

**MEDIA UPDATE • MEDIA UPDATE • MEDIA UPDATE**

## **Novartis to present new Entresto HFpEF and HFrEF data at ESC Congress 2019**

- *PARAGON-HF trial will provide Entresto® (sacubitril/valsartan) Phase III full results in heart failure with preserved ejection fraction (HFpEF)<sup>1</sup>*
- *New PROVE-HF and EVALUATE-HF studies will highlight Entresto's direct impact on the heart in heart failure with reduced ejection fraction (HFrEF)<sup>2,3</sup>*
- *New PIONEER-HF and TRANSITION-HF findings will advance understanding of Entresto use in patients hospitalized for decompensated HFrEF following stabilization<sup>4,5,6,7</sup>*

**Basel, August 19, 2019** – Novartis will present data for Entresto® (sacubitril/valsartan) in both types of chronic heart failure – HFpEF and HFrEF – at the upcoming ESC Congress 2019, the annual meeting of the European Society of Cardiology (ESC), taking place from August 31 to September 4 in Paris.

Key Entresto outcomes will be shared via three late-breaking trial presentations, three oral/rapid fire presentations and one poster. Late-breaking presentations include the first full readout from PARAGON-HF, the largest Phase III HFpEF trial to date, which evaluated Entresto against an active comparator<sup>8</sup>.

"Novartis is a pioneer in reimagining outcomes in heart failure treatment, and we are excited by the wealth of Entresto data being presented during this year's ESC congress," said John Tsai, M.D., Head of Global Drug Development and Chief Medical Officer, Novartis. "We are pleased to share the latest outcomes exploring this important medication's role as a first-choice HFrEF treatment and the full primary results from our landmark PARAGON-HF trial in HFpEF. We are proud of the positive impact Entresto is having on the lives of HFrEF patients, and we will be equally proud of its robust contribution to the scientific body of evidence during the ESC Congress 2019."

### **Highlights of Entresto data at the ESC Congress 2019 include:**

**The first in-depth readout of PARAGON-HF, which is the largest HFpEF clinical trial conducted to date<sup>8</sup>.** The randomized, double-blind, Phase III outcome study evaluated the long-term efficacy and safety profile of Entresto against an active comparator (valsartan) in HFpEF<sup>8</sup>. It represents the largest-ever Phase III study in HFpEF and, despite the narrowly missed statistical significance for its composite primary endpoint of reducing cardiovascular death and total heart failure hospitalizations, the totality of evidence suggests that treatment with sacubitril/valsartan may result in clinically important benefits in select patients with HFpEF, a disease with high unmet need and no currently approved treatment<sup>1,8,9,10</sup>.

- **PARAGON-HF - Angiotensin Receptor Neprilysin Inhibition in Heart Failure with Preserved Ejection Fraction**

*S. Solomon*

**Time:** Sun 01 Sept., 15:02 – 15:25

**Session & location:** Hot Line Session 1, Paris - Main Auditorium

**Cardiac remodeling data from the PROVE-HF and EVALUATE-HF trials in HFrEF**, which assessed whether Entresto improves the structure and function of the heart, providing additional insight into Entresto's unique mechanism of action and whether these effects may underlie its clinical benefits<sup>2,3</sup>. Cardiac remodeling refers to changes that occur in the heart as a result of disease or after injury and leads to poor prognosis due its negative effects on heart function<sup>11</sup>. The ability to reverse cardiac remodeling may restore function and improve clinical outcomes<sup>11,12</sup>.

- **Effects of Sacubitril-Valsartan Compared with Enalapril on Arterial Hemodynamics and Cardiac Remodeling in Patients with Heart Failure and Reduced Ejection Fraction (EVALUATE-HF)**

*A. Desai*

**Time:** Mon 02 Sept., 08:48 – 09:06

**Session & location:** Late Breaking Science in Heart Failure 1, Budapest - Village 5

- **Effects of Angiotensin Receptor/Neprilysin Inhibitor Therapy on NT-proBNP and Cardia Remodelling in Heart Failure with Reduced Ejection Fraction: Primary results of the PROVE-HF study**

*J. Januzzi*

**Time:** Mon 02 Sept., 09:06 – 09:24

**Session & location:** Late Breaking Science in Heart Failure 1, Budapest - Village 5

**Oral and rapid fire presentations, as well as poster presentations, showcasing new data from the PIONEER-HF and TRANSITION trials in acutely decompensated HFrEF patients<sup>4,5,6,7</sup>**, which build on data presented [at ACC 2019](#) and [at AHA 2018](#). PIONEER-HF and TRANSITION data are included in the [expert consensus meeting report of The Heart Failure Association of the European Society of Cardiology](#), supporting the use of Entresto in every eligible HFrEF patient stabilized in hospital<sup>13</sup>.

- **Angiotensin receptor-neprilysin inhibition in patients with de novo acute decompensated heart failure: a prespecified subgroup analysis of the PIONEER-HF trial**

*A. Ambrosy*

**Time:** Sun 01 Sept., 08:48 – 09:06

**Session & location:** Treatment of conundrum in acute heart failure, Sarajevo - Village 5

- **Safety and efficacy of sacubitril/valsartan by dose level in patients hospitalized with acute heart failure: Observations from PIONEER-HF**

*D. Morrow*

**Time:** Mon 02 Sept., 17:22 – 17:36

**Session & location:** Acute heart failure: new treatment updates, Science Box 2 - Poster Area

- **Clinical predictors of NT-proBNP response to early initiation of sacubitril/valsartan after hospitalisation for decompensated heart failure: An analysis of the TRANSITION study**

*D. Pascual-Figal*

**Time:** Sun 01 Sept., 11:45 – 11:54

**Session & location:** New treatment studies in heart failure, Agora 1 - Poster Area

- **Rehospitalisations during 26 weeks of follow up from initiation of sacubitril/valsartan after acute decompensated heart failure: An analysis of the TRANSITION study**

*D. Pascual-Figal*

**Time:** Sun 01 Sept., 08:30 – 12:30 (presenter at poster 10:05 - 10:55)

**Session & location:** Poster Session 2: Heart failure outcome, poster area

Throughout the ESC Congress 2019, Novartis will host dedicated content on Twitter, Facebook and LinkedIn.

