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PRESS RELEASE

Twice-yearly* Leqvio® (inclisiran) reduced cardiovascular event risk in first outcomes study of an siRNA therapy in ASCVD

- *ORION-4 met its primary endpoint, with Leqvio® demonstrating a statistically significant and clinically meaningful reduction in major adverse cardiovascular events (MACE) when added to standard-of-care*[1]
- *ORION-4 and ongoing VICTORION-2 PREVENT trial comprise one of the largest advanced lipid-lowering cardiovascular outcomes programs in secondary prevention*[1-3]
- *Full results planned to be published in H1 2027*

Basel, November 23, 2026 – Novartis today announced positive topline results from the Phase III ORION-4 trial, providing the first cardiovascular outcomes evidence for Leqvio® (inclisiran) in patients with established atherosclerotic cardiovascular disease (ASCVD)[1]. The results demonstrate that adding Leqvio to standard-of-care lipid-lowering therapy reduced cardiovascular risk, reinforcing the potential of sustained LDL-C lowering with twice-yearly Leqvio to transform the management of ASCVD[1].

"People living with cardiovascular disease face a lifelong risk of another heart attack, stroke or other cardiovascular event," said Ruchira Glaser, Head, Cardiovascular, Renal and Metabolism Development Unit, Novartis. "ORION-4 marks a meaningful advance demonstrating for the first time the potential to significantly reduce cardiovascular risk with a twice-yearly therapy."

“ORION-4 provides evidence that inclisiran is well tolerated and can reduce the risk of major cardiovascular events in people with established vascular disease,’’ said Louise Bowman, BA, MBBS, MD, FRCP, Professor of Medicine and Clinical Trials, and Honorary Consultant Physician (Lipidology), Oxford Population Health, and lead ORION-4 investigator. “These findings are particularly important given the substantial burden of cardiovascular disease and the continued need for effective approaches to reducing cardiovascular risk.”

These findings represent an important milestone in the broader VictORION siRNA clinical development program. Together, ORION-4 and the ongoing VICTORION-2 PREVENT trial have enrolled more than 33,000 participants worldwide, forming one of the largest cardiovascular outcomes programs of its kind in secondary prevention[1-3].

ASCVD remains one of the leading causes of death worldwide, with millions of people continuing to experience cardiovascular events each year[4]. Despite availability of therapies, up to 80% of people with ASCVD do not achieve guideline recommended LDL-C targets, highlighting the need for treatment approaches that support sustained LDL-C lowering and long-term cardiovascular risk reduction[5-8].

Full results from ORION-4 are planned for publication in the first half of 2027 with VICTORION-2 PREVENT also expected in 2027[2-3].

*After an initial dose and another at three months.

About Atherosclerotic Cardiovascular Disease (ASCVD)
Cardiovascular disease (CVD) affects hundreds of millions of people and claims more lives globally than cancer, chronic lung disease and diabetes combined[9]. Around 80% of premature cardiovascular deaths can be prevented by addressing factors that cause or worsen CVD[10].

ASCVD accounts for 85% of all CV deaths[4]. It is the primary cause of mortality in the European Union and its burden in the US is greater than that of any other chronic diseases[11,12]. ASCVD is caused by the development and growth of plaques in the inner lining of the arteries[13]. The atherosclerotic plaque is mainly composed of low-density lipoprotein cholesterol (LDL-C) that accumulates over time[14]. Cumulative exposure to LDL-C can increase one's risk of cardiovascular events such as a heart attack or stroke[13-14].

About Leqvio
Leqvio® (inclisiran) is the first and only small interfering RNA (siRNA) therapy to lower low-density lipoprotein cholesterol (LDL-C)[15,16]. It is a subcutaneous injection given by a healthcare provider (HCP) with an initial dose, another at three months, and then every six months[15,16]. 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 approved in more than 100 countries, including the US, EU, Japan and China[15-18]. Novartis obtained global rights to develop, manufacture and commercialize Leqvio under a license and collaboration agreement with Alnylam Pharmaceuticals, a leader in RNA interference (RNAi) therapeutics.

About ORION-4
ORION-4 is a Phase III, randomized, double-blind, placebo-controlled cardiovascular outcomes trial evaluating whether Leqvio® (inclisiran) reduces the risk of major adverse cardiovascular events (MACE), defined as coronary heart disease death, myocardial infarction, fatal or non-fatal ischemic stroke, or urgent coronary revascularization, in people with established atherosclerotic cardiovascular disease (ASCVD)[2].

The study is led by the University of Oxford in collaboration with the TIMI Study Group and co-sponsored by the University of Oxford and Novartis. Over 16,000 participants were randomized to receive inclisiran or placebo on Day 1, at three months and then every six months[2]. Secondary outcomes include MACE among participants taking high-intensity statins at baseline, the composite of coronary heart disease death or myocardial infarction, and cardiovascular death[1].

The topline results reported by Novartis are based on analyses conducted by the University of Oxford and presented to the ORION-4 Steering Committee.

About Novartis in Cardiovascular Disease
At Novartis, we're redefining cardiovascular care, shifting toward earlier action, expanding how we understand and treat cardiovascular disease, and pushing the boundaries of what's possible so more people can live longer, healthier lives. Building on our 40-year legacy, we're committed to shaping what's next in cardiovascular care through bold science and a diverse, industry-leading pipeline.

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 300 million people worldwide.

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

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