Novartis Phase III study shows RLX030 improved symptoms and reduced deaths by one-third in patients with acute heart failure

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- RELAX-AHF study met one of its two primary endpoints in reducing dyspnea or shortness of breath, and was therefore positive under pre-specified criteria
- Newly presented data show that at six months, RLX030 reduced all-cause and cardiovascular mortality by 37% in patients with acute heart failure (AHF)
- RLX030 is the first in a new class of medicines and the only agent to show a reduction in mortality in AHF
- Within one year after hospitalization for AHF, approximately 20-30% of patients die from various causes

East Hanover, November 6, 2012 – The Phase III RELAX-AHF study has shown that investigational RLX030 (serelaxin) improved symptoms and reduced deaths by one-third at the end of six months in patients with acute heart failure (AHF). Most of these deaths were due to cardiovascular causes. RLX030 is the first in a new class of medicines and is believed to act through multiple mechanisms on the heart, kidneys and blood vessels.

RELAX-AHF demonstrated that RLX030 significantly reduced dyspnea (i.e. shortness of breath), the most common symptom of AHF and the primary endpoint of the study. As one of two co-primary endpoints was met, the study achieved its primary objective based on pre-specified protocol criteria.

Results of the study were presented today at the American Heart Association (AHA) Scientific Sessions in Los Angeles and published simultaneously in The Lancet.

“This study with serelaxin is important because it may offer the prospect of a much-needed new medicine for acute heart failure, where the death rate remains high and there have been few new therapies for several decades,” said Professor John R. Teerlink, MD of the Section of Cardiology, San Francisco Veterans Affairs Medical Center, University of California, San Francisco, the co-lead investigator of the RELAX-AHF study.

Professor Marco Metra, Director of the Institute of Cardiology at the University and Civil Hospital of Brescia, Italy, the other co-lead investigator of the study, said: “The reduction in mortality seen with serelaxin is supported by the decreases in episodes of worsening of heart failure, as well as by the biomarker data collected during the study, suggesting that the clinical effects of serelaxin may be linked to a beneficial effect on organs such as the heart and kidneys.”

Novartis has begun discussing the results of this single Phase III study with health authorities worldwide.

“The survival results with RLX030 are encouraging for patients, their families and society at large,” said Tim Wright, Global Head of Development, Novartis Pharmaceuticals. “Novartis is committed to significantly improving treatment outcomes for patients with heart failure, and these results support our research into this therapeutic area which may lead to better management of the disease.”

Study details
RELAX-AHF was an international randomized, double-blind study involving 1,161 patients and was designed to compare the efficacy and safety profile of RLX030 to placebo in addition to standard therapy for the treatment of AHF. RLX030 was given upon hospitalization in the form of an intravenous infusion (30 mcg per kg per day) for 48 hours in addition to conventional therapy for AHF, i.e. loop diuretics and other medicines.

The study had two primary endpoints using different scales to measure reduction in dyspnea. The visual analog scale (VAS) showed a significant benefit up to day five (p=0.0075), whereas the Likert scale (a baseline-related short-term assessment of dyspnea relief) did not reach significance at 6, 12 and 24 hours (p=0.702). As one of the primary endpoints was met the study was positive according to protocol criteria.

The study did not meet its secondary efficacy endpoints, namely days alive and out of hospital up to day 60 (p=0.37), and cardiovascular death or re-hospitalization due to heart or kidney failure up to day 60 (p=0.89).

Results showed that 7.3% of patients died from all causes in the RLX030 group compared to 11.3% in the placebo group (p=0.02) at 180 days of follow-up. All-cause mortality up to day 180 was a safety endpoint of the study. The number of deaths due to cardiovascular causes to day 180 (an additional pre-specified efficacy endpoint) was also significantly lower with RLX030 than placebo (6.1% vs. 9.6%, p=0.028). RLX030 was therefore associated with a 37% reduction in all-cause and cardiovascular mortality at the end of six months.

