.
11. Press release entitled, "Repurchase of Shares in AstraZeneca PLC", dated 18 December 2003.
12. Press release entitled, "Repurchase of Shares in AstraZeneca PLC", dated 19 December 2003.
13. Press release entitled, "Exanta™ (Ximelagatran) Regulatory Filings Submitted in United States (US) and European Union (EU) For Key Chronic Indications", dated 23 December 2003.
14. Press release entitled, "Exanta™ (Ximelagatran) Receives First Approval. First indication for prevention of venous thromboembolic events in major orthopaedic surgery", dated 23 December 2003.

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SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

AstraZeneca PLC

Date: 8 January 2004

By: /s/ G H R Musker

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Name: G H R Musker

Title: Company Secretary & Solicitor

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Item 1

REPURCHASE OF SHARES IN ASTRAZENECA PLC

AstraZeneca PLC announced that on 28 November 2003, it purchased for cancellation 300,000 ordinary shares of AstraZeneca PLC at a price of 2638 pence per share. Upon the cancellation of these shares, the number of shares in issue will be 1,696,147,717.

G H R Musker  
Company Secretary  
1 December 2003

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Item 2

REPURCHASE OF SHARES IN ASTRAZENECA PLC

AstraZeneca PLC announced that on 1 December 2003, it purchased for cancellation 200,000 ordinary shares of AstraZeneca PLC at a price of 2643 pence per share. Upon the cancellation of these shares, the number of shares in issue will be 1,695,947,717.

G H R Musker  
Company Secretary  
2 December 2003

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Item 3

REPURCHASE OF SHARES IN ASTRAZENECA PLC

AstraZeneca PLC announced that on 3 December 2003, it purchased for cancellation 200,000 ordinary shares of AstraZeneca PLC at a price of 2666 pence per share. Upon the cancellation of these shares, the number of shares in issue will be 1,695,761,944.

G H R Musker  
Company Secretary  
4 December 2003

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Item 4

REPURCHASE OF SHARES IN ASTRAZENECA PLC

AstraZeneca PLC announced that on 5 December 2003, it purchased for cancellation 700,000 ordinary shares of AstraZeneca PLC at a price of 2660 pence per share. Upon the cancellation of these shares, the number of shares in issue will be 1,695,066,044.

G H R Musker  
Company Secretary  
8 December 2003

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## Item 5

### **Further data supports safety and efficacy of oral direct thrombin inhibitor, Exanta™ (ximelagatran) in prevention of venous thromboembolism**

AstraZeneca today announced further evidence to support the strong efficacy and safety profile of Exanta™ (ximelagatran), following a presentation at the American Society of Haematology (ASH) Annual Meeting 2003, San Diego, US.

The EXULT B randomised, double-blind study, involving 2303 patients across five countries, compared oral fixed dose Exanta, 36 mg, given post-operatively twice daily, to standard anticoagulant treatment, dose adjusted warfarin, in patients undergoing total knee replacement surgery. Exanta was shown to provide superior efficacy to warfarin in preventing total venous thromboembolism (VTE) and all-cause mortality (22.5 per cent Exanta vs. 31.9 per cent warfarin,  $p < 0.001$ ), with no significant difference in bleeding compared with dose-adjusted warfarin.

Exanta is in development as the first oral treatment in a new class of direct thrombin inhibitors (DTIs) to prevent and treat thrombosis, one of the largest causes of morbidity and mortality in the western world. Those at greatest risk of VTE include patients undergoing orthopaedic surgery. More than half of patients undergoing major total hip or knee replacement currently develop VTE in the absence of preventative anticoagulant treatment. The most frequently used oral anticoagulant currently, warfarin, is effective, but it is limited by a number of factors including slow onset and offset of action, frequent dose adjustment, numerous drug and food interactions, and the need for routine coagulation monitoring. In contrast, oral Exanta has a rapid onset of action, a fixed dose regimen and no requirement for coagulation monitoring.

These results confirm the findings of the EXULT A study, presented at the ASH Annual Meeting 2002, with both studies now showing that oral Exanta 36 mg twice daily is clinically effective and superior compared to well-controlled warfarin in reducing total VTE and all-cause mortality among patients undergoing total knee replacement surgery, with no increase in bleeding.

