New analysis of Novartis’ Entresto® data shows long-term benefits on heart failure readmissions and total cardiovascular deaths

- Entresto reduced the risk of first and subsequent events of heart failure hospitalizations and cardiovascular deaths following heart failure hospitalization by 20%-24% compared to enalapril.

- These findings are consistent with the benefit Entresto showed in reducing the risk of a first event, which was the primary endpoint of the PARADIGM-HF trial.

- Additional new analyses show that compared to enalapril, Entresto was associated with more diuretic dose reductions, lower risk of severe hyperkalemia in patients taking an MRA, and reduced risk among HFrEF patients with the most severe symptoms.

Basel, November 15, 2016 – Novartis announced today results of a new analysis demonstrating that Entresto® (sacubitril/valsartan) tablets reduced the risk of all events – first and repeat heart failure (HF) hospitalizations as well as cardiovascular (CV) deaths that followed HF hospitalization – compared to enalapril among heart failure patients with reduced ejection fraction (HFrEF). The findings are from a post-hoc analysis of PARADIGM-HF, the largest clinical trial ever conducted in HF. and are being presented at the American Heart Association (AHA) Scientific Sessions 2016 in New Orleans.

“In PARADIGM-HF, about one-third of heart failure patients with a first event experienced subsequent events – underscoring the substantial risks faced by patients with this life-threatening condition,” said Professor John McMurray of the University of Glasgow, and co-principal investigator for PARADIGM-HF. “The fact that sacubitril/valsartan not only reduced the risk of a first event, but also of repeat events – which are at least as serious and costly, and all too common – is highly significant and reinforces why this medicine is now guideline-directed therapy.”

Investigators conducted a comprehensive analysis of all heart failure hospitalizations and all CV deaths that took place in the PARADIGM-HF trial. A total of 3,181 primary endpoint events (including 1,251 CV deaths) were observed during the median 27-month double-blinded follow-up period of PARADIGM-HF, and about one-third of patients with a primary event also experienced a repeat event (defined as repeat HF hospitalizations or a CV death that followed HF hospitalization). Using multiple statistical analysis models, investigators found that Entresto demonstrated a risk reduction of between 20%-24% for all events (first-time and repeat events) compared to enalapril. These findings are consistent with the proven benefit of Entresto for reducing the risk of a first event in PARADIGM-HF (a 20% risk reduction compared to enalapril on the primary endpoint, a composite measure of time to CV death or first HF hospitalization).

“These analyses further support our knowledge that Entresto can keep many heart failure patients with reduced ejection fraction alive and out of the hospital for longer,” said Vas Narasimhan, Global Head of Development and Chief Medical Officer for Novartis. “As we
continue to analyze the results of the PARADIGM-HF study, we become more and more confident in the benefit that Entresto can bring to patients and to potentially reducing costs of care to healthcare systems."

Additional post-hoc analyses from PARADIGM-HF also presented at AHA Scientific Sessions further support the efficacy and safety benefits of Entresto among a range of HFrEF patients compared to enalapril. These analyses found:

- Treatment with Entresto was associated with fewer diuretic dose increases and more dose reductions compared to enalapril.
- Patients receiving Entresto and a mineralocorticoid receptor antagonist (MRA) had a lower risk of severe hyperkalemia (high potassium levels, >6) compared to those taking enalapril and an MRA.
- In patients with severe HF symptoms (NYHA functional class IV), Entresto showed consistent benefit when compared to the overall patient population of PARADIGM-HF.

About Heart Failure

Heart failure is a debilitating and life-threatening condition, which impacts over 60 million people worldwide. About half of people with heart failure have heart failure with reduced ejection fraction (HFrEF). Reduced ejection fraction means the heart does not contract with enough force, so less blood is pumped out. Heart failure presents a major and growing health-economic burden that currently costs the world economy $108 billion every year, which accounts for both direct and indirect costs.

Novartis has established the largest global clinical program in the heart failure disease area across the pharma industry to date, FortiHFy, comprising over 40 active or planned clinical studies designed to generate an array of additional data on symptom reduction, efficacy, quality of life benefits and real world evidence with Entresto, as well as to extend understanding of heart failure.

About Entresto

Entresto is a twice-a-day medicine that reduces the strain on the failing heart. It does this by enhancing the protective neurohormonal systems (natriuretic peptide system) while simultaneously inhibiting the harmful effects of the overactive renin-angiotensin-aldosterone system (RAAS). Other heart failure medicines only block the harmful effects of the overactive RAAS. Entresto contains the nepriyslin inhibitor sacubitril and the angiotensin receptor blocker (ARB) valsartan.

In Europe, Entresto is indicated in adult patients for the treatment of symptomatic chronic heart failure with reduced ejection fraction. In the U.S., Entresto is indicated for the treatment of heart failure (NYHA class II-IV) in patients with systolic dysfunction. It has been shown to reduce the rate of cardiovascular death and heart failure hospitalization compared to enalapril, and also to reduce the rate of all-cause mortality compared to enalapril. Entresto is usually administered in conjunction with other heart failure therapies, in place of an ACE inhibitor or other angiotensin receptor blocker (ARB). Approved indications may vary depending upon the individual country.

Disclaimer

The foregoing release contains forward-looking statements that can be identified by words such as “can,” “continue to analyze,” “confident,” “growing,” “to date,” “planned,” “designed,” or similar terms, or by express or implied discussions regarding potential new indications or labeling for Entresto, or regarding potential future revenues from Entresto. You should not place undue reliance on these statements. Such forward-looking statements are based on the current beliefs and expectations of management regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no
guarantee that Entresto will be submitted or approved for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that Entresto will be commercially successful in the future. In particular, management’s expectations regarding Entresto could be affected by, among other things, the uncertainties inherent in research and development, including unexpected clinical trial results and additional analysis of existing clinical data; unexpected regulatory actions or delays or government regulation generally; the company’s ability to obtain or maintain proprietary intellectual property protection; general economic and industry conditions; global trends toward health care cost containment, including ongoing pricing pressures; unexpected safety, quality or manufacturing issues, and other risks and factors referred to in Novartis AG’s current Form 20-F on file with the US Securities and Exchange Commission. 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.

About Novartis
Novartis 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 and cost-saving generic pharmaceuticals. Novartis is the only global company with leading positions in these areas. In 2015, the Group achieved net sales of USD 49.4 billion, while R&D throughout the Group amounted to approximately USD 8.9 billion (USD 8.7 billion excluding impairment and amortization charges). Novartis Group companies employ approximately 118,000 full-time-equivalent associates. Novartis products are available in approximately 180 countries around the world. For more information, please visit http://www.novartis.com.

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