

MEDIA & INVESTOR RELEASE

World-first agreement between Novartis and the NHS enables broad and rapid access to first-in-class cholesterol-lowering medicine Leqvio[®] ▼ (inclisiran)

- *Agreement follows positive NICE recommendation and commits to deliver Leqvio[®] (inclisiran) access via a population health management approach identifying eligible patients across England¹*
- *Over three years ~300,000 patients at high risk of a second cardiovascular event are expected to be treated with inclisiran, a small interfering RNA therapy administered as a 6-monthly maintenance dose[‡], in the community setting*
- *Long-term elevated LDL cholesterol (LDL-C) is a known cause of atherosclerotic cardiovascular disease (ASCVD) and a key modifiable risk factor in the prevention of cardiovascular disease²*
- *Cardiovascular disease, which can lead to heart attack and stroke, causes more than 1 in 4 deaths across the UK and places a considerable financial burden on the NHS and wider society^{3,4}. It is estimated that there are over 3.5 million people living with ASCVD in the UK⁵*
- *NHS agreement is a strong demonstration of Novartis' commitment to increasing access to innovative medicines through pioneering partnerships with health systems*

Basel, September 01, 2021 — Novartis has reached a commercial agreement with the NHS in England as part of a collaboration to pioneer a first-of-its-kind population health management approach to address elevated LDL-C in eligible patients with ASCVD across England.

The NHS and Novartis collaboration moves into the implementation phase following the positive final recommendation from the National Institute for Health and Care Excellence (NICE) for use of inclisiran in primary care for the treatment of adult patients within its licenced indication^{*} who also have persistently elevated LDL-C levels (2.6 mmol/l or more despite maximum tolerated statins with or without ezetimibe) and a history of certain cardiovascular events[†].

“This population health management approach is potentially game-changing, seeking to improve a nation’s health by proactively identifying individuals ‘at highest risk’ and introducing effective solutions that will improve their future health state. This represents a significant advance in patient care through effective lipid management,” said Prof Kausik Ray, MD,

*:† See endnotes for further details

‡ See ‘About inclisiran’ section later in release for details

Professor of Public Health at Imperial College London and Honorary Consultant Cardiologist at the Imperial College NHS Trust. “As a clinician, I see many patients where their cholesterol levels are insufficiently controlled for their level of risk, often despite optimal use of available therapies, putting them at increased risk of a heart attack or stroke. Having faster and broader access to a medicine like inclisiran, which offers the combination of a convenient twice-a-year maintenance dosing schedule, as well as the ability to be used in primary care – where most patients are cared for – and provide sustained reductions in LDL-C is a hugely positive milestone in patient care.”

Novartis will work with the NHS Accelerated Access Collaborative and the Academic Health Science Network (with the support of NHS Digital) to help them proactively identify, treat and monitor eligible individuals with ASCVD who have experienced a cardiovascular event, such as a heart attack or stroke, and have high cholesterol despite treatment with maximal tolerated statins.

“Cardiovascular disease has long been the number one cause of human mortality, and this intractable health issue requires a reimagining of how we treat heart health, said Vas Narasimhan, Novartis CEO. This pioneering collaboration with the NHS in England has the potential to spur a step-change improvement in cardiovascular health across the UK, and it demonstrates Novartis’ commitment to working with healthcare systems around the world to improve patient outcomes by co-creating novel access solutions for innovative medicines.”

With around 7.6 million people across the UK living with heart and circulatory diseases, causing more than a quarter (27%) of all deaths each year, the NHS has recognised CVD as the single biggest area in which lives can be saved over the next 10 years^{3,4}. This collaboration aims to contribute towards meeting the goals of the NHS Long Term Plan which calls for a proactive approach to identifying and treating patients with high-risk conditions to help prevent cardiovascular disease⁶.

“High cholesterol is a major cause of cardiovascular disease – disease of the heart and blood vessels. It is very common and can affect anyone including those who are young, slim, fit and active. HEART UK looks forward to continuing our leading role in helping people effectively manage their cholesterol and we warmly welcome the collaboration between Novartis and the NHS to enable more people to access this innovative medicine.” comments Jules Payne, Chief Executive at HEART UK, the cholesterol charity.

The NICE recommendation was based on results from the Novartis ORION clinical research program, including Phase III trials ORION-9, ORION-10 and ORION-11, which involved over 3,600 patients and assessed the safety, efficacy and tolerability of inclisiran in lowering LDL-Cholesterol levels^{7,8,9}.

Endnotes:

Inclisiran is licenced in Europe for use in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet:

- in combination with a statin or statin with other lipid-lowering therapies in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin or,
- along or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated.

The criteria set out by NICE are for use in patients only if:

- There is a history of any of the following cardiovascular events:
 - o Acute coronary syndrome (such as myocardial infarction or unstable angina needing hospitalisation)
 - o Coronary or other arterial revascularisation procedures
 - o Coronary heart disease
 - o Ischaemic stroke or
 - o Peripheral arterial disease, and:

- Low density lipoprotein cholesterol (LDL-C) concentrations are persistently 2.6 mmol/l or more, despite maximum tolerated lipid-lowering therapy (that being maximum tolerated statins with or without ezetimibe).