In addition to its effects on mortality and symptoms, RLX030 met several other efficacy endpoints including significantly reducing the worsening signs and symptoms of heart failure up to day 14 (p=0.024), thereby decreasing the need for intensified heart failure treatment. RLX030 also reduced the mean length of stay in hospital by 0.9 days (p=0.039) and in the intensive/cardiac care unit by 0.4 days (p=0.029).

RLX030 was well tolerated and adverse events (AEs), including low blood pressure (hypotension), were generally comparable between RLX030 and placebo. There was a lower incidence of adverse events related to renal impairment with RLX030 than placebo (4.6% vs. 8.6%). The most common AEs in both treatment groups were cardiac disorders, metabolism and nutrition disorders, and gastrointestinal disorders. No clinically significant differences in the incidence of serious adverse events were seen between treatment groups.

Heart failure is a disease in which the heart is unable to supply enough blood to meet the body's needs. The disease leads to a spiral of physical decline often leading to acute episodes in which patients' symptoms suddenly become worse and urgent hospital treatment is needed. These episodes are called acute heart failure (AHF) and are also referred to as acute decompensated heart failure. Acute heart failure (AHF) places an enormous burden on healthcare systems. It is the most frequent cause of hospitalization in patients over 65 years of age in the United States. Death rates remain high despite currently available treatments. In 2009, there were more than 650,000 AHF hospitalizations in the United States.

Novartis progress in heart failure

RLX030 (serelaxin) is a recombinant form of the human hormone relaxin-2 which occurs naturally in both men and women. The results presented at AHA are consistent with those of a Phase II dose-ranging study called Pre-RELAX-AHF which investigated RLX030 in 234 patients with AHF. This study indicated that RLX030 improved dyspnea and suggested the potential for longer-term benefits.

Novartis and its wholly owned subsidiary Corthera Inc. have the exclusive worldwide rights to RLX030 (except in Canada).

Disclaimer

The foregoing release contains forward-looking statements that can be identified by terminology such as "may," "prospect," "suggesting," "encouraging," "committed," "potential," or similar expressions, or by express or implied discussions regarding potential marketing submissions or approvals for RLX030, or the timing of any such submissions or approvals, or regarding potential future revenues from RLX030. You should not place undue reliance on these statements. Such forward-looking statements reflect the current views of management regarding future events, and involve known and unknown risks, uncertainties and other factors that may cause actual results with RLX030 to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that RLX030 will be submitted or approved for sale in any market, or at any particular time. Nor can there be any guarantee that RLX030 will achieve any particular levels of revenue in the future. In particular, management's expectations regarding RLX030 could be affected by, among other things, unexpected clinical trial results, including unexpected new clinical data and unexpected additional analysis of existing clinical data; unexpected regulatory actions or delays or government regulation generally; competition in general; government, industry and general public pricing pressures; unexpected manufacturing issues; the company's ability to obtain or maintain patent or other proprietary intellectual property protection; the impact that the foregoing factors could have on the values attributed to the Novartis Group's assets and liabilities as recorded in the Group's consolidated balance sheet, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those anticipated, believed, estimated or expected. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

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Located in East Hanover, New Jersey, Novartis Pharmaceuticals Corporation is an affiliate of Novartis AG, which provides innovative healthcare solutions that address the evolving needs of patients and societies. Headquartered in Basel, Switzerland, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, eye care, cost-saving generic pharmaceuticals, preventive vaccines and diagnostic tools, over-the-counter and animal health products. Novartis is the only global company with leading positions in these areas. In 2011, the Group’s continuing operations achieved net sales of USD 58.6 billion, while approximately USD 9.6 billion (USD 9.2 billion excluding impairment and amortization charges) was invested in R&D throughout the Group. Novartis Group companies employ approximately 127,000 full-time-equivalent associates and operate in more than 140 countries around the world. For more information, please visit http://www.novartis.com.

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