New Novartis data show early addition of twice-yearly* Leqvio® (inclisiran) following maximally tolerated statin therapy significantly reduces LDL-C in ASCVD patients in real-world setting

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- V-INITIATE trial demonstrates that early initiation with Leqvio, prior to guideline-recommended ezetimibe, for ASCVD patients unable to achieve LDL-C goal on statin therapy alone led to significant LDL-C reduction vs. clinician-determined usual care (60% vs. 7% respectively)[1]
- A significantly greater proportion of the ASCVD patients receiving Leqvio achieved guideline-recommended LDL-C goal vs. the usual care arm while maintaining adherence to statin treatment[1]
- Results from usual care arm reinforce the urgent need for more aggressive LDL-C lowering in ASCVD patients, 92% of whom did not reach their LDL-C goal with statins alone[1]
- The Leqvio safety profile was consistent with the Phase III clinical studies and long-term open-label extension trials for up to 6 years of treatment[1-4]

EAST HANOVER, N.J., April 6, 2024 Novartis today announced new data demonstrating the early addition of twice-yearly* Leqvio® (inclisiran) to maximally tolerated statin therapy, prior to guideline-recommended ezetimibe, in a real-world setting significantly reduced low-density lipoprotein cholesterol (LDL-C) in patients with atherosclerotic cardiovascular disease (ASCVD), including those with a history of an ASCVD-related event, who could not reach their goal on statin therapy alone[1]. The late-breaking data were presented at the 2024 American College of Cardiology's Annual Scientific Session & Expo and simultaneously published in the Journal of the American College of Cardiology.

"V-INITIATE evaluated a solution to the important challenge seen in clinical practice of too many patients with ASCVD not achieving guideline-recommended LDL-C goal on statins alone and effective non-statin therapies being markedly underutilized," said Michael Koren, M.D., Medical Director and CEO of Jacksonville Center for Clinical Research, and the primary investigator of the study. "Given the urgent need to more aggressively manage LDL-C, the results from V-INITIATE show that when added earlier in the treatment continuum, the structured use of effective non-statin therapies like Leqvio can significantly reduce LDL-C for ASCVD patients who are struggling to reach or maintain their LDL-C goal."

In the V-INITIATE study, patients receiving Leqvio experienced significant reductions in LDL-C compared to those receiving usual care (60% vs. 7%, respectively; $p<0.001$), which consisted mostly of statin therapy alone (73%)[1]. Four in five patients receiving Leqvio achieved the guideline-recommended LDL-C goal of <70 mg/dL compared to just one in five patients receiving usual care (81.8% vs. 22.2%, respectively; $p<0.001$)[1]. Notably, patients receiving health care provider (HCP)-administered Leqvio maintained adherence to existing lipid-lowering therapy, and the discontinuation rate of background statin therapy did not differ between the Leqvio and usual care arms (5.8% vs. 16.7%, respectively)[1].

The safety results from V-INITIATE were consistent with findings from the pivotal Phase III clinical trial program and long-term open-label extension trials, ORION-3 and ORION-8, which demonstrated sustained safety for up to six years of treatment[1-4].

"The data from V-INITIATE illustrate that earlier initiation of innovative non-statin therapies, like Leqvio, presents a real opportunity to do better for ASCVD patients and improve the way we approach LDL-C lowering," said David Soergel, M.D., Global Head of Cardiovascular, Renal and Metabolic Drug Development at Novartis. "This study adds data from a real-world setting to the growing body of evidence for Leqvio being generated through our robust VictORION program, and further reinforces the clinical value of this twice-yearly HCP-administered therapy."

V-INITIATE is a 12-month Phase IIIb open-label study evaluating the effectiveness of adding Leqvio earlier, following a patient's failure to reach LDL-C goal on maximally tolerated statin therapy, compared to usual care, in a setting that reflects U.S. clinical practice. It was designed to more accurately represent the diversity of the U.S. general population across age, sex, race, ethnicity, insurance status, income level, education, prior medical history and statin intolerance[1]. Unlike placebo arms in typical double-blind trials, the usual care arm reflected U.S. clinical practice by allowing treating physicians to make changes to lipid-lowering treatment based on LDL-C measurements. Usual care was defined as clinician determined based on the 2018 American College of Cardiology/American Heart Association guideline recommendations[1].

*After an initial dose and another at three months.

Indication
LEQVIO (inclisiran) is an injectable prescription medicine used along with diet and other cholesterol-lowering medicines in adults with high blood cholesterol levels called primary hyperlipidemia (including a type of high cholesterol called heterozygous familial hypercholesterolemia [HeFH]) to reduce low-density lipoprotein (LDL-C) or "bad" cholesterol.

Important Safety Information:
The most common side effects of Leqvio were: injection site reaction (including pain, redness, and rash), arthralgia (joint pain), bronchitis (chest cold).

