

WE ARE A WORLD LEADER IN CV MEDICINES, BACKED BY OVER 40 YEARS' EXPERIENCE. WE AIM TO BUILD ON OUR STRONG POSITION, FOCUSING ON THE GROWTH AREAS OF DYSLIPIDAEMIA, THROMBOSIS, TYPE 2 DIABETES/OBESITY, ATHEROSCLEROSIS AND ATRIAL FIBRILLATION.

PRODUCTS

Crestor has now been approved in 91 countries and launched in 76, including the US, Canada, Japan and the majority of EU countries. *Crestor* was launched in China in April 2007.

Dyslipidaemia is increasingly recognised as a major health issue. Of those people currently being treated for high cholesterol, only about half reach their cholesterol goal on existing treatments. In multiple clinical studies, *Crestor* has been shown to be highly effective in lowering low-density lipoprotein cholesterol or 'bad cholesterol' (LDL-C), allowing the majority of patients to reach their LDL-C goals with the 10mg usual starting dose. Additionally, *Crestor* produces an increase in high-density lipoprotein cholesterol or 'good cholesterol' (HDL-C), an effect that is observed across the 5, 10, 20 and 40mg doses. At its usual 10mg starting dose, *Crestor* has been shown to reduce LDL-C by up to 52% and raise HDL-C by up to 14%.

Our extensive, long-term global clinical research programme (GALAXY), which began in 2002, includes studies that investigate the effect of *Crestor* on CV risk reduction and patient outcomes. The programme involves over 63,000 patients in over 55 countries.

The GALAXY programme was designed to address important unanswered questions in statin research by investigating links between optimal lipid control, atherosclerosis and CV morbidity and mortality. So far, a number of the studies have been completed and we have seen data from three atherosclerosis studies, ORION, ASTEROID and METEOR. The ORION study examined the potential for *Crestor* to shrink the lipid-rich necrotic core of plaques and so improve their stability, while the ASTEROID study examined the effect of *Crestor* on coronary atherosclerosis. The METEOR data, reported in March 2007, showed that *Crestor* significantly slowed progression of atherosclerosis compared with placebo in people with early signs of carotid artery disease and at low risk of coronary heart disease. In November 2007, the US Food and Drug Administration approved *Crestor* as an adjunct to diet for slowing the progression of atherosclerosis in patients with elevated cholesterol. *Crestor* is the only statin with a broad atherosclerosis indication in the US (irrespective of disease severity

or location and not restricted to patients with coronary heart disease), an important differentiation from other cholesterol-lowering products. In addition, the *Crestor* prescribing information in Europe was updated in July 2007 to incorporate positive atherosclerosis data from the METEOR study. In January 2008, we announced the launch of a new clinical trial for *Crestor*, called SATURN, designed to measure the impact of *Crestor* 40mg and atorvastatin (Lipitor™) 80mg on the progression of atherosclerosis in high-risk patients. The study is expected to enrol more than 1,000 patients across the world and should be completed in 2011.

Data from the CORONA multi-national study in patients with advanced heart failure were presented at the American Heart Association 2007 Scientific Sessions in November 2007. CORONA was a novel study that examined the effect of adding *Crestor* 10mg to optimised treatment on CV mortality and morbidity and overall survival in elderly patients with advanced heart failure who were not candidates for statin therapy. CORONA showed an 8% reduction in the combined primary endpoint of CV death, myocardial infarction or stroke in patients with heart failure taking *Crestor* 10mg, which did not reach statistical significance. This reduction was primarily driven by a decrease in atherosclerotic events, such as stroke and myocardial infarctions. In addition, significantly fewer hospitalisations occurred in patients on *Crestor* compared to placebo, whether due to any cause, cardiovascular causes, or worsening heart failure. *Crestor* 10mg was well-tolerated, with a safety profile similar to placebo in a very high-risk study population. Further clinical trials of *Crestor* as part of the GALAXY programme are continuing and are due to report over the next few years.

Data from two pharmacoepidemiological observational studies investigating the incidence of CV events in over 470,000 patients taking statins (including *Crestor*) in routine clinical practice were presented in October 2007. The results from one study, conducted in The Netherlands, with a median duration of therapy of 11 months suggest that patients taking *Crestor* had significantly fewer CV events compared to patients taking simvastatin and pravastatin. The results from the other study, conducted in the US, showed

that *Crestor* users had a similar incidence of CV events to users of other statins at a median duration of therapy of 100 days. However, amongst patients who were on statin therapy for nine months or longer, the incidence of events was significantly lower in *Crestor* users. These studies have limitations typical of observational research. The large *Crestor* post-marketing surveillance programme in Japan was successfully completed in April 2007, when it was confirmed that the safety of *Crestor* for Japanese patients was in line with other statins.

In December 2007, we filed patent infringement actions against seven generic drug manufacturers in response to receiving notices stating that they had filed abbreviated new drug applications (ANDAs) in the US certifying their intent to market generic copies of *Crestor* before the 2016 expiry of our patent covering the active ingredient in *Crestor*. We did not file patent infringement actions against two other generic drug manufacturers that similarly filed ANDAs seeking approval to market generic copies of *Crestor*. Those ANDAs seek approval to market products only after expiration of the patent covering the active ingredient in 2016. Further information about the ANDAs in respect of *Crestor* is set out in Note 27 to the Financial Statements on page 158. We continue to have full confidence in our intellectual property protecting *Crestor* and will vigorously defend and enforce it.

Atacand continues to be well accepted and competes in the fastest growing sector by value (angiotensin II antagonists – plain and combinations with diuretic) of the global hypertension market. A 32mg dose is available to support the use of *Atacand* in hypertension and congestive heart failure. Launches of the 32mg dosage strength outside the US continued during the year, and this strength is now available in most major markets. The clinical programme (DIRECT) investigating the effect of *Atacand* (up to 32mg dosage) on retinopathy in hypertensive and normotensive diabetic patients continued during 2007.

PIPELINE

Diabetes/obesity

In January 2007, we announced a worldwide (except Japan) collaboration with Bristol-Myers Squibb Company (BMS) to develop and commercialise two investigational compounds discovered by BMS being studied for the treatment of Type 2 diabetes – saxagliptin and dapagliflozin. We will set the development and commercial strategy for the two compounds jointly with BMS.

Saxagliptin is being studied as a once-daily oral anti-diabetic to determine its efficacy and safety profile. Saxagliptin was specifically