### **About Our Longstanding Commitment to Heart Failure**

Sacubitril/valsartan (approved as Entresto® since 2015) is a first-choice treatment in heart failure with reduced ejection fraction (HFrEF), based on its superiority to the angiotensin-converting enzyme (ACE) inhibitor enalapril and its ability to significantly reduce CV death and HFrEF hospitalizations<sup>13,14</sup>. Entresto plays a critical role in keeping people with HFrEF out of the hospital and helps reduce the staggering economic burden of the disease, which is estimated to be \$108 billion globally on an annual basis (accounting for both direct and indirect costs)<sup>15</sup>.

Novartis undertook the largest global clinical program in the HF disease area across the pharmaceutical industry to date, called FortiHFy. The program comprises 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.

Through the Entresto scientific program, Novartis is reimagining the standard of care for HFrEF patients and the use of Entresto as a first-choice therapy in HFrEF as well as its potential in HFpEF, a condition for which there is currently no approved treatment<sup>9,10</sup>. Beyond PARAGON-HF, additional studies investigating Entresto on other relevant endpoints in HFpEF are ongoing.

### **About PARAGON-HF**

PARAGON-HF is the largest clinical trial in heart failure with preserved ejection fraction (HFpEF) conducted to date<sup>8</sup>. The Phase III randomized, double-blind, parallel group, active-controlled, 2-arm, event-driven trial compared the long-term efficacy and safety of sacubitril/valsartan versus valsartan in 4,822 patients with HFpEF<sup>8</sup>. The patients in the study represented ambulatory patients with established HFpEF being treated for symptoms and comorbidities, approximately half of whom had a history of heart failure hospitalizations<sup>1, 8</sup>. The primary endpoint of the trial is the composite of total (first and recurrent) heart failure hospitalizations and cardiovascular death<sup>8</sup>. PARAGON-HF is part of FortiHFy, the largest global clinical program in the heart failure disease area across the pharmaceutical industry to date. Established by Novartis, the FortiHFy program comprises more than 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 sacubitril/valsartan, as well as to extend understanding of heart failure.

PARAGON-HF follows the only positive Phase II trial in HFpEF, PARAMOUNT-HF, which demonstrated that sacubitril/valsartan reduced NT-proBNP (a biomarker of cardiac strain) to a greater extent than valsartan at 12 weeks and was associated with improvement in NYHA class at 36 weeks<sup>16,17</sup>. Additional studies investigating sacubitril/valsartan on other relevant endpoints in HFpEF are ongoing.

### **About Heart Failure**

Heart failure (HF) is a progressive and serious condition, affecting approximately 26 million people worldwide, where the heart cannot pump enough blood to the body<sup>9,15,18</sup>. There are two distinct types of heart failure: preserved ejection fraction (HFpEF) and reduced ejection fraction (HFrEF)<sup>19</sup>.

#### **About HFpEF**

HFpEF is a distinct type of heart failure where the heart muscle contracts normally but the ventricles do not relax as they should during ventricular filling (or when the ventricles relax)<sup>20</sup>. HFpEF can be associated with high hospitalization rates, poor quality of life and increased mortality<sup>21</sup>, and it is emerging as the predominant form of HF<sup>22</sup>. There is currently no approved treatment for HFpEF<sup>9,10</sup>.

#### **About HFrEF**

HFrEF is a certain type of long-lasting heart failure, also known as systolic HF<sup>23,24</sup>. HFrEF means the heart does not contract with enough force, so less blood is pumped out<sup>20</sup>. There are approved treatment options for people living with HFrEF<sup>9,10</sup>.

#### **About Entresto for Heart Failure with Reduced Ejection Fraction (HFrEF)**

Entresto is a twice-a-day medicine that reduces the strain on the failing heart<sup>25</sup>. 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)<sup>25,26</sup>. 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. Entresto contains the neprilysin inhibitor sacubitril and the ARB valsartan<sup>25,27</sup>.

In Europe, Entresto is indicated in adult patients for the treatment of symptomatic chronic heart failure with reduced ejection fraction<sup>25</sup>. 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<sup>27</sup>. It has been shown to reduce the rate of cardiovascular death, heart failure hospitalization and 30-day hospital readmission compared to enalapril, to reduce the rate of all-cause mortality compared to enalapril, and to improve aspects of health-related quality of life (including physical and social activities) compared to enalapril<sup>28,29,30</sup>. Entresto is usually administered in conjunction with other heart failure therapies, in place of an ACE inhibitor or other ARB<sup>25,27</sup>. Approved indications may vary depending upon the individual country.

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### **About Novartis**

Novartis is reimagining medicine to improve and extend people's lives. As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of great medical need. In our quest to find new medicines, we consistently rank among the world's top companies investing in research and development. Novartis products reach more than 750 million people globally and we are finding innovative ways to expand access to our latest treatments. About 108,000 people of more than 140 nationalities work at Novartis around the world. Find out more at [www.novartis.com](http://www.novartis.com).

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