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MEDIA & INVESTOR RELEASE

FDA approves Novartis Leqvio® (inclisiran), first-in-class siRNA to lower cholesterol and keep it low with two doses a year

Ad hoc announcement pursuant to Art. 53 LR

- *With two maintenance doses a year, Leqvio is the first and only FDA-approved small interfering RNA (siRNA) therapy for LDL-C (bad cholesterol) reduction*[1]
- *Leqvio provides effective and sustained LDL-C reduction of up to 52% vs. placebo for certain people with atherosclerotic cardiovascular disease (ASCVD) on maximally tolerated statin therapy*[2,3]
- *Approximately 16 million Americans with ASCVD taking statins to lower cholesterol—including those who have experienced a heart attack or stroke—are not at recommended LDL-C target*[4,5]

Basel, December 22, 2021 — Novartis today announced the US Food and Drug Administration (FDA) approval of Leqvio® (inclisiran), the first and only small interfering RNA (siRNA) therapy to lower low-density lipoprotein cholesterol (also known as bad cholesterol or LDL-C) with two doses a year, after an initial dose and one at three months.

“Leqvio is a revolutionary approach to lower LDL-C, and creates new possibilities for how healthcare systems can impact cardiovascular disease, a defining public health challenge of our time,” said Vas Narasimhan, Novartis CEO. “We now have the opportunity, working together with partners, to provide this first-ever approved LDL-C–lowering siRNA-based therapy to tackle ASCVD at scale across the United States.”

Leqvio is indicated in the United States as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with clinical atherosclerotic cardiovascular disease (ASCVD) or heterozygous familial hypercholesterolemia (HeFH) who require additional lowering of LDL-C. The effect of Leqvio on cardiovascular morbidity and mortality is being explored in clinical trials currently underway.

“ASCVD is a substantial public health burden affecting 30 million Americans,” said Norman Lepor, MD, a Los Angeles based cardiologist and a clinical investigator in the Phase III clinical program for Leqvio. “As a first-of-its-kind siRNA therapy, Leqvio works differently than other cholesterol treatments, with twice-yearly dosing that makes it a compelling option for the millions of people with ASCVD already on cholesterol-lowering medications struggling to reach their LDL-C target.”

Leqvio reduces the amount of LDL-C in the bloodstream by improving the liver’s natural ability to prevent the production of a protein that plays a role in keeping circulating cholesterol levels high[6,7]. It is a subcutaneous injection given by a healthcare provider with an initial dose, then

again at three months, and then every six months[1]. This approach may help those who have trouble sticking to medicines that are self-administered and have greater dosing frequency. Leqvio will be available in early January 2022.

“People with ASCVD have most likely experienced a heart attack or stroke from high cholesterol, causing a burden on the family and having a negative impact on lives,” said Andrea Baer, Executive Director of The Mended Hearts, Inc. “One of the first steps to improving patients’ health is to manage high cholesterol and we’re encouraged that this new twice-a-year treatment offers a new option.”

The FDA approval was based on results from the comprehensive Phase III ORION-9, -10 and -11 clinical trials, in which all 3,457 participants with ASCVD or HeFH had elevated LDL-C while receiving a maximally tolerated dose of statin therapy[2,3]. In the Phase III trials at month 17, Leqvio delivered effective and sustained LDL-C reduction of up to 52% vs. placebo and was reported to be well-tolerated with a safety profile shown to be comparable to placebo[2,3]. The most common side effects were mild to moderate injection site reaction (including pain, redness and rash), joint pain, urinary tract infection, diarrhea, chest cold, pain in legs or arms and shortness of breath[2,3].

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

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,” “believe,” “keep,” “taking on,” next-generation,” “enables,” “to explore,” “innovative,” “to help,” “improving,” “keeping,” “to develop,” “possible,” “goal,” or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for Leqvio, or regarding potential future revenues from Leqvio. 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 Leqvio 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 Leqvio will be successfully launched in the markets where it is approved, or at any particular time. Neither can there be any guarantee that Leqvio will be commercially successful in the future. In particular, our expectations regarding Leqvio 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 in cardiovascular renal metabolism
Cardiovascular (CV), renal and metabolic diseases are a global health crisis[8-11].

These chronic, complex and often hereditary diseases are frequently inter-related, and come with healthcare and treatment barriers and a lack of transformative medicines, and almost always lead to the same outcome: death due to CV disease[8-11].

CV disease is the number one killer in the world[8]. Taking more lives than all cancers combined, it contributes to one in every three deaths globally[8,12]. Of all CV events, 80% can be prevented[13]. Patients and their families deserve better, and our society deserves more.

Thanks to a combination of our legacy, global footprint and leading science, Novartis is uniquely positioned to help change this landscape. We are transforming the way we think about the relationship between these diseases and how they are managed throughout life. Our efforts include the use of early interventions and the development of pioneering treatments that address the spectrum of CV, renal and metabolic diseases, from prevention to management, as well as the creation of innovative access models. By re-writing the way we work with society, we will lead a worldwide effort to improve health outcomes and roll back the crisis of CV death.

Our goal is to bend the curve of life by reducing and stopping premature death from CV disease.

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 108,000 people of more than 140 nationalities work at Novartis around the world. Find out more at https://www.novartis.com.

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