PROMISE Trial Substudy Demonstrates That the Corus CAD Blood Test Is Associated With Clinical Events Among Patients Being Evaluated for Suspected Obstructive Coronary Artery Disease

Data from Large NHLBI-Sponsored, Multi-center Study Presented at the

65th American College of Cardiology Annual Scientific Meeting

REDWOOD CITY, Calif. – April 4, 2016 – CardioDx, Inc., a molecular diagnostics company specializing in cardiovascular genomics, announced today results from a genomic substudy of the NHLBI-funded Prospective Multicenter Imaging Study for Evaluation of Chest Pain (PROMISE) trial in nondiabetic patients receiving the Corus CAD blood test. The test integrates age, sex and gