Important new analysis shows that Novartis' Entresto® is associated with higher relative health-related quality of life scores among HFrEF patients

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- New analysis of PARADIGM-HF data shows that among patients who had been hospitalized for heart failure, those on Entresto reported higher relative health-related quality of life (HRQL) scores compared to those taking ACE inhibitor enalapril (1)
- In the overall study population, declines in HRQL scores were associated with an increased risk of worse outcomes, including CV death or heart failure hospitalization, a second analysis reported (2)
- Findings further support clinical benefits of Entresto and reinforce the urgency to treat appropriate patients with reduced ejection fraction (HFrEF)

EAST HANOVER, N.J., Sept. 19, 2016 /PRNewswire/ -- A new post-hoc analysis demonstrates that the decline in health-related quality of life (HRQL) scores associated with a heart failure (HF) hospitalization among patients taking Novartis' Entresto® (sacubitril/valsartan) was lower – approximately 50% less of a decline – compared to those taking ACE inhibitor enalapril.[1] A second post-hoc analysis in the overall study population shows an association between decline in HRQL score and increased risk of cardiovascular (CV) death and HF hospitalization.[2] The findings are based on data from PARADIGM-HF, the largest clinical trial ever conducted in HF,[3] and are being presented at the Heart Failure Society of America (HFSA)'s 20th Annual Scientific Meeting in Orlando.

"Heart failure hospitalizations can significantly decrease a patient's quality of life and lead to poorer outcomes," said Eldrin F. Lewis, MD, MPH, Associate Physician at Brigham and Women's Hospital and Associate Professor of Medicine, Harvard Medical School. "Heart failure management must focus on strategies to reduce this decline by better managing symptoms which can lead to hospitalization. These analyses suggest that sacubitril-valsartan may help mitigate the impact of heart failure hospitalization on a patient's health-related quality of life, and make a strong case for it as part of optimal treatment of heart failure with reduced ejection fraction."

Regardless of treatment, patients experienced a decrease in HRQL following a HF hospitalization.[1] The first analysis demonstrated that the decline in HRQL associated with a HF hospitalization among Entresto patients was significantly less compared to that of patients taking enalapril.[1]

- 6,981 patients in PARADIGM-HF completed a Kansas City Cardiomyopathy Questionnaire (KCCQ) to measure HRQL at baseline and at 8 months of treatment; during those 8 months, 305 patients were hospitalized for HF.[1]
- Among patients who had been hospitalized for HF, those on Entresto experienced lower declines in HRQL (approximately half) compared to those on enalapril (5.11 point decline vs. 10.77 point decline in KCCQ Clinical Summary Score (KCCQ-CSS) for Entresto and enalapril, respectively; p=0.003).[1]

Patients in the PARADIGM-HF study completed a KCCQ at randomization, 4 months, 8 months and annually.[1] KCCQ is a self-administered HRQL measure for HF patients, and the clinical summary score of the KCCQ uses a scale from 0 to 100, with higher scores indicating fewer symptoms and physical limitations associated with HF.[4] In PARADIGM-HF, at 8 months of treatment, HRQL, as measured by the KCCQ clinical summary score, declined less

in patients treated with Entresto than those patients treated with enalapril (2.99 point decline vs. 4.63 point decline for Entresto and enalapril, respectively; least squares mean of the between-group difference 1.64; 95% CI 0.63–2.65; p=0.001).[4]

A second post-hoc analysis examined the association between HRQL and patient outcomes in the overall patient population, and found that clinically meaningful worsening in HRQL scores (defined as a ≥ 5 point decrease in the KCCQ clinical summary score) after 4 months of treatment was associated with an increased risk of worse clinical outcomes, including CV death or HF hospitalization.[2]

- 7,155 patients completed a KCCQ at baseline and at 4 months of treatment.[2]
- Patients with a decline in HRQL, defined by a decrease of at least 5 points in the KCCQ clinical summary score at 4 months, were subsequently at a 24% higher risk of CV death (p=0.009) or 28% higher risk of HF hospitalization (p=0.004).[2]

"Entresto has already been shown to reduce the risk of cardiovascular death and heart failure hospitalization in heart failure patients with reduced ejection fraction. Now, we have further evidence that reinforces the importance to treat patients with this medication," said Fabrice Chouraqui, president of Novartis Pharmaceuticals Corporation. "Patients with heart failure face risks of hospitalization which can lower quality of life, and Entresto may help improve their outcomes."

