

Novartis Cardiovascular & Metabolism

a report by

Novartis Diovan

High blood pressure and its consequences affect one in four adults, more than a billion people worldwide, and kill more than 7 million people every year. Type 2 diabetes causes 3 million deaths annually. Both diseases remain under-diagnosed and poorly treated, but Novartis is poised to expand its broad cardiovascular and metabolism portfolio by offering patients and physicians breakthrough innovations with the potential to transform treatment.

US regulatory approval of Exforge in December culminated a year packed with submissions and decisions for Novartis, setting the stage for a series of major launches over the next two years.

Exforge is the first treatment for high blood pressure to combine the two most commonly prescribed antihypertensive medicines in their classes: Diovan and the calcium channel blocker amlodipine besylate.

Tentative approval by the US Food and Drug Administration (FDA) will permit the launch of Exforge in September 2007, after the expiration of market exclusivity for amlodipine besylate.

In an extensive clinical program involving over 5,000 patients, Exforge helped up to 9 out of 10 patients reach their treatment goal (diastolic blood pressure under 90mmHg or more than a 10mmHg reduction in diastolic pressure from baseline). That high proportion of treatment success stands in sharp contrast to the estimated 7 out of 10 people with high blood pressure today who either remain undiagnosed or fail to reach their blood pressure targets.

“Exforge offers a potential solution to many people with high blood pressure who currently need two or more medicines to control their illness,” says James Shannon, MD, Head of Pharmaceutical Development at Novartis.

Meanwhile, two additional breakthrough medicines from Novartis are poised to fortify the dynamic portfolio of the Cardiovascular and Metabolism Franchise. Galvus (vildagliptin) and Tekturna (aliskiren) completed clinical testing last year and are now under regulatory review in

both the US and Europe for treatment of type 2 diabetes and hypertension, respectively.

“We are very confident of the efficacy and safety profiles of Galvus and Tekturna,” says Thomas Ebeling, Head of the Pharmaceuticals Division and member of the Executive Committee of Novartis, “and we are ready to roll as soon as we receive the go-ahead from regulators.”

Both medicines have innovative mechanisms of action and may offer patients the added promise of delaying or perhaps even preventing disease onset. Novartis has embarked on major ‘outcome’ trial programs for Galvus and Tekturna to realize their full medical and commercial potential. Tekturna was developed in collaboration with Speedel.

Outcome studies can span several years, involve thousands of patients and cost hundreds of millions of dollars, but they are viewed as the gold standard in demonstrating safety and efficacy of a drug to patients and physicians. They are also considered the gold standard of value for money by cost-conscious governments, insurers, and other payers.

“We drove Diovan’s success by creating and continuously adding to outcome data,” says John Glasspool, Head of the Cardiovascular and Metabolism Business Franchise at Novartis. “We aim to do the same for Galvus and Tekturna and move medical practice forward with studies we believe will demonstrate that these novel therapies can prevent and modify progression of type 2 diabetes and hypertension and ultimately help save lives.”

The Diovan Heritage

Exforge builds upon the heritage of Diovan, the flagship antihypertensive treatment from Novartis. Diovan sustained buoyant growth during 2006 as sales climbed 15% to US\$4.2 billion. Already the world’s most prescribed angiotensin receptor blocker (ARB), Diovan is expected to pass branded amlodipine this year and become the top-selling medication for high blood pressure worldwide.

The success of Diovan has been fueled by powerful efficacy and a broad range of approved indications. Those multiple applications reflect a comprehensive program of outcome studies, involving more than 40,000 patients across the cardiovascular continuum.

The megatrial program delivered new results in 2006, when the biggest clinical study of an ARB to date, in Japan, confirmed the efficacy of Diovan as well as its excellent cardiovascular profile, compared with the other studied antihypertensive therapies. The JIKEI Heart Study, involving more than 3,000 patients and conducted by the Jikei University School of Medicine in Tokyo, was halted early for ethical reasons after an interim statistical analysis showed Diovan had reduced stroke by 40% and heart failure by 46% compared with non-ARB therapies being used as comparators.

According to Professor Sebu Mochizuki, MD, of Jikei University, Chairman of the JIKEI Heart Study executive committee, the significantly reduced incidence of stroke shown in the trial “will be of particular interest to clinicians because there is a higher prevalence of stroke in the Japanese population than in Western society.”

Biggest Killer

High blood pressure and its consequences affect an estimated one in four adults, a billion people worldwide. The disorder is the leading cause of risk-attributable death, accounting for more than 7 million deaths per year. A person dies somewhere in the world from a hypertension-related disease every five seconds.

“Blood pressure is very poorly controlled,” says Matthew Weir, MD, Professor of Medicine at University of Maryland. “Even using a relatively unchallenging definition of normal blood pressure,” Dr Weir adds, “only 30% of patients in the US achieve their goal

blood pressure. America does better than anywhere else. Our friends in Europe have much lower percentages of people with high blood pressure under control.”

Clinical studies have clearly demonstrated that effective treatment of high blood pressure reduces coronary and renal events and strokes. Yet to the frustration of health authorities around the world, it’s a formidable challenge to keep patients on therapy long enough to reap those benefits.

Physicians increasingly view combination therapy as an important tool to improve patient compliance. “If you use two drugs as a single entity, as opposed to giving them as multiple tablets, there is significantly better adherence to therapy,” Dr. Weir explains. “I think this is the way we have to go in the future and I suspect that sooner or later we will see the development of triple combinations as well.”

In the Exforge clinical trial program, involving more than 5,000 people with hypertension, clinically significant blood pressure reductions and a good safety and tolerability profile were observed. “Exforge really starts to separate from other highly effective agents in treatment of poorly controlled patients with severe hypertension,” says Ameet Nathwani, MD, Head of Clinical Development and Medical Affairs, Cardiovascular and Metabolism Business Franchise. One example, he says, is a study where Exforge produced greater blood pressure reductions than treatment with a combination of lisinopril and hydrochlorothiazide.

“We believe Exforge may become the most efficacious agent in the antihypertensive category,” Dr. Nathwani adds.

For more information, please refer to our annual report: http://www.novartis.com/downloads/investors/report_s/AR06-E-advance-web.pdf ■