

# Nine new analyses show Novartis' LCZ696 could change course of heart failure for patients

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- - New data from PARADIGM-HF shows LCZ696 cut incidence of sudden deaths, emergency room visits, hospitalizations, worsening symptoms and need for more intense treatment in HFrEF patients versus enalapril(1,2)
- - Patients' and doctors' assessments of disease severity were also significantly better with LCZ696 than enalapril(1)
- - Effects on certain heart biomarkers indicate that compared to enalapril, LCZ696 reduced cardiac stress and damage(1)
- - Heart failure is highly debilitating and life-threatening(3) - up to half of patients who die from cardiovascular causes will die suddenly when their heart stops pumping, before medical intervention is possible(4)

EAST HANOVER, N.J., Nov. 17, 2014 /PRNewswire/ -- New data on Novartis' investigational medicine, LCZ696, for patients with heart failure with reduced ejection fraction (HFrEF) shows it has the potential to change the course of the disease for patients.<sup>1,2</sup> In August 2014, Novartis presented topline results from the landmark PARADIGM-HF study showing LCZ696 was superior to ACE inhibitor enalapril on key endpoints, including significantly reducing the risk of cardiovascular (CV) death or heart failure hospitalization.<sup>5</sup>

The new analyses being presented for the first time at the American Heart Association Scientific Sessions 2014, with a paper being simultaneously published in *Circulation*, show that versus enalapril, LCZ696 significantly:<sup>1,2</sup>

- reduced the risk of dying suddenly by 20% – in HFrEF patients, 45% of CV deaths and 36% of all-cause deaths were sudden<sup>6</sup>
- reduced first and subsequent HFrEF hospitalizations by 21% and 23%, respectively
- reduced hospitalizations for a CV reason or for any reason both by 16%
- reduced the need for more intense outpatient treatment by 16%
- reduced emergency room visits because of rapid symptom worsening by 30%

When hospitalized, LCZ696 and enalapril patients remained under care for approximately the same amount of time, but those on LCZ696 had 18% fewer stays in intensive care and were 31% less likely to need IV drugs to help their heart pump. Patients' reports of how well they felt and doctors' assessments of disease severity were also significantly better with LCZ696 than enalapril.<sup>1</sup>

"These results provide strong evidence that we may be able to do more than reduce risk of death or hospitalization with LCZ696 versus enalapril. This therapy offers hope to millions of people living with HFrEF that they can also reduce or slow the decline in their heart function, potentially altering the progression of their disease," said David Epstein, Division Head, Novartis Pharmaceuticals.

Analysis of cardiac biomarkers (NTpro-BNP and troponin), substances that indicate risk and progression of cardiac disease, showed levels were consistently lower with LCZ696 than enalapril, reflecting reduced heart

stress and subsequent damage.<sup>1</sup>

LCZ696, a twice-a-day medicine being investigated for heart failure, acts to enhance the protective neurohormonal systems of the heart (NP system) while simultaneously suppressing the harmful effects of the overactive renin-angiotensin-aldosterone system (RAAS). Currently available medicines for HFrEF only block the harmful effects and mortality remains very high, with up to 50% of patients dying within 5 years of a diagnosis of heart failure.<sup>7,8,9</sup>

Novartis plans to complete the New Drug Application for LCZ696 with the US Food and Drug Administration (FDA) by the end of 2014.

#### About the PARADIGM-HF study

PARADIGM-HF is a randomized, double-blind, Phase III study that evaluated the efficacy and safety profile of LCZ696 versus enalapril (a widely studied ACE inhibitor) in 8,442 patients with HFrEF.<sup>5</sup> The baseline characteristics showed the patients enrolled were typical HFrEF patients with NYHA Class II-IV heart failure.<sup>10</sup> PARADIGM-HF was specifically designed to see if LCZ696 could decrease CV mortality by at least 15% versus enalapril.<sup>11</sup> Patients received LCZ696 or enalapril in addition to current best treatment regimen. The primary endpoint was a composite of time to first occurrence of either CV death or heart failure hospitalization, and it is the largest heart failure study ever done.<sup>10,11</sup>

#### About LCZ696 in heart failure

LCZ696 is an ARNI (Angiotensin Receptor Neprilysin Inhibitor) and has a unique mode of action which is thought to reduce the strain on the failing heart.<sup>8,11</sup>

