Novartis joins the Global Chagas Disease Coalition and also announces first multinational, prospective, randomized study in people with chronic Chagas cardiomyopathy

- Study is planned to assess efficacy and safety of Entresto® (sacubitril / valsartan) vs enalapril in 900 patients with chronic Chagas cardiomyopathy; recruitment is planned to commence within 2019

- Chagas disease is a potentially life-threatening neglected disease, affecting approximately six million people worldwide¹,², mostly in Latin America; up to 30% of chronically infected people develop cardiac disorders³

- Chagas cardiomyopathy is the most important clinical manifestation of the disease, resulting in the majority of morbidity and mortality⁴

- The Global Chagas Disease Coalition is a collaborative alliance, which aims to increase awareness of Chagas disease and foster synergies in controlling the disease and promoting access to diagnosis and treatment⁵

Basel, Switzerland, March 14, 2019 – At the Annual Meeting of the Global Chagas Disease Coalition in Barcelona, Spain, Novartis announced that it is joining the Coalition as a member contributor. In addition, the company announced its commitment to launch a multinational, prospective, randomized study with heart failure drug, Entresto® (sacubitril / valsartan), in people with chronic Chagas cardiomyopathy, one form of heart failure with reduced ejection fraction. This is the first definitive morbidity and mortality study to assess a potential therapy for cardiac disease in this underserved patient population.

“Today marks another milestone in our longstanding commitment to the fight against neglected tropical diseases, and we are proud to partner with the Global Chagas Disease Coalition and its members to help improve access to diagnosis and reimagine treatment for people with Chagas disease,” said Patrice Matchaba, Group Head, Global Health and Corporate Responsibility at Novartis. “It is only by joining forces that we can succeed in bringing our innovation to the people that need it.”

The clinical trial will assess the efficacy and safety of Entresto vs. enalapril and is expected to start within 2019, with the aim of recruiting approximately 900 patients with confirmed Chagas disease in Latin America. The primary endpoint is time to occurrence of a composite of cardiovascular events, including cardiovascular death or first hospitalization due to heart failure. This definitive study follows an exploratory post hoc analysis from the PARADIGM-HF trial⁶, which suggested that Entresto may have beneficial effects in people with chronic Chagas cardiomyopathy and heart failure with reduced ejection fraction.

At the same time, Novartis is working with stakeholders in endemic countries to co-develop tailored access-to-medicine programs and health system strengthening strategies to help ensure lower-income patients suffering from chronic Chagas cardiomyopathy can benefit from the best available treatment.

Chagas disease, also known as American trypanosomiasis, is a potentially life-threatening neglected tropical disease estimated to affect approximately six million people globally and is
responsible for approximately 12 000 deaths annually\textsuperscript{1,2,3}. The disease is endemic in 21 Latin American countries, where it is the second leading cause for developing chronic heart failure\textsuperscript{7}. Due to population mobility, in the past decades, Chagas disease has been increasingly detected in the United States, Canada, and many European and some Western Pacific countries\textsuperscript{3}. Chagas cardiomyopathy is the most important clinical manifestation of the disease, resulting in the majority of morbidity and mortality\textsuperscript{4}.

“We are pleased to welcome Novartis as one of our member contributors,” said Javier Sancho, Coordinator of the Global Chagas Disease Coalition. “It is only by openly sharing our experience and knowledge and fostering synergies that we can hope to achieve our common goal of controlling and potentially eliminating Chagas disease.”

Novartis is also taking steps to advance research efforts around the disease and is committed to providing mentorship opportunities for scientists from Latin America to help strengthen capacity for relevant research regionally. The Novartis Institute for Tropical Diseases (NITD), the Genomics Institute of the Novartis Research Foundation (GNF) and collaborators have developed a promising portfolio of novel drug candidates for the treatment of kinetoplastid diseases. The proteasome inhibitor LXE408 was recently advanced as a promising drug candidate for the treatment of visceral leishmaniasis\textsuperscript{8}. This novel mechanism of action is also being explored for other indications, including Chagas disease.

