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MEDIA & INVESTOR RELEASE

Novartis receives complete response letter from U.S. FDA for inclisiran

- *The U.S. Food and Drug Administration (FDA) has not raised any concerns related to the efficacy or safety of inclisiran. The complete response letter is due to unresolved facility inspection-related conditions*

- *No onsite inspection was conducted of the single third-party facility in question. If a facility inspection is needed, FDA will define an approach once safe travel may resume based on public health need and other factors*

- *Novartis will work with FDA and the third-party manufacturing facility in Europe to complete the inclisiran review, to bring this potential first-in-class siRNA to patients in the U.S. as quickly as possible*

Basel, December 18, 2020 — The U.S. Food and Drug Administration (FDA) has issued a complete response letter (CRL) regarding the new drug application (NDA) for inclisiran, a potential treatment for hyperlipidemia in adults who have elevated low-density lipoprotein cholesterol (LDL-C) while being on a maximum tolerated dose of a statin therapy. The FDA stated that the agency cannot approve the NDA by the Prescription Drug User Fee Act (PDUFA) action date of December 23, 2020, due to unresolved facility inspection-related conditions. The conditions will be conveyed to the European manufacturing facility within 10 business days. The third-party facility is responsible for drug product manufacturing. Satisfactory resolution of the unresolved facility inspection-related conditions is required before the Novartis NDA may be approved. No onsite inspection was conducted. If it is determined that a facility inspection is needed to approve the application, the FDA will define an approach for scheduling once safe travel may resume based on public health need and other factors.

“Novartis is confident in the quality of the regulatory submission for inclisiran, which includes a robust body of evidence related to efficacy and safety. We look forward to meeting with the FDA and our third-party manufacturing partner to discuss the feedback received and next steps,” said John Tsai, Head Global Drug Development and Chief Medical Officer, Novartis. “We are committed to bringing this potential first-in-class small interfering RNA cholesterol-lowering treatment to patients as soon as possible.”

The European Commission (EC) recently granted Novartis marketing authorization for Leqvio® (inclisiran) in Europe on December 11, 2020.

About inclisiran
Inclisiran (KJX839) is the first and only small interfering RNA (siRNA) therapy to reduce low-density lipoprotein cholesterol (LDL-C) levels via an RNA interference (RNAi) mechanism of action and could help improve outcomes for patients with atherosclerotic cardiovascular disease (ASCVD), a deadly form of cardiovascular disease[1-3]. With two doses a year and effective and sustained LDL-C reduction, inclisiran works as a complement to statins.

Inclisiran works differently from other therapies by preventing the production of the target protein in the liver, increasing hepatic uptake of LDL-C and clearing it from the bloodstream[3]. Inclisiran is dosed initially, again at 3 months, and then once every 6 months. In three clinical trials, patients taking inclisiran maintained LDL-C reduction throughout each 6-month dosing interval[1,2]. Administered in-office as a subcutaneous injection, inclisiran is expected to integrate seamlessly into a patient's healthcare routine[1,2].

In the Phase III trials, inclisiran was well-tolerated[1,2]. The most common adverse events reported (≥3% of patients treated with inclisiran and occurring more frequently than placebo) were injection site reaction, arthralgia, urinary tract infection, diarrhea, bronchitis, pain in extremity and dyspnea[1,2]. Among those, injection site reactions were the most frequent ones. Those were generally mild and none were severe or persistent[1,2].

Novartis has obtained global rights to develop, manufacture and commercialize inclisiran under a license and collaboration agreement with Alnylam Pharmaceuticals, a leader in RNAi therapeutics.

About Novartis in Cardiovascular-Renal-Metabolism
Bending the curve of life requires addressing some of society's biggest public health concerns. Novartis has an established and expanding presence in diseases covering the heart, kidney and metabolic system. In addition to essential treatment Entresto® (sacubitril/valsartan), Novartis has a growing pipeline of potentially first-in-class molecules addressing cardiovascular, metabolic and renal diseases.

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 "will," "may," "as quickly as possible," "potential," "confident," "look forward," "committed," "potential," "as soon as possible," "could," "expected," "investigational," "pipeline," "launch," or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for inclisiran and the other investigational and 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 inclisiran will be approved for sale in the United States, or if approved, at any particular time. Neither can there be any guarantee that inclisiran or the other 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 inclisiran and such other products could be affected by, among other things, regulatory actions or delays or government regulation generally; the uncertainties inherent in research and development, including clinical trial results and additional analysis of existing clinical data; 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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