Heart failure is a debilitating and life-threatening disease in which the heart cannot pump enough blood around the body. Symptoms such as breathlessness, fatigue and fluid retention can appear slowly and worsen over time, significantly impacting quality of life.<sup>3</sup>

Heart failure represents a major and growing health-economic burden that currently exceeds \$30 billion in the United States, which accounts for both direct and indirect costs.<sup>12</sup> Hospitalizations account for 80% of the \$21 billion spent on the direct costs of heart failure.<sup>12</sup>

#### Disclaimer

The foregoing release contains forward-looking statements that can be identified by words such as "could," "will," "investigational," "potential," "may," "hope," "potentially," "being investigated," "plans," "thought," "growing," or similar terms, or by express or implied discussions regarding potential marketing approvals for LCZ696, or regarding potential future revenues from LCZ696. 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 LCZ696 will be approved for sale in any market, or submitted for approval in any additional markets, or at any particular time. Neither can there be any guarantee that LCZ696 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 LCZ696 will be commercially successful in the future. In particular, management's expectations regarding LCZ696 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 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.

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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, over-the-counter and animal health products. Novartis is the only global company with leading positions in these areas. In 2013, the Group achieved net sales of USD 57.9 billion, while R&D throughout the Group amounted to approximately USD 9.9 billion (USD 9.6 billion excluding impairment and amortization charges). Novartis Group companies employ approximately 133,000 full-time-equivalent associates and sell products in more than 150 countries around the world. For more information, please visit <http://www.novartis.com>.

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#### References:

1. Packer M, McMurray JJV, Desai AS, et al. Angiotensin-Nepriylsin Inhibition and Clinical Progression in Surviving Patients with Heart Failure. *Circulation*. 2014.  
  
McMurray JJV. The Prospective Comparison of Angiotensin Receptor Nepriylsin Inhibitor (ARNI) With ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure (PARADIGM-HF) Trial. Abstract: American Heart Association Scientific Sessions 2014.
2. ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure (PARADIGM-HF) Trial. Abstract: American Heart Association Scientific Sessions 2014.
3. Fauci A and Longo D. Disorders of the Heart. *Harrison's 'Principles of Internal Medicine*. 17<sup>th</sup> ed. 2008;4:1442-55.
4. Poole-Wilson PA, Uretsky BF, Thygesen K, et al. Mode of death in heart failure: findings from the ATLAS trial. *Heart*. 2003;89:42-48.
5. McMurray JJV, Packer M, Desai AS, et al. Angiotensin-Nepriylsin Inhibition versus Enalapril in Heart Failure. *N Engl J Med*. 2014;371:993-1004. DOI: 10.1056/NEJMoa1409077.
6. Novartis data on file.
7. Go A, Mozaffarian D, Roger V, et al. Heart Disease and Stroke Statistics—2014 Update: A Report From

the American Heart Association. *Circulation*. 2014;4(129):e28-e292.

Langenickel TH and Dole WP. Angiotensin receptor-neprilysin inhibition with LCZ696: a novel approach for the treatment of heart failure. *Drug Discovery Today: Therapeutic Strategies*. 2012;9(4):e131-e139. doi: 10.1016/j.ddstr.2013.11.002.

Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2013;128:e240-e327.

McMurray JJV, Packer M, Desai AS, et al. Baseline characteristics and treatment of patients in Prospective comparison of ARNI with ACEI to Determine Impact on Global Mortality and morbidity in Heart Failure trial (PARADIGM-HF). *Eur J Heart Fail*. 2014;16:817-825.

McMurray JJV, Packer M, Desai AS, et al. Dual angiotensin receptor and neprilysin inhibition as an alternative to angiotensin-converting enzyme inhibition in patients with chronic systolic heart failure: rationale for and design of the Prospective comparison of ARNI with ACEI to Determine Impact on Global Mortality and morbidity in Heart Failure trial (PARADIGM-HF). *Eur J Heart Fail*. 2013;15:1062-73. doi:10.1093/eurjhf/hft052.

Heidenreich PA, Albert NM, Allen LA, et al. Forecasting the impact of heart failure in the United States: a policy statement from the American Heart Association. *Circ Heart Fail*. 2013;6(3):606-619.

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