



PROMISE Substudy Results, Published in the *American Heart Journal*, Provide Independent Validation of the Clinical Value of the Corus® CAD Blood Test to Accurately Identify Patients with Obstructive CAD

Large NHLBI-Sponsored Substudy Corroborate Findings from Previous Validation Studies Demonstrating that Corus CAD Significantly Identifies Obstructive CAD and Predicts Future Clinical Events

REDWOOD CITY, Calif. – February 6, 2017 – [CardioDx, Inc.](#), a molecular diagnostics company specializing in [cardiovascular genomics](#), announced today the publication of a peer-reviewed substudy of the National Heart, Lung and Blood Institute (NHLBI)-funded PROMISE (Prospective Multicenter Imaging Study for Evaluation of Chest Pain) trial in the *American Heart Journal*, which assessed the Corus CAD test's ability to predict future clinical events.¹ Previously validated for the detection of obstructive* coronary artery disease (CAD) with a 96% negative predictive value and 89% sensitivity, Corus CAD is a simple blood test, incorporating age, sex, and gene expression measurements into a single score (1-40 scale) that indicates the current likelihood of obstructive CAD.²

“The PROMISE study findings are important because they provide clinicians with additional information regarding their patients with suspected obstructive CAD using a non-invasive blood test that come from a pragmatic clinical trial setting,” said Deepak Voora, M.D., lead author and substudy investigator, Associate Professor of Medicine and member of the Duke Center for Applied Genomics & Precision Medicine in the Department of Medicine, Duke University School of Medicine. “What many don’t realize is that it is often difficult to diagnose CAD because many patients do not have typical symptoms. Our substudy, which included more than 2,000 patients, demonstrated that patients with low scores not only had a low likelihood of obstructive CAD but also were at lower risk for undergoing revascularization in the near term. Study results suggest this test could provide additional assurance for clinicians to pursue alternate causes of symptoms and to defer the need for advanced cardiac testing in patients with low scores.”

“The results of the PROMISE substudy reinforce the clinical validity of the Corus CAD test over a range of scores,” said Mark Monane, M.D., FACP, Chief Medical Officer of CardioDx. “The PROMISE substudy, with a median patient follow-up of greater than two years, highlights and strengthens the clinical value of the Corus CAD blood test and its ability to help clinicians safely and accurately identify patients who may be at a low or elevated risk of obstructive CAD. The totality of Corus CAD data to date provides the key stakeholders – patients, physicians and payers – with a broad range of evidence needed in order to integrate the test into the care and management of patients presenting with symptoms suggestive of obstructive CAD.”

The study, published in the *American Heart Journal* on February 2017, showed that patients with low Corus CAD test scores had a lower likelihood of obstructive CAD in the arteries, and the opposite is true for higher scores. The primary analysis found that the clinical event rate (defined as the composite rate of death, myocardial infarction (MI), hospitalization for unstable angina, or revascularization) was lower



in patients with low Corus CAD test scores (1-15, n=1058 patients) as compared to patients with higher Corus CAD test scores (>15, n=1312 patients) (odds ratio of 2.6, $p<0.001$).

Additionally, the clinical event rate for patients with low Corus CAD test scores (≤ 15) compared to noninvasive cardiac testing, was low and no different from a negative or normal cardiac stress test or CT-angiography (3.2% vs. 2.6%, $p=0.29$) at 25-month median follow-up.

The study included 2,370 non-diabetic patients from the PROMISE trial biobank repository and nearly half of the patients in the substudy were randomized to the coronary CT-angiography (CTA) arm (n=1,137). In this group, 10.1% of patients (n=115 of 1,137) were found to have obstructive CAD, and a Corus CAD score > 15 was associated with an increased likelihood of obstructive CAD (OR 2.5, $p<0.001$).

Finally, the relationship between Corus CAD test scores and clinical event rates remained significant even after adjusting for common clinical risk factors using the Framingham Risk Score (FRS). When the Corus CAD test was added to functional (stress testing) or anatomical (CTA) testing, the Corus CAD test score provided independent and incremental information beyond that of noninvasive diagnostic imaging and helped to accurately reclassify patients to their appropriate risk levels. The increased risk of clinical events seen with elevated Corus CAD test scores were largely driven by a higher rate of revascularization procedures in this group, thus reaffirming that the likelihood of obstructive CAD (defined as >70% stenosis by CTA) increased with higher Corus CAD test scores.

“The results from the PROMISE substudy represent an opportunity to learn more about the integration of the test into clinical practice to help direct heart evaluations and care of patients with chest pain,” said Pamela Douglas, Principal Investigator of the PROMISE study, Professor of Medicine, Ursula Geller Professor for Research in Cardiovascular Disease, Duke University Medical Center and member, Duke Clinical Research Institute.

For an external point of view on the impact of the PROMISE substudy results from cardiologist Andrew Waxler, MD, FACC, Berks Cardiologists, Ltd., [click here](#).

