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MEDIA & INVESTOR RELEASE

Novartis Entresto® granted expanded indication in chronic heart failure by FDA

- *Entresto is the first and only therapy approved in the US to treat patients diagnosed with guideline-defined heart failure to include both those with heart failure with reduced ejection fraction (HFrEF) and many with heart failure with preserved ejection fraction (HFpEF)*[1-3]

- *Expanded indication enables potential treatment of more adults with left ventricular ejection fraction (LVEF) below normal, the group where benefits are most clearly evident*[1]

- *Of the more than 6 million Americans suffering from chronic heart failure (CHF), approximately 5 million may be appropriate for treatment with Entresto*[3,4]

Basel, February 16, 2021 — Novartis today announced that the US Food and Drug Administration (FDA) has approved the following expanded indication for Entresto® (sacubitril/valsartan): *to reduce the risk of cardiovascular death and hospitalization for heart failure in adult patients with chronic heart failure*[1]*. Benefits are most clearly evident in patients with left ventricular ejection fraction (LVEF) below normal*[1]*.* The label also states LVEF is a variable measure and clinical judgment should be used in deciding whom to treat[1].

For the first time, there is a treatment with benefit for patients diagnosed with guideline-defined heart failure that includes both those with heart failure with reduced ejection fraction (HFrEF) and many with heart failure with preserved ejection fraction (HFpEF)[1-3].

“This approval is a significant advancement, providing a treatment to many patients who were not eligible for treatment before because their ejection fraction was above the region we normally considered reduced. Until now, treatment for these patients was largely empiric,” said Scott Solomon, MD, Professor of Medicine at Harvard Medical School and Brigham and Women's Hospital, and PARAGON-HF Executive Committee Co-Chair. “We can now offer a treatment to a wider range of patients who have an LVEF below normal.”

This label expansion is based on efficacy and safety evidence observed in PARAGON-HF, the largest and only Phase III active-controlled study to date in patients with guideline-defined HFpEF[2,5,6]. The greatest benefit was shown in patients with LVEF below normal[6].

Approximately 6 million Americans are living with chronic heart failure (CHF)[4]. Approximately 3 million have HFrEF, and of the remaining 3 million, about 2 million have HFpEF with LVEF below normal[2-4]. The prevalence of heart failure (HF) is increasing as the population ages[4]. Patients often face worsening symptoms that result in frequent HF hospitalizations[7]. Each

hospitalization event is associated with worsening long-term prognosis[7]. Approximately one in four patients are re-admitted for HF and 10 percent may die within 30 days of discharge[8,9]. Overall CHF death rates remain significantly high, with up to half of patients dying within five years of a HF diagnosis[4].

“We are proud of our goal to reimagine medicine. This commitment has enabled us to bring Entresto to millions more heart failure patients in the US, many of whom did not have an approved treatment option until now,” said Marie-France Tschudin, President, Novartis Pharmaceuticals. “This achievement would not have been possible without tremendous dedication from investigators, patients in our clinical trials and the advocacy community, to whom we are extremely grateful.”

About our longstanding commitment to heart failure
Our goal is 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 the spectrum of heart failure, such as PARADIGM-HF, PIONEER-HF, TRANSITION, PROVE-HF, PARAGON-HF and PARAMOUNT. Worldwide, it is estimated that more than 30,000 patients have participated in the Entresto clinical trials program, and it is estimated that more than 2.8 million patients are on treatment with Entresto today.

About Entresto
In Europe, Entresto is indicated in adult patients for the treatment of symptomatic chronic HF with reduced ejection fraction[10]. In the United States, Entresto is indicated to reduce the risk of cardiovascular death and hospitalization for heart failure in adult patients with chronic heart failure[1]. Benefits are most clearly evident in patients with left ventricular ejection fraction (LVEF) below normal[1]. LVEF is a variable measure, so use clinical judgment in deciding whom to treat[1]. Approved indications may vary depending upon the individual country.

Entresto is a twice-a-day medicine that reduces the strain on the failing heart[10]. It does this by enhancing protective neurohormonal systems (i.e., natriuretic peptide system) while simultaneously inhibiting the harmful effects of the overactive renin-angiotensin-aldosterone system (RAAS)[10,11]. 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[1,10].

Disclaimer
This press release contains forward-looking statements within the meaning of the United States Private Securities Litigation Reform Act of 1995. Forward-looking statements can generally be identified by words such as “potential,” “can,” “will,” “may,” “could,” “would,” “commitment,” “to reduce,” “increasing,” “goal,” “to generate,” or similar terms, or by express or implied discussions regarding potential marketing approvals, 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 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 Entresto 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 Entresto will be commercially successful in the future. In particular, our expectations regarding Entresto 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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