Novartis International AG
Novartis Global Communications
CH-4002 Basel
Switzerland

http://www.novartis.com

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Novartis announces new analysis demonstrating Entresto helped preserve kidney function in patients with chronic heart failure, especially those with diabetes

- *Heart failure (HF) patients with reduced ejection fraction treated with Entresto experienced significantly less reduction in kidney function compared to patients treated with standard of care ACE inhibitor enalapril*[1]
- *Magnitude of benefit was twice as high in a sub group of patients with HF and diabetes*[1]
- *Up to 40% of HF patients have diabetes, which is associated with greater risk of developing chronic kidney disease leading to poorer cardiovascular outcomes*[2,3,4]
- *In addition to the established benefits on mortality and HF hospitalizations, Entresto treatment also helps to preserve kidney function, especially in diabetic patients*

Basel, April 16, 2018 – Novartis today announced a new post hoc analysis of the pivotal Phase III heart failure study, PARADIGM-HF, demonstrating that treatment with Entresto® (sacubitril/valsartan) helped to preserve kidney function, as assessed by estimated glomerular filtration rate (eGFR), in patients with heart failure with reduced ejection fraction (HFrEF).[1] HFrEF patients treated with Entresto had a slower rate of decline in eGFR than those treated with ACE inhibitor enalapril.[1] In a sub group of patients who had both HFrEF and diabetes, the magnitude of benefit was twice as high.[1] The findings of the analysis are published today in *The Lancet Diabetes & Endocrinology*.

“These results suggest that in addition to the established benefits on heart failure, Entresto treatment also helps to preserve kidney function. This is important because impaired kidney function is associated with poorer outcomes in patients with heart failure,” said Shreeram Aradhye, Chief Medical Officer and Global Head, Medical Affairs, Novartis Pharmaceuticals. “The benefit is particularly significant for people with chronic heart failure who also have diabetes, which is an independent risk factor for kidney damage.”

Non-diabetic HFrEF patients in the PARADIGM-HF study were shown to lose kidney function twice as fast as the general population.[1] This was further accelerated in HFrEF patients with diabetes, who experienced a decline in kidney function that was twice as fast as the non-diabetic patients.[1] When compared with enalapril, treatment with Entresto significantly slowed this decline in all HFrEF patients (-1.3 vs -1.8 ml/min/1.73m^2 per year).[1] In HFrEF patients who also had diabetes, the benefit of treatment with Entresto was doubled vs. those without diabetes (+0.6 (0.4, 0.8) vs. +0.3 (0.2, 0.5) ml/min/1.73m^2 per year).[1]

Heart failure is associated with both diabetes and kidney disease, which lead to poorer outcomes for patients, including increased risk of morbidity and mortality.[2,3,4] More than half of all heart failure patients are expected to experience moderate to severe chronic kidney disease (CKD), and up to 40% of heart failure patients will have a diagnosis of diabetes.[2,4]

Diabetes significantly increases an individual's risk for CKD. Added to this, many anti-diabetic medications are known to increase the risk of heart failure hospitalization or mortality.[2,5]

Primary data from PARADIGM-HF, the largest clinical trial ever conducted in heart failure, showed that treatment with Entresto reduced the risk of dying from a cardiovascular cause by 20%, reduced heart failure hospitalizations by 21% and reduced the risk of dying from any cause by 16% as compared to enalapril.[6] This new analysis adds to the growing evidence that Entresto has important clinical benefits for heart failure patients beyond improving their cardiovascular outcomes, and validates findings from a further post hoc analysis of PARADIGM-HF, published online in the *Journal of the American College of Cardiology: Heart failure* (*JACC-HF*) on 12 April 2018, which found that Entresto helped slow the rate of renal function decline, even in heart failure patients with chronic kidney disease, as compared to enalapril.[7] Entresto is indicated for the treatment of chronic heart failure (NYHA II-IV) with reduced ejection fraction.[8] It is not indicated to treat diabetes.

About Heart Failure
Heart failure is a debilitating and life-threatening condition, which impacts over 60 million people worldwide.[9] It is the leading cause of hospitalization in people over the age of 65.[10,11] About half of people with heart failure have heart failure with reduced ejection fraction (HFrEF).[12] Reduced ejection fraction means the heart does not contract with enough force, so less blood is pumped out.[13] 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.[10,14]

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® (sacubitril/valsartan)
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).[8,15] Other common heart failure medicines, called angiotensin converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs), only block the harmful effects of the overactive RAAS.[16] Entresto contains the neprilysin inhibitor sacubitril and the angiotensin receptor blocker (ARB) valsartan.[8]

In Europe, Entresto is indicated in adult patients for the treatment of symptomatic chronic heart failure with reduced ejection fraction. In the United States, Entresto is indicated for the treatment of heart failure (New York Heart Association class II-IV) in patients with systolic dysfunction.[8] 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.[6] Entresto is usually administered in conjunction with other heart failure therapies, in place of an ACE inhibitor or other angiotensin receptor blocker (ARB).[8] Approved indications may vary depending upon the individual country.

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on these statements. Such forward-looking statements are based on our current beliefs and expectations 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 the investigational or approved products described in this press release will be submitted or approved for sale or for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that such products will be commercially successful in the future. In particular, our expectations regarding such products could be affected by, among other things, the uncertainties inherent in research and development, including clinical trial results and additional analysis of existing clinical data; regulatory actions or delays or government regulation generally; global trends toward health care cost containment, including government, payor and general public pricing and reimbursement pressures; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; general political and economic conditions; safety, quality or manufacturing issues; potential or actual data security and data privacy breaches, or disruptions of our information technology systems, 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, cost-saving generic and biosimilar pharmaceuticals and eye care. Novartis has leading positions globally in each of these areas. In 2017, the Group achieved net sales of USD 49.1 billion, while R&D throughout the Group amounted to approximately USD 9.0 billion. Novartis Group companies employ approximately 122,000 full-time-equivalent associates. Novartis products are sold in approximately 155 countries around the world. For more information, please visit http://www.novartis.com.

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Novartis Media Relations
Central media line: +41 61 324 2200
E-mail: media.relations@novartis.com

Eric Althoff
Novartis Global Media Relations
+41 61 324 7999 (direct)
+41 79 593 4202 (mobile)
eric.althoff@novartis.com

Agnes Estes
Novartis Pharma Communications
+41 61 324 1896 (direct)
+41 79 644 1062 (mobile)
agnes.estes@novartis.com

Novartis Investor Relations
Central investor relations line: +41 61 324 7944
E-mail: investor.relations@novartis.com

Central		North America	
Samir Shah	+41 61 324 7944	Richard Pulik	+1 212 830 2448
Pierre-Michel Bringer	+41 61 324 1065	Cory Twining	+1 212 830 2417
Thomas Hungerbuehler	+41 61 324 8425		
Isabella Zinck	+41 61 324 7188		