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The EXULT A and B studies, comparing Exanta to warfarin in around 5,000 patients, will form the basis of a FDA regulatory submission for this indication, to be submitted by the end of 2003. The outcome of the EU regulatory submission for Exanta for prevention of VTE in patients undergoing elective hip or knee replacement surgery is expected shortly. The European licence submission includes data involving almost 7,500 patients that reflect the typical treatment regimen in Europe, and is based on studies that compare Exanta with the injectable low molecular weight heparin (LMWH), enoxaparin.

The ASH Annual Meeting 2003 also included a further presentation of the longer term THRIVE Treatment study in patients with VTE and at risk of recurrent thromboembolic events. First presented at the International Society of Haemostasis and Thrombosis (ISTH) in July 2003, THRIVE Treatment compares oral fixed dose Exanta 36 mg twice daily to the current standard treatment for acute VTE: in this study, the injectable LMWH, enoxaparin, followed by oral dose-adjusted warfarin, was given over six months. The study aimed to evaluate treatment of DVT with or without PE, and prevention of further VTE events.

The THRIVE Treatment study showed oral Exanta to be as effective and well tolerated as the standard treatment, but without limitations such as coagulation monitoring and dose titration. Laboratory blood tests in this long-term study showed an incidence of transient liver enzyme elevations in 9.6 per cent of patients receiving Exanta. These elevations decreased spontaneously whether treatment continued or discontinued and as has been seen in previous studies, were not typically associated with any specific clinical symptoms.

Exanta is the first oral anticoagulant to reach late-stage clinical development in almost 60 years, and has been the subject of the most extensive clinical development programme to date, involving approximately 30,000 patients. It is currently in phase III development for the key indications of stroke prevention in atrial fibrillation, treatment of VTE and long-term secondary prevention of VTE, with regulatory submissions to be filed in Europe and the US by the end of the year. The current worldwide market for antithrombotics is \$9.6 billion.

8th December 2003

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Item 6

REPURCHASE OF SHARES IN ASTRAZENECA PLC

AstraZeneca PLC announced that on 8 December 2003, it purchased for cancellation 600,000 ordinary shares of AstraZeneca PLC at a price of 2643 pence per share. Upon the cancellation of these shares, the number of shares in issue will be 1,694,466,044.

G H R Musker  
Company Secretary  
9 December 2003

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Item 7

REPURCHASE OF SHARES IN ASTRAZENECA PLC

AstraZeneca PLC announced that on 9 December 2003, it purchased for cancellation 400,000 ordinary shares of AstraZeneca PLC at a price of 2615 pence per share. Upon the cancellation of these shares, the number of shares in issue will be 1,694,066,044.

G H R Musker  
Company Secretary  
10 December 2003

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Item 8

REPURCHASE OF SHARES IN ASTRAZENECA PLC

AstraZeneca PLC announced that on 11 December 2003, it purchased for cancellation 350,000 ordinary shares of AstraZeneca

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PLC at a price of 2604 pence per share. Upon the cancellation of these shares, the number of shares in issue will be 1,693,716,544.

G H R Musker  
Company Secretary  
12 December 2003

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Item 9

AstraZeneca Prilosec® Patents Upheld by Federal  
Appeals Court

AstraZeneca today announced that a three judge panel of the United States Court of Appeals for the Federal Circuit upheld the October 2001 decision by U.S. District Court Judge Barbara S. Jones, finding that Andrx, Genpharm and Cheminor infringed AstraZeneca's patents for Prilosec® (omeprazole), and that the two formulation patents are not invalid. The Court also upheld the judgment that Kudco's formulation did not infringe.

AstraZeneca is pleased with the Court's decision upholding the validity of our patents, again reaffirming the strength of our intellectual property.

Prilosec is a treatment for acid-related stomach disorders.

12 December 2003

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Item 10

REPURCHASE OF SHARES IN ASTRAZENECA PLC

AstraZeneca PLC announced that on 12 December 2003, it purchased for cancellation 600,000 ordinary shares of AstraZeneca PLC at a price of 2581 pence per share. Upon the cancellation of these shares, the number of shares in issue will be 1,693,116,544.

G H R Musker  
Company Secretary  
15 December 2003

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Item 11

REPURCHASE OF SHARES IN ASTRAZENECA PLC

AstraZeneca PLC announced that on 17 December 2003, it purchased for cancellation 300,000 ordinary shares of AstraZeneca PLC at a price of 2579 pence per share. Upon the cancellation of these shares, the number of shares in issue will be 1,692,816,544.