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About Atherosclerotic Cardiovascular Disease (ASCVD)

Atherosclerosis corresponds to the accumulation of lipids over time, mainly low-density lipoprotein cholesterol (LDL-C) in the inner lining of the arteries. Unexpected rupture of the atherosclerotic plaque can cause an atherosclerotic cardiovascular event such as a heart attack or stroke^{10,11}. ASCVD accounts for over 85% of all cardiovascular disease deaths¹². ASCVD is the primary cause of death in the European Union^{15,16}. ASCVD risk equivalent corresponds to conditions that confer a similar risk for an ASCVD event (e.g., diabetes, heterozygous familial hypercholesterolemia)^{9,15}.

About inclisiran

Inclisiran (KJX839) is the first and only small interfering ribonucleic acid (siRNA) therapy for the reduction of low-density lipoprotein cholesterol (LDL-C) levels via an RNA interference (RNAi) mechanism of action^{7,8,9}. It works, in combination with maximally-tolerated statins and a lipid-lowering diet, by preventing the production of the target protein in the liver, increasing hepatic uptake of LDL-C and clearing it from the bloodstream. Inclisiran is dosed initially, again at three months and then once every six months thereafter¹⁶. In three clinical trials, patients taking inclisiran maintained LDL-C reduction throughout each six-month dosing interval^{8,9}. Inclisiran is administered by a healthcare professional as a subcutaneous injection.

In the Phase III trials, inclisiran was generally well-tolerated^{8,9}. The most common adverse events reported ($\geq 3\%$ 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. Among those, injection site reactions were the most frequent ones. Those were generally mild, and none were severe or persistent^{8,9}.

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.

Inclisiran was granted marketing authorization by the European Commission on December 9, 2020.

About the Global Novartis Population Health Management Approach

The Novartis population health management approach is anchored in building partnerships between Novartis and systems of care around the world that accelerate patient access to a therapy, with the goal of improving the CV health of the system's defined population at speed and scale.

Novartis is committed to co-creating innovative solutions, anchored in an LDL-C lowering approach, that can address public health needs and deliver responsible budget impact and return on healthcare-spending investment. Optimizing cholesterol levels can be done through a central management model for which inclisiran is a suitable candidate, thereby helping to reach a large number of at-risk patients^{6,7,8}.

About Novartis in Cardiovascular-Renal-Metabolism

Novartis is committed to 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. Novartis is committed to researching molecules with the potential to address cardiovascular, metabolic and renal diseases.

About Novartis

As a leading global medicines company, we use innovative science and digital technologies to create 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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References

1. National Institute for Health and Care Excellence. Inclisiran for treating primary hypercholesterolaemia or mixed dyslipidaemia [ID1647] <https://www.nice.org.uk/guidance/indevelopment/gid-ta10703>.
2. Mach F. et al. *European Heart Journal*. 2020;1(41):111–188.
3. British Heart Foundation. CVD Factsheet. Available at: <https://www.bhf.org.uk/-/media/files/research/heart-statistics/bhf-cvd-statistics-uk-factsheet.pdf?la=en> [Last accessed: August 2021].
4. NHS England. Cardiovascular disease (CVD). Our ambition for CVD prevention. Available at: <https://www.england.nhs.uk/ourwork/clinical-policy/cvd/> [Last accessed: August 2021].
5. Data on file. INC_DOF-014.
6. NHS long-term plan summary. Available at: <https://www.longtermplan.nhs.uk/wp-content/uploads/2019/01/the-nhs-long-term-plan-summary.pdf>. [Last accessed: July 2021].
7. Stoekenbroek RM, Kallend D, Wijngaard PL, et al. Inclisiran for the treatment of cardiovascular disease: the ORION clinical development program. *Future Cardiol*. 2018;14(6):433–442.
8. Raal F, Kallend D, Ray K, et al. Inclisiran for Heterozygous Familial Hypercholesterolemia. *N Engl J Med*. 2020;382(16):1520–1530.
9. Ray K, Wright R, Kallend D, et al. Two Phase 3 Trials of Inclisiran in Patients with Elevated LDL Cholesterol. *N Engl J Med*. 2020;382(16):1507–1519.

10. Mayo Clinic. Arteriosclerosis / atherosclerosis. Available from: <https://www.mayoclinic.org/diseases-conditions/arteriosclerosis-atherosclerosis/symptoms-causes/> [Last accessed: July 2021].
11. Goldstein J, Brown M. A century of cholesterol and coronaries: from plaques to genes to statins. *Cell*. 2015;161(1):161–172.
12. World Health Organization. Cardiovascular diseases (CVDs): Factsheet [online] May 17, 2017. Available from: [https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-\(cvds\)](https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)) [Last accessed: July 2021].
13. Roger VL, Go AS, Lloyd-Jones DM, et al. Heart disease and stroke Statistics–2012 update: A report from the American Heart Association. *Circulation*. 2012;125(1):e2–e220.
14. Kim H, Kim S, Han S, et al. Prevalence and incidence of atherosclerotic cardiovascular disease and its risk factors in Korea: a nationwide population-based study. *BMC Public Health*. 2019;19(1):1112.
15. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation*. 2002;106(25):3143–3421.
16. Inclisiran Summary of product characteristics.

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