These are not all the possible side effects of Leqvio. Ask your health care provider for medical advice about side effects. You are encouraged to report negative side effects of prescription drugs to the FDA.
Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please click here for Leqvio full Prescribing Information.

About Leqvio
Leqvio is a subcutaneous injection given by a health care provider (HCP) with an initial dose, another at three months, and then every six months[2,5]. As a twice-yearly, HCP-administered treatment, Leqvio may help to circumvent the challenges of treatment adherence, a common issue in cholesterol management. Leqvio is the first and only small interfering RNA (siRNA) therapy to lower LDL-C. It is approved in over 90 countries, including the U.S., EU, Japan and China[1,5,6].

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.

About V-INITIATE
V-INITIATE is a 12-month, randomized, multicenter, open-label Phase IIIb study in 450 atherosclerotic cardiovascular disease (ASCVD) patients in the U.S. with elevated LDL cholesterol (LDL-C) ≥70 mg/dL. The study evaluated the effectiveness of adding HCP-administered Leqvio earlier, following a patient's failure to reach LDL-C goal on maximally tolerated statin therapy, compared to usual care[1]. Usual care was determined by the clinicians and based on the 2018 American College of Cardiology/American Heart Association guideline recommendations; most patients (73%) in the usual care arm remained on statins only[1]. The co-primary endpoints were the percentage change in LDL-C from baseline to Day 330 and the discontinuation of statin therapy, defined as no statin use ≥30 days before the end of study visit[1]. This is the first Novartis trial where all patients have been tokenized with the intention of following their outcomes for two additional years post-trial completion, providing additional insights on the

real-world effectiveness of Leqvio[7].

About VictORION

The V-INITIATE trial is part of VictORION, an innovative and robust clinical program for Leqvio, comprising more than 30 trials and enrolling over 60,000 patients in more than 50 countries worldwide[7]. The program is designed to expand on the foundational evidence of LDL-C reduction with Leqvio in diverse patient populations to include randomized clinical trials, implementation research, real-world evidence, and trials that aim to establish its potential benefits on cardiovascular outcomes in primary and secondary prevention. A growing number of studies are planned to generate a vast array of data with major trials such as ORION-4 (secondary prevention), V(VictORION)-2-PREVENT (secondary prevention), V-1-PREVENT (high-risk primary prevention), V-INCEPTION and V-MONO.

About Atherosclerotic Cardiovascular Disease (ASCVD)

ASCVD refers to a variety of diseases caused by the development and growth of plaques in the inner lining of the arteries[8]. The atherosclerotic plaque is mainly composed of low-density lipoprotein cholesterol (LDL-C) which accumulates over time[8]. Cumulative exposure to LDL-C is proportionally related to arterial plaque growth and progression leads to subsequent risk of cardiovascular events such as a heart attack or stroke[8,9]. Accounting for 85% of all cardiovascular disease deaths, ASCVD is the primary cause of mortality in the European Union and its burden in the United States is greater than that of any other chronic diseases[10-13]. ASCVD risk-equivalent corresponds to conditions that confer a similar risk for an ASCVD event (e.g., diabetes and heterozygous familial hypercholesterolemia)[4,13].

About Novartis in Cardiovascular

Cardiovascular disease (CVD) affects hundreds of millions of people and claims more lives globally than cancer, chronic lung disease and diabetes combined[14]. It is time to change that. Around 80% of premature cardiovascular deaths can be prevented by addressing factors that cause or worsen CVD[15]. We have a responsibility to make that a reality for more people.

Novartis has been advancing the scientific understanding and treatment of CVD for more than four decades. Through early intervention, pioneering science and technological innovation, we are addressing factors that increase the risk of heart attacks and strokes, improving the function of damaged hearts and easing the burden of care for patients. We also collaborate with healthcare professionals, patient communities and diverse organizations to improve preventive CV care worldwide. Together, we will help more people with CVD get the right treatments at the right time and live longer and healthier lives.

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," "plan," "may," "could," "would," "expect," "anticipate," "look forward," "believe," "committed," "investigational," "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; 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 an innovative medicines company. Every day, we work to reimagine medicine to improve and extend people's lives so that patients, healthcare professionals and societies are empowered in the face of serious disease. Our medicines reach more than 250 million people worldwide.

Reimagine medicine with us: Visit us at https://www.novartis.com and https://www.novartis.us and connect with us on LinkedIn, LinkedIn US, Facebook, X/Twitter, X/Twitter US and Instagram.

Novartis previously filed its 2023 annual report with the Swiss SIX exchange in Switzerland, as well as its 2023 Annual Report on Form 20-F with the US Securities and Exchange Commission, and posted these documents on www.novartis.com. Novartis shareholders may receive a hard copy of either of these documents, each of which contains our complete audited financial statements, free of charge, upon request.

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