G H R Musker  
Company Secretary  
18 December 2003

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Item 12

REPURCHASE OF SHARES IN ASTRAZENECA PLC

AstraZeneca PLC announced that on 18 December 2003, it purchased for cancellation 200,000 ordinary shares of AstraZeneca PLC at a price of 2585 pence per share. Upon the cancellation of these shares, the number of shares in issue will be 1,692,623,745.

G H R Musker  
Company Secretary  
19 December 2003

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Item 13

EXANTA™ (XIMELAGATRAN) REGULATORY FILINGS SUBMITTED IN UNITED STATES (US) AND EUROPEAN UNION (EU) FOR KEY CHRONIC INDICATIONS

AstraZeneca has submitted Exanta™ the first oral direct thrombin inhibitor, for regulatory review in the EU and US in key chronic-use indications. In the US, submissions have been made to the Food and Drug Administration (FDA) for Exanta in the prevention of stroke and other thromboembolic complications associated with atrial fibrillation (AF) and long-term secondary prevention of venous thromboembolism (VTE), after standard treatment for an episode of acute VTE. In Europe, regulatory submissions have been made to the Reference Member State, France, as part of the Mutual Recognition Procedure for use of Exanta in prevention of stroke and other thromboembolic complications associated with AF and the treatment of VTE.

Exanta is the first oral treatment in a new World Health Organisation class of direct thrombin inhibitors (DTIs) and is the first new oral anticoagulant to reach regulatory review since the introduction of warfarin almost 60 years ago. These submissions collectively comprise one of the largest-ever regulatory filings and are based on an extensive clinical study programme involving around 30,000 patients.

Exanta has the potential to meet an important unmet medical need in these long-term chronic indications involving prevention or treatment of venous thromboembolic events. For example, in the prevention of stroke in patients with AF, studies have shown that

the risk of stroke can be reduced by 62 per cent in patients taking oral anticoagulant therapy, and that around 50 per cent of eligible patients do not currently receive optimal treatment.

Exanta benefits from administration as a fixed oral dose, has a rapid onset and offset of action and shows low potential for food and drug interactions. Importantly, coagulation monitoring and dose titration are also not necessary in treatment with Exanta. Although existing anticoagulant treatments are effective, they are also associated with many limitations. While some require subcutaneous or intravenous administration, the current standard oral treatment, warfarin, is limited by extensive drug and food interactions and the need for routine coagulation monitoring and dose titration.

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A submission for the prevention of venous thromboembolic events in major elective orthopaedic (knee replacement) surgery has also been submitted in the US to the FDA this month.

23 December 2003

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## Item 14

### EXANTA™ (XIMELAGATRAN) RECEIVES FIRST APPROVAL

First indication for prevention of venous thromboembolic events in major orthopaedic surgery

AstraZeneca has received its first regulatory approval for Exanta™ (ximelagatran) in France for the prevention of venous thromboembolic events in major orthopaedic (hip or knee replacement) surgery. France is the Reference Member State for the European Union (EU) Mutual Recognition Procedure for Exanta. Subject to approval, launches of Exanta in this first 'proof of principle' indication are expected to take place later in 2004.

Exanta is the first oral treatment in a new World Health Organisation class of direct thrombin inhibitors (DTIs) and is the first new oral anticoagulant approved since the introduction of warfarin almost 60 years ago. Exanta benefits from administration as a fixed oral dose, has a rapid onset and offset of action and shows low potential for food and drug interactions. Importantly, coagulation monitoring is also not necessary in treatment with Exanta.

The approval of Exanta for this first indication in France is based on the METHRO study programme, involving an early postoperative start of Exanta treatment, with initial injectable dosing administered at least four hours after the completion of surgery, followed by oral Exanta 24mg twice daily for up to 11 days. This approval reflects clinical practice that is becoming increasingly common in Europe and allows use in conjunction with spinal anaesthesia with the oral dosing route enabling treatment to be easily continued following discharge from hospital. More than half of patients undergoing major orthopaedic surgery develop VTE in the absence of preventative anticoagulant treatment, and while effective treatments are available, no treatment regimen to date has successfully balanced efficacy and bleeding risk with oral dosing.

Regulatory submissions for Exanta in key chronic treatment indications, for prevention of stroke in atrial fibrillation and treatment of VTE, have already been filed in France as part of the EU Mutual Recognition Procedure. In the US, the Food and Drug Administration (FDA) submissions for use of Exanta in stroke prevention in

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patients with atrial fibrillation and long-term secondary prevention of VTE have also been filed alongside the orthopaedic surgery file for use of Exanta in prevention of VTE in total knee replacement.

23 December 2003

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