Investigator: Dr. Richard Burkimsher **Centre number:** 3656 **Contact for queries** If you have any questions about this study, you can contact: **Daytime:** Research team on 01736 805460 **Out of hours:** Research team on 07398182935	Mounts Bay Medical Hub Connor Downs Surgery Turnpike Road TR27 5DT 01736 805460

Dear potential participant:

We are inviting you to be in a research study to find out if the study treatment, called inclisiran, can help prevent cardiovascular events (such as heart attacks, strokes, procedures to improve blood flow, and death) in adults who are at high cardiovascular risk but have not had a major cardiovascular event, and who also have high cholesterol. This is often referred to as "primary prevention". Having a lot of LDL-cholesterol (also known as "bad" cholesterol) in your blood can lead to build up on your artery walls (a condition called atherosclerotic cardiovascular disease), creating a thick and fatty deposit (or plaque) that can block blood flow. Blocked arteries can lead to important cardiovascular events, such as heart attack, stroke, or cardiovascular-related death. Inclisiran has been shown to be safe and effective at lowering LDL-cholesterol. This study will help understand if a reduction in LDL-cholesterol with inclisiran will also prevent these important cardiovascular events from occurring. Approximately 14,000 participants in approximately 45 countries will participate in this study.

A summary of the information is below.

Summary of the study

What is the purpose of this study? The purpose of the study is to find out if inclisiran will prevent cardiovascular events in participants at high cardiovascular risk and who have elevated cholesterol but have not yet had a major cardiovascular event.
What study treatment will I get? You have a 1 in 2 (50%) possibility of receiving the study treatment, called inclisiran, or of receiving placebo. Placebo is something that will look like the study treatment, but it has no active ingredients. Both treatments are administered by a healthcare professional via a pre-filled syringe. Regardless of which study treatment you will receive as part of this study, if you are already taking a medication to lower your cholesterol that was prescribed to you before starting this study, you will continue taking that medication for the duration of the study.
Who is paying for this study? The study is being organised and funded by Novartis Pharma AG, Lichstrasse 35, 4056 Basel Switzerland and is being run by the medical staff in hospital outpatient clinics. Novartis will make payments into your study doctor's hospital research fund to cover the costs of this study.

What happens at my study visits? This study is expected to last for approximately 6 years. Your participation in this study will likely be at least 3 years. If you have any questions about this, your Study Doctor can explain this further. During the first year of the study, you will meet with your Study Doctor 5 times at the Study Site. You will receive an injection of either inclisiran or placebo at 3 of these visits. After the first year, you will go to your Study Doctor every 6 months (twice a year) and receive an injection of inclisiran or placebo at each of these visits. Your Study Doctor will take a fasted blood sample at every visit. If you do not attend the screening visit fasted you will be asked to return on another day to have your fasted blood sample collected
Have others received this study treatment before? Inclisiran has been studied in people with atherosclerotic cardiovascular disease or who are at risk for atherosclerotic cardiovascular disease in multiple clinical trials to assess inclisiran' s ability to reduce LDL-cholesterol, in which 3,968 adult participants have received inclisiran. However, this is the first study to see if inclisiran can prevent cardiovascular events in patients who are at high cardiovascular risk but have not yet had a major cardiovascular event, so we do not know if it will work for you. Your condition may improve, may get worse, or there may be no change.
Do I have to join this study? You do not need to join this study to be treated for your risk of cardiovascular events or high LDL-cholesterol. Your Study Doctor and/or your personal doctor will discuss your treatment options and their risks and benefits with you before you make your decision. If you choose not to join the study or choose to leave the study at any time, there will be no penalty or loss of benefits.
Are there any side effects? There may be side effects (or risks) from the study treatment and from blood collection during the study. You should tell your Study Doctor if you have any new complaints, side effects, or had other doctor visits or hospitalisations outside of the study. The most common risk of study medication administration is injection site reactions (local skin reactions at the injection site), occurring in less than 10% of patients. As with any drug, it is possible that you may have an allergic reaction to inclisiran. However, no allergic reactions were seen in three large previous clinical trials.
Are there any benefits to me? Taking part in this research study may not benefit you directly, but we may learn new things that could help treat people in the future. If you receive inclisiran during this study, you may also benefit from preventing cardiovascular events and/or lowering of your LDL-cholesterol (also known as "bad" cholesterol).
What happens if I am hurt during the study? The Sponsor's insurance will pay for study-related injuries under the conditions mentioned in the patient information sheet and consent form
Who has the rights to my data? The Sponsor owns all rights to the study results and your data collected throughout the trial.
Will my information remain confidential? The Sponsor will follow all applicable laws to ensure your identity remains confidential.

Thank you in advance for your time and interest in our research study. If you would like more information, you can contact the Study Doctor or nurse whose name and number are shown on the front page of this document and they will provide the full Information Sheet and Consent Form.