Novartis presents new long-term Leqvio® (inclisiran) data demonstrating consistent efficacy and safety beyond six years

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- Results from the ORION-8 open-label extension trial show twice-yearly* Leqvio, in addition to statin therapy, provides consistent low-density lipoprotein cholesterol (LDL-–C) reduction beyond six years of treatment[1]
- Eight in ten patients achieved target LDL-C threshold**, in line with previously reported Phase III data[1-3]
- Long-term safety data was consistent with previous findings, confirming the well-established and favorable safety profile of Leqvio[1-3]
- Approximately four in five ASCVD patients using statins alone to lower cholesterol, including those who already experienced a heart attack or stroke, do not reach recommended LDL-C target[4]

EAST HANOVER, N.J., Aug. 28, 2023 - Novartis today announced new long-term data from ORION-8, a Phase III open-label extension of ORION-9, ORION-10, ORION-11 and ORION-3 trials. The data demonstrated that with twice-yearly* dosing, Leqvio, in addition to statin therapy, provides consistent low-density lipoprotein cholesterol (LDL-C) reduction beyond six years in patients with atherosclerotic cardiovascular disease (ASCVD), increased risk of ASCVD or heterozygous familial hypercholesterolemia (HeFH)[1]. The results were presented in a late-breaking session at the European Society of Cardiology (ESC) Congress 2023 in Amsterdam.

ORION-8, the largest clinical trial completed to date with Leqvio, continues to support the consistent long-term efficacy, safety, and tolerability of Leqvio, with a total exposure of more than 8,500 patient-years during the trial's three-year follow-up[1]. Patients from four previous completed Novartis trials (ORION-9, ORION-10, ORION-11 and ORION-3) received Leqvio every six months* for up to an additional three years[1,5]. Nearly 80% (78.4% (95% CI: 76.8, 80.0)) of patients reached their pre-specified LDL-C targets**, and on average, LDL-C levels were reduced by approximately 50% (49.4% (95% CI: 48.3, 50.4))[1]. These results demonstrate consistent efficacy as they are comparable to the LDL-C reductions observed at the end of the initial trials[1-3,6]. In addition, the long-term safety data was consistent with previous findings, confirming the well-established and favorable safety profile of Leqvio.[1-3,6].

"These long-term results show that twice-yearly inclisiran, when used in addition to statin therapy, provides consistent LDL-C reduction in patients with ASCVD, and those at increased risk of developing cardiovascular disease," said Norman Lepor, M.D., a Los Angeles based cardiologist and Director of the National Heart Institute. "While LDL-C is one of the most readily modifiable risk factors for heart disease, many patients do not reach their recommended LDL-C target through use of statin therapy alone. The demonstrated long-term efficacy of inclisiran indicates that after administration by a health care provider (HCP), both patient and HCP

can be confident that a dose has been received for six months."

ORION-8 is part of VictORION, a large dynamic clinical trial program co-created with healthcare partners worldwide to generate evidence on the impact of cholesterol-lowering with Leqvio. The program is enrolling over 60,000 patients, across more than 50 countries and more than 30 clinical trials[7].

"The ORION-8 results affirm the benefits of Leqvio in helping patients achieve sustained LDL-C reduction, which is important as cumulative exposure to LDL-C leads to the growth of plaque in the arteries and an increased risk of cardiovascular events," said David Soergel, M.D., Global Head of Cardiovascular, Renal and Metabolic Drug Development, Novartis. "The trial is part of a growing body of evidence for Leqvio being generated through our ongoing VictORION program that is examining the use of Leqvio in broad and varied patient populations affected by ASCVD."

Leqvio is the first and only small interfering RNA (siRNA) therapy to lower LDL-C. It is approved in over 80 countries, including the US, EU and China[8,9,10]. In the US, the FDA approved a label update in July 2023 that allows for earlier use of Leqvio to help reduce LDL-C as an adjunct to diet and statin therapy for patients with elevated LDL-C who have not had a cardiovascular event but are at an increased risk of heart disease[8,11].

* After an initial dose and another at three months.
** <70 mg/dL, the target for patients with ASCVD or <100mg/dL for patients with increased risk of ASCVD.

About Leqvio
Leqvio is an injectable prescription medicine indicated as an adjunct to diet and statin therapy for the treatment of adults with primary hyperlipidemia, including heterozygous familial hypercholesterolemia (HeFH), to reduce low-density lipoprotein cholesterol (LDL-C)[8,10].

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.

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 ORION-8
ORION-8 (NCT03814187) is a three-year open-label extension of the placebo-controlled 18-month Phase III trials ORION-9, ORION-10, and ORION-11 and the four-year Phase II ORION-3 trial (an extension of the on-year Phase II ORION-1 trial)[5,13]. ORION-8 evaluated the long-term safety, efficacy and tolerability of Leqvio in 3,274 patients with atherosclerotic cardiovascular disease (ASCVD), increased risk of ASCVD (includes patients with who have comorbidities such as diabetes and hypertension) or heterozygous familial hypercholesterolemia (HeFH) and elevated low density lipoprotein cholesterol (LDL-C), despite maximum tolerated dose of LDL-C lowering therapies[5]. 2,446 patients completed the trial to Day 1080 (three years)[1]. The primary endpoint of the study was the proportion of patients achieving pre-specified LDL-C targets at the end of the study, either Day 1080 or 90 days after the last injection[5]. Patients received 284 mg inclisiran sodium twice yearly* (every 6 months) for up to an additional three years after baseline studies[3]. Adverse events at the injection site occurred in 5.9% of patients, compared with 8% in the Leqvio arm of the pooled analysis of ORION-9, ORION-10, and ORION-11 trials[1,8].

About VictORION

VictORION is 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-INITIATE, V-INCEPTION, V-REAL, V-DIFFERENCE, and V-PLAQUE.

About atherosclerotic cardiovascular disease (ASCVD)

Atherosclerotic cardiovascular disease (ASCVD) refers to a variety of diseases caused by the development and growth of plaques in the inner lining of the arteries[14]. The atherosclerotic plaque is mainly composed of low-density lipoprotein cholesterol (LDL-C) which accumulates over time[14]. 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[14,15]. 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 from any other chronic diseases[16-19]. ASCVD risk-equivalent corresponds to conditions that confer a similar risk for an ASCVD event (e.g., diabetes, heterozygous familial hypercholesterolemia)[2,19].

About Novartis in Cardiovascular

Cardiovascular (CV) disease is a global health crisis[16,20]. CV disease is the number one killer in the world[16]. Taking more lives than all cancers combined, it contributes to one in every three deaths globally[16,20]. Of all CV events, 80% can be prevented[21]. 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 how CV disease is managed throughout life. Our efforts include the use of early interventions and the development of pioneering treatments that address the spectrum of CV disease, 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.

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About Novartis
Novartis is reimagining medicine to improve and extend people's lives. We deliver high-value medicines that alleviate society's greatest disease burdens through technology leadership in R&D and novel access approaches. In our quest to find new medicines, we consistently rank among the world's top companies investing in research and development. Novartis employs about 14,000 people in the United States. For more information, please visit https://www.novartis.us

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