In addition, Novartis is partnering with the World Heart Federation to develop an end-to-end roadmap for addressing Chagas disease. The final roadmap is expected to be launched within 2019. In parallel, we are working together with different stakeholders in Latin American countries, such as Argentina and Colombia, to support existing national plans for an integrated care approach to Chagas disease.

The Novartis commitment to neglected tropical diseases

Novartis is a signatory to the London Declaration on Neglected Tropical Diseases, which aims to control, eliminate or eradicate 10 diseases by 2020. Since 1999, Novartis has donated multidrug therapy for the treatment of leprosy through the WHO, reaching more than seven million people worldwide. In addition, since 2005, we have donated Egaten\textsuperscript{®} for the treatment of fascioliasis (liver fluke infestation) to the WHO, helping to treat around 2 million people in more than 30 countries. In 2018, we renewed our agreement with the WHO to extend the drug donation until 2022, expected to reach 300 000 patients per year.

We have a strong commitment to research and development for tropical diseases. In 2018, we announced an investment of USD 100 million to advance research and development of next-generation antimalarials over the next five years. The Novartis Institute for Tropical Diseases, founded in 2001, is dedicated to finding new medicines to treat infectious and neglected diseases. In addition to malaria, research currently focuses on parasitic diseases such as cryptosporidiosis (diarrheal disease) and three major kinetoplastid diseases: human African trypanosomiasis (sleeping sickness), Chagas disease and leishmaniasis. Together with our leprosy elimination efforts, this strategic focus on kinetoplastid parasitic diseases would address four out of 10 diseases in scope of the London Declaration.

Building on our experience in neglected and infectious diseases, Novartis also implements programs to expand access to medicines for chronic diseases and, most recently, to address sickle cell disease in sub-Saharan Africa, starting in Ghana.

About Chagas disease\textsuperscript{3}

Chagas disease, also known as American trypanosomiasis, is a potentially life-threatening illness caused by the protozoan parasite \textit{Trypanosoma cruzi} (\textit{T. cruzi}), which is carried by the triatomine bug, commonly known as “the kissing bug”. It is recognized by the World Health Organization as one of the world’s 13 most neglected tropical diseases\textsuperscript{5}. It is estimated to affect approximately six million people globally and to cause approximately 12 000 deaths annually. The disease is endemic in 21 Latin American countries; however, due to population...
mobility, in the past decades, it has been increasingly detected in the United States, Canada, and many European and some Western Pacific countries.

Chagas disease presents in an initial acute phase, where a high number of parasites circulate in the blood. In most cases, symptoms are absent or mild and nonspecific. During the chronic phase, the disease mainly affects the heart and digestive muscles, leading to cardiac disorders in up to 30% of patients and digestive, neurological or mixed alterations in up to 10% of patients. The infection can eventually lead to sudden death due to cardiac arrhythmias or progressive heart failure.

Chagas cardiomyopathy is the most important clinical manifestation of Chagas disease, resulting in the majority of morbidity and mortality. The patients, despite being younger, tend to have a worse quality of life and higher hospitalization and mortality rates compared with other etiologies.

About Entresto
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). 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 nepriyslin inhibitor sacubitril and the angiotensin receptor blocker (ARB) valsartan.

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. 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. Entresto is usually administered in conjunction with other heart failure therapies, in place of an ACE inhibitor or other angiotensin receptor blocker (ARB). 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 800 million people globally and we are finding innovative ways to expand access to our latest treatments. About 130 000 people of nearly 150 nationalities work at Novartis around the world. Find out more at 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          Katerina Kontzalis
Novartis Global Media Relations  Novartis Global Health & CR Communications
+41 61 324 7999 (direct)  +41 61 324 1631 (direct)
+41 79 593 4202 (mobile)  +41 79 797 8393 (Mobile)
eric.althoff@novartis.com  katerina.kontzalis@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