About Heart Failure
Heart failure is a debilitating and life-threatening condition, which impacts nearly 6 million Americans and is the leading cause of hospitalization among Americans over the age of 65.[5,6] About half of people with heart failure have heart failure with reduced ejection fraction (HFrEF).[7] Reduced ejection fraction means the heart does not contract with enough force, so less blood is pumped out.[8] Heart failure presents a major and growing health-economic burden that currently exceeds $30 billion in the United States, which accounts for both direct and indirect costs.[9]

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).[10,11] Other heart failure medicines only block the harmful effects of the overactive RAAS.[12] Entresto contains the neprilysin inhibitor sacubitril and the angiotensin receptor blocker (ARB) valsartan.[10]

Entresto is indicated in the US to reduce the risk of cardiovascular death and hospitalization for heart failure in patients with chronic heart failure (NYHA Class II-IV) and reduced ejection fraction.[10] Entresto is usually administered in conjunction with other heart failure therapies, in place of an Angiotensin Converting Enzyme (ACE) inhibitor or an angiotensin II receptor blocker (ARB).[10] Entresto film-coated tablets are available in three dosage strengths: 24/26 mg, 49/51 mg, and 97/103 mg (sacubitril/valsartan).[10] These doses are referred to as 50 mg, 100 mg, and 200 mg in the clinical trial literature including the New England Journal of Medicine publication of the results of PARADIGM-HF. The target treatment dose of Entresto is 97/103 mg twice daily.[10]

Novartis is committed to providing patients with affordable access and resources through Entresto Central. For more information, please call 1-888-ENTRESTO or visit www.entresto.com.

Please visit http://www.pharma.us.novartis.com/product/pi/pdf/entresto.pdf for Entresto full Prescribing Information.

IMPORTANT SAFETY INFORMATION
Entresto can harm or cause death to an unborn baby. Patients should talk to their doctor about other ways to treat heart failure if they plan to become pregnant. If a patient gets pregnant while taking Entresto, she should tell her

doctor right away.

Patients are not to take Entresto if they are allergic to sacubitril or valsartan or any of the ingredients in Entresto; have had an allergic reaction including swelling of the face, lips, tongue, throat or trouble breathing while taking a type of medicine called angiotensin-converting enzyme (ACE) inhibitor or angiotensin II receptor blocker (ARB); or take an ACE inhibitor medicine. Patients are not to take Entresto for at least 36 hours before or after they take an ACE inhibitor medicine. Patients should talk with their doctor or pharmacist before taking Entresto if they are not sure if they take an ACE inhibitor medicine. Patients are not to take Entresto if they have diabetes and take a medicine that contains aliskiren.

Before they take Entresto, patients should tell their doctor about all of their medical conditions, including if they have kidney or liver problems; are pregnant or plan to become pregnant; are breastfeeding or plan to breastfeed. Patients should either take Entresto or breastfeed. They should not do both.

Patients should tell their doctor about all the medicines they take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. They should especially tell their doctor if they take potassium supplements or a salt substitute; nonsteroidal anti-inflammatory drugs (NSAIDs); lithium; or other medicines for high blood pressure or heart problems such as an ACE inhibitor, ARB, or aliskiren.

Entresto may cause serious side effects including serious allergic reactions causing swelling of the face, lips, tongue, and throat (angioedema) that may cause trouble breathing and death. Patients are to get emergency medical help right away if they have symptoms of angioedema or trouble breathing. Patients are not to take Entresto again if they have had angioedema while taking Entresto. People who are black or who have had angioedema may have a higher risk of having angioedema if they take Entresto. Entresto may cause low blood pressure (hypotension). Patients are to call their doctor if they become dizzy or lightheaded, or they develop extreme fatigue. Entresto may cause kidney problems or an increased amount of potassium in the blood.

The most common side effects were low blood pressure, high potassium, cough, dizziness, and kidney problems.

Please see full Prescribing Information, including Boxed WARNING available at http://www.pharma.us.novartis.com/product/pi/pdf/entresto.pdf.

Patients are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Disclaimer

The foregoing release contains forward-looking statements that can be identified by words such as "support," "potential," "being presented," "can," "lead to," "strategies," "suggest," "may," "make a strong case," "evidence," "growing," "committed," 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 Pharmaceuticals Corporation offers a broad range of medicines for cancer, cardiovascular disease, endocrine disease, inflammatory disease, infectious disease, neurological disease, organ transplantation, psychiatric disease, respiratory disease and skin conditions.

Located in East Hanover, NJ 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 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 more than 180 countries around the world. For more information, please visit http://www.novartis.com.

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