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MEDIA & INVESTOR RELEASE

Novartis announces positive FDA Advisory Committee recommendation for use of Entresto® to treat patients with HFpEF

- *The Committee voted 12 to 1 that the data presented support the use of Entresto in treatment of patients with heart failure with preserved ejection fraction (HFpEF)*

- *Potential Q1 2021 sNDA approval could make Entresto the first therapy indicated for use in treatment of patients with both major types of chronic heart failure: HFpEF and HFrEF; and the only chronic heart failure treatment studied in both conditions against active comparators*[1,2]

- *HFpEF patients currently have no approved treatment options and face worsening symptoms that result in frequent HF hospitalizations, emergency room and urgent office visits*[1,3,4]

Basel, December 16, 2020 — Novartis today announced that the US Food and Drug Administration (FDA) Cardiovascular and Renal Drugs Advisory Committee (CRDAC) voted 12 to 1 that the data presented support the use of Entresto® (sacubitril/valsartan) in treatment of patients with heart failure with preserved ejection fraction (HFpEF). This was based on data supporting the benefit of Entresto in reducing worsening heart failure (total heart failure [HF] hospitalizations and urgent HF visits) in patients studied in PARAGON-HF. If approved by the FDA, Entresto could become the first therapy indicated for use in treatment of patients with HFpEF, as well as the first medication approved for both major types of chronic heart failure, HFpEF and heart failure with reduced ejection fraction (HFrEF), both based on trials that included active comparators (valsartan and enalapril, respectively)[1,2].

With no approved therapies for HFpEF to address the prevention of HF hospitalizations and urgent visits, a significant unmet medical need exists for a treatment to reduce the burden associated with this debilitating condition. The FDA is expected to make a decision on the supplemental New Drug Application (sNDA) in the first quarter of 2021.

“Managing HFpEF has historically been a clinical and scientific challenge due to the heterogeneity of the condition,” said Scott Solomon, MD, Professor of Medicine at Harvard Medical School and Brigham and Women's Hospital, and PARAGON-HF Executive Committee Co-Chair. “Today’s vote represents much needed progress in this area of unmet need and is a positive step toward bringing a potential therapy to millions of patients suffering from this type of heart failure.”

The Committee’s positive decision is based on the totality of evidence from efficacy and safety analyses, including findings presented from a pre-specified subgroup analysis of PARAGON-HF, the largest and only Phase III active-controlled study to date in patients with HFpEF and additional evidence from PARAMOUNT (a Phase II trial in HFpEF), as well as PARADIGM-HF

(a Phase III trial in HFrEF)[5-7]. Data from PARAGON-HF demonstrated a favorable safety profile for Entresto in patients with HFpEF, which is in line with the vast clinical and post-marketing experience in HFrEF, and showed clinical benefit of Entresto in HFpEF patients[2].

“Our commitment to reimagine medicine through our extensive clinical trials program on heart failure has been unwavering, and we are encouraged by the Committee’s response today,” said David Soergel, MD, Global Head of Cardiovascular, Renal and Metabolic Drug Development, Novartis. “We appreciate the valuable insights shared by the patient and advocacy community about this devastating disease, and we look forward to FDA’s decision on the potential approval of this new indication.”

HFpEF affects more than 3 million Americans, and is increasing in prevalence as the population ages[3,8]. It is a complex disease for which it is difficult to develop treatments due to its heterogeneous pathophysiology and the varied impact of symptoms among patients, despite decades of research[9]. HFpEF can change the structure of the heart and occurs when the muscle tissue of the heart thickens and stiffens so that it cannot expand to fill with enough blood to meet the body’s needs[10]. HFpEF is associated with high rates of recurring heart failure hospitalizations, emergency room visits and urgent doctor’s office appointments[3,4]. Each hospitalization event is associated with worsening long-term prognosis, and approximately one in four patients are re-admitted for heart failure within one year of discharge[11,12].

Entresto is approved in 115 countries worldwide for the treatment of HFrEF, with more than 2.6 million patient-years of exposure to date[13].

About our longstanding commitment to heart failure
To reimagine medicine for heart failure patients, Novartis established the largest global clinical program in the HF disease area across the pharma industry to date. Known as FortiHFy, it is comprised of more than 40 clinical studies designed to generate an array of additional data on efficacy, quality of life, patient-reported outcomes and real-world evidence with Entresto, as well as to extend understanding of heart failure. FortiHFy includes trials across HFpEF, including PARAGON-HF, PARAMOUNT and PARAGLIDE-HF, as well as Entresto’s current indication in HFrEF, such as PARADIGM-HF, PIONEER-HF, TRANSITION and PROVE-HF.

About Entresto for heart failure with reduced ejection fraction
In Europe, Entresto is indicated in adult patients for the treatment of symptomatic chronic HF with reduced ejection fraction[14]. In the United States, Entresto is indicated for the treatment of HF (New York Heart Association class II-IV) in patients with systolic dysfunction[15]. It has been shown to reduce the rate of cardiovascular death and HF hospitalization, to reduce the rate of all-cause mortality and to improve aspects of health-related quality of life (including physical and social activities), compared to enalapril[7,16,17]. Entresto is usually administered in conjunction with other HF therapies, in place of an ACE inhibitor or other angiotensin receptor blocker (ARB)[14]. Approved indications may vary depending upon the individual country.

Entresto is a twice-a-day medicine that reduces the strain on the failing heart[14]. 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)[14,18]. Other common HF medicines, called angiotensin converting enzyme inhibitors (ACEi) and angiotensin II receptor blockers (ARBs), only block the harmful effects of the overactive RAAS. Entresto contains the neprilysin inhibitor sacubitril and the angiotensin receptor blocker (ARB) valsartan[14,15].

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“pipeline,” “launch,” or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for the investigational or approved products described in this press release, or regarding potential future revenues from such products. You should not place undue reliance 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 and requirements for increased pricing transparency; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; general political, economic and business conditions, including the effects of and efforts to mitigate pandemic diseases such as COVID-19; safety, quality, data integrity 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 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 nearly 800 million people globally and we are finding innovative ways to expand access to our latest treatments. About 110,000 people of more than 140 nationalities work at Novartis around the world. Find out more at https://www.novartis.com.

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