PROCORALAN® REDUCES RISK OF DEATH AND HOSPITALISATION FOR HEART FAILURE IN CHRONIC HEART FAILURE PATIENTS BY MORE THAN A QUARTER

STOCKHOLM, Sweden, August 29th 2010 – The largest-ever morbi-mortality study of treatments for chronic heart failure has shown that adding the specific heart rate lowering agent Procoralan® (ivabradine) to standard therapy significantly reduces the risk of death and hospitalisation for heart failure.[1] Results from this new study, SHIFT (**S**ystolic **H**eart Failure Treatment with the $\mathbf{I_f}$ Inhibitor Ivabradine **T**rial), were presented today at the European Society of Cardiology Congress[1] in Stockholm and published in *The Lancet.*[2]

SHIFT involved over 6,500 patients from 37 countries with moderate to severe heart failure and heart rate above 70 bpm who were followed up for an average of 23 months. The results showed that Procoralan® reduces the primary endpoint, a composite of cardiovascular death or hospitalisation for worsening heart failure, by 18% ($p<0.0001$). Procoralan® also reduced the likelihood of death from heart failure by over a quarter (26%, $p=0.014$) and the risk of hospitalisation due to worsening heart failure by the same amount (26%,$p<0.0001$). These benefits were evident in just three months of treatment with Procoralan® and despite the fact that patients were already receiving guideline recommended therapy (beta-blockers, angiotensin converting enzyme (ACE) inhibitors, diuretics or aldosterone antagonists). The study also confirmed that Procoralan® has a good tolerability profile in these fragile patients.

"Twenty years after Angiostensin Converting Enzyme Inhibitors and ten years after beta-blockers, we now have a new life-saving drug available for our patients", pointed out SHIFT executive committee co-chairman Professor Michel Komajda, Professor of Cardiology, University Pierre et Marie Curie Paris 6, France.

Chronic heart failure is a common and growing problem affecting 15 million patients in Europe (2% to 3% of the overall population). It impairs the heart's ability to pump effectively and maintain sufficient circulation to meet the body's needs. Heart failure presents a major healthcare and economic burden. Heart failure represents 10% of all hospital admissions and half of heart failure patients die within 4 years.

Procoralan® is an innovative treatment that is currently used in angina patients as it relieves symptoms, myocardial ischemia and reduces the risk of coronary events. The SHIFT study

has now also demonstrated the prognostic benefits of Procoralan® in chronic heart failure patients.

The SHIFT study is also the first study to specifically confirm that, due to Procoralan®, isolated heart rate reduction reduces the risk of death or hospitalisation for heart failure. This finding confirms that heart rate plays a key role in the progression of disease.

SHIFT co-chairman, Professor Karl Swedberg from the Head of the Department of Emergency and Cardiovascular Medicine at University of Gothenburg, Sweden, said: *"The SHIFT study has important implications for our clinical practice. It tells us that having a high heart rate is bad for heart failure patients. So we should routinely measure heart rate in all heart failure patients and, if it is above 70 beats per minute, heart rate lowering with Procoralan® should be considered, irrespective of their background treatment".*

SHIFT Trial Design

SHIFT is a randomised, double-blind study that compares Procoralan® with placebo on outcomes in patients with moderate to severe chronic heart failure (most commonly caused by ischaemia), poor left-ventricular ejection function and heart rate above 70 bpm. The study was designed to assess whether the I_f inhibitor can improve cardiovascular outcomes and symptoms and quality of life when added to standard therapy in patients with CHF and systolic dysfunction.

Patients received Procoralan® or placebo in addition to their standard chronic heart failure treatment. These included ACE inhibitors and/or ARBs, beta-blockers, diuretics and aldosterone antagonists. A total of 89% of patients in the study received ACE inhibitors and beta-blockers, with more than half of them who received at least 50% of the target dose.

SHIFT was funded by Servier, France's leading independent pharmaceutical company with a long history of successful drug development for cardiovascular diseases, and coordinated by the SHIFT executive committee, an international group of heart failure experts.

Procoralan®***** was developed by Servier and is indicated for the treatment of angina. It is the first agent of a new therapeutic class known as the selective and specific I_f inhibitors.

**Depending on the country, ivabradine is available as Procoralan®, Coralan®, Coraxan®, or Corlentor®*

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2. Swedberg K, et al. Beneficial effects of ivabradine on outcomes in chronic heart failure. The Systolic Heart Failure Treatment with the If Inhibitor Ivabradine Trial (SHIFT). Lancet. Online 29th August 2010

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