

GENinCode Plc
(**"GENinCode" or the "Company"**)

CARDIO inCode-Score® presentation on polygenic risk of Coronary Heart Disease
at 2024 European Society of Cardiology (ESC) Annual Congress, London

Oxford, UK. GENinCode Plc (AIM: GENI), the polygenics company focused on the prevention of cardiovascular disease and ovarian cancer, announces the presentation by Kaiser Permanente on the interplay between family history and polygenic risk on the incidence of coronary heart disease ("CHD") which will take place at the 2024 Annual Congress of the European Society of Cardiology ("ESC") in London from 30 August to 2 September 2024.

Following the March 2024 milestone publication in the American Journal of Preventive Cardiology¹, this latest study shows CARDIO inCode-Score® PRS and family history in first degree relatives independently contribute to the risk of incident CHD, with a 42% increase in risk in the presence of a positive family history and a 64% increase where the patient has a high polygenic risk score ("PRS"). Importantly, the study showed the joint effect of positive family history and a high polygenic risk increased the hazard or incidence of CHD by 2.3 times. Thus, relying solely on self reported (patient) family history is insufficient to fully characterise the genetic contribution to CHD and PRS is recommended.

The Kaiser Permanente Division of Research study investigated more than 63,000 adult individuals with no history of CHD who are part of the Kaiser Permanente Northern California Genetic Epidemiology Resource in Adult Health and Aging ("GERA") multi-ethnic cohort. The GERA cohort followed the membership over an average of 14 years, using CARDIO inCode-Score® to assess the polygenic risk of CHD and future incidence of risk of CHD.

Individuals with a high polygenic risk of CHD should be prioritised for lifestyle advice and where appropriate therapeutic intervention as those at the highest polygenic risk will benefit most from earlier and/or more intensified treatment, especially where they have family history. Previous data on CARDIO inCode-Score® presented at last year's ESC showed that where individuals have a high polygenic risk, a favourable lifestyle is associated with a 52% lower rate of CHD compared with an unfavourable lifestyle. The latest study continues to underline the need for 'polygenic risk score' lifetime risk assessment in conjunction with traditional clinical risk assessment (including family history) to optimise preventive care strategies and lower the future risk of CHD.

Polygenic risk assessment can be undertaken in younger people, before conventional clinical risk factors (such as high blood pressure, diabetes, etc.) have developed, and can be combined with conventional risk scoring in older people. In this way clinicians can more accurately identify those most likely to benefit from lifestyle and therapeutic intervention (precision medicine).

In the UK around 7.6 million people live with heart and circulatory disease, which causes 25% of all UK deaths annually. Cardiovascular Disease ("CVD") can be reduced by identifying and treating individuals at risk, with the NHS 10 Year Plan (2019) setting out to address CVD prevention.

Matthew Walls, CEO of GENinCode said:*"This latest ESC presentation on CARDIO inCode-Score® continues to strengthen the clinical utility and importance of polygenic risk assessment to identify individuals in the population at high genetic risk enabling targeted treatment to prevent coronary heart disease."*

1. <https://www.sciencedirect.com/science/article/pii/S266667724000291>

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About GENinCode:

GENinCode Plc is a UK based company specialising in genetic risk assessment of cardiovascular disease. Cardiovascular disease is the leading cause of death and disability worldwide.

GENinCode operates business units in the UK, Europe through GENinCode S.L.U, and in the United States through GENinCode U.S. Inc.

GENinCode predictive technology provides patients and physicians with globally leading preventive care and treatment strategies. GENinCode CE marked invitro-diagnostic molecular tests combine clinical algorithms and bioinformatics to provide advanced patient risk assessment to predict and prevent cardiovascular disease.

About CARDIO inCode-Score® (CIC-SCORE)

CIC-SCORE is a first in class in-vitro diagnostic test used to assess an individuals genetic risk of CHD. The test is based on published clinical evidence amassed over 15 years which, combined with traditional clinical risk factors, provides a comprehensive risk assessment of CHD for use in primary preventive care. GENinCode labs process patient DNA (extracted from saliva or blood samples) and deliver the CARDIO inCode-Score® test results to physicians via an online cloud based algorithmic (AI) reporting system ('SITAB').

CIC-SCORE also addresses the well-recognised need for improvement in the cardiovascular disease (CVD) standard of care across ethnicities where individuals from certain racial and ethnic groups face higher risks of CVD. The CIC-SCORE test provides an improved estimation of an individual's risk of heart attack over their lifetime, particularly within a 10-year period post testing when combined with traditional clinical risk assessment. The CIC-SCORE polygenic risk score enables a major improvement in patient CVD risk assessment, preventive care and personalised treatment to reduce the incidence of major adverse cardiovascular events (MACE), such as heart attack.

About Cardiovascular Disease (CVD):

Heart and circulatory disease also known as cardiovascular disease (CVD) is the leading cause of death globally, taking an estimated 17.9 million lives each year, with Coronary Heart Disease (CHD) representing the leading cause of death for men, women, and people of most racial and ethnic groups in the United States. CVD is a group of disorders of the heart and blood vessels that include coronary heart disease, cerebrovascular disease, rheumatic heart disease and other conditions. More than four out of five CVD deaths are due to heart attacks and strokes, and one third of these deaths occur prematurely in people under 70 years of age. By 2030 the global cost of CVD is set to rise from approximately US\$863 billion in 2010 to US\$1,044 billion and is both a major health issue and global economic burden.

Cardiovascular disease, causes a quarter of all deaths in the UK and is the largest cause of premature mortality in deprived areas and is the single biggest area where the NHS can save lives over the next 10 years. CVD is largely preventable, through lifestyle changes and a combination of public health and action on smoking and tobacco addiction, obesity, tackling alcohol misuse and food reformulation. Lifestyle "risks factors" are measured in primary care facilities and indicate an increased risk of heart attack, stroke, heart failure and other complications.

Identifying those at highest risk of CVDs and ensuring they receive appropriate treatment can prevent premature deaths.

The current standard of care for assessing cardiovascular risk is primarily based on traditional clinical risk factors such as age, sex, smoking, body mass, blood pressure and cholesterol levels from which individuals

are categorised as being at low, moderate or high risk of a CVD event. This categorisation is imperfect as CVD events frequently occur in those thought to be at low or moderate risk. The size of the populations at low or moderate risk are much larger than those at high or very high risk so whilst the relative risk of a CVD event may be small, the absolute number of CVD events in low and moderate risk populations is much greater than the number of events in higher risk categories. It is clear that the earlier in life preventive measures can be put in place the lower the future risk.

Clinicians have for many years recognised the importance of prior CVD events within the families of their patients because genetic factors contribute to the development of atherosclerosis and a patient's family history has become a surrogate for their inherited genetic risk. In recent years, with the advances of genomics, it has proved possible to add genetic profiling to conventional CVD risk factors, the combination of the two (genetics and conventional clinical risk factors) enhancing the predictive capability of patient risk thereby resulting in a personalised and preventive approach to CVD.

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