About Obstructive Coronary Artery Disease

Coronary artery disease (CAD) is a very common heart condition in the United States. One in seven deaths among Americans is caused by CAD.³ CAD can cause a narrowing or blockage of the coronary arteries (vessels to the heart that supply the heart with blood, oxygen, and nutrients), reducing blood flow to the heart muscle. This narrowing or blockage in the coronary arteries is often referred to as obstructive CAD, characterized by the presence of atherosclerosis, or plaque.

About the PROMISE Trial

Sponsored by Duke University in collaboration with the National Heart Lung and Blood Institute (NHLBI) the Prospective Multicenter Imaging Study for Evaluation of Chest Pain (PROMISE) is the first large randomized trial using clinical outcomes to compare alternative diagnostic strategies for assessment of patients with new stable symptoms suggestive of coronary artery disease (CAD).⁴



As part of the trial, a genomic archive of blood samples from study patients was obtained which included genetic material (DNA), genomic material (RNA) and plasma. CardioDx purified and isolated DNA and RNA using proprietary methods. In addition, the company's Corus CAD blood test was used to evaluate blood samples from an estimated 2,500 to 3,000 non-diabetic patients enrolled in the trial, with the goal of determining the test's ability to predict major clinical cardiovascular events.

About the Corus CAD Test

Corus CAD is the first and only commercially available blood test that can safely and conveniently help primary care clinicians and cardiologists assess whether or not a stable non-diabetic patient's symptoms may be due to obstructive coronary artery disease. The test incorporates age, sex and gene expression measurements into a single score that indicates the likelihood of obstructive CAD. Clinicians use the Corus CAD score, along with other clinical information, to determine whether further cardiac testing is necessary, which can help patients avoid unnecessary exposure to radiation associated with medical imaging testing, as well as possible reactions to imaging dyes and/or potential complications from invasive cardiac tests requiring catheterization. The test involves a routine blood draw that is conveniently administered in the clinician's office or clinical laboratory patient service center. The Corus CAD test is the only sex-specific test for the evaluation of obstructive CAD because it accounts for cardiovascular differences between men and women.

The test has been clinically validated in independent male and female patient cohorts, including two prospective, multicenter U.S. studies, PREDICT and COMPASS.^{5,2} In the COMPASS study, the Corus CAD test outperformed myocardial perfusion imaging (MPI) as a diagnostic tool to exclude obstructive CAD by demonstrating a higher negative predictive value (96% vs. 88%, $p < 0.001$) than MPI for assessing the presence of obstructive CAD.⁶ To date, over 200,000 Corus CAD test results have been provided to clinicians. CardioDx processes all Corus CAD test samples at its CLIA-certified and CAP-accredited clinical laboratory in Redwood City, California.

The Corus CAD test has been recognized by *The Wall Street Journal's* Technology Innovation Awards, honored as a Gold Edison Award recipient, and named one of *TIME's* Top 10 Medical Breakthroughs.

About CardioDx

CardioDx, Inc., a molecular diagnostics company specializing in cardiovascular genomics, is committed to developing clinically validated tests that empower clinicians to better tailor care to each individual patient. Strategically focused on coronary artery disease, CardioDx is committed to expanding patient access and improving healthcare quality and efficiency through the commercialization of genomic technologies. Please visit www.cardiodx.com for additional information.

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* Obstructive CAD is defined as at least one atherosclerotic plaque causing $\geq 50\%$ luminal diameter stenosis in a major coronary artery (≥ 1.5 mm lumen diameter) as determined by invasive quantitative coronary angiography (QCA) or coronary computed tomography angiography (CTA) (≥ 2.0 mm).

¹ Voora D, Coles A, Lee KL, et al. An Age- and Sex-Specific Gene Expression Score is Associated With Revascularization and Coronary Artery Disease: Insights From the Prospective Multicenter Imaging Study for Evaluation of Chest Pain (PROMISE) Trial. *Am Heart J*. 2017;184:133-140.

² Thomas GS, Voros S, McPherson JA, et al. A Blood-Based Gene Expression Test for Obstructive Coronary Artery Disease Tested in Symptomatic Nondiabetic Patients Referred for Myocardial Perfusion Imaging: The COMPASS Study. *Circ Cardiovasc Genet*. 2013;6(2):154-162.

³ Mozaffarian D, Benjamin EJ, Go AS, et al. On Behalf of the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart Disease and Stroke Statistics – 2016 Update: A Report from the American Heart Association. *Circulation*. 2016;133(4):e38-e360.

⁴ Douglas PS, Hoffman U, Patel MR, et al. Outcomes of Anatomical Versus Functional Testing for Coronary Artery Disease. *N Engl J Med*. 2015;372(14):1291-1300.

⁵ Rosenberg S, Elashoff MR, Beineke P, et al. Multicenter Validation of the Diagnostic Accuracy of a Blood-Based Gene Expression Test for Assessing Obstructive Coronary Artery Disease in Nondiabetic Patients. *Ann Intern Med*. 2010;153:425-434.

⁶ The COMPASS study demonstrated that the Corus CAD algorithm has an NPV of 96% at the pre-specified threshold of 15 in a population of men and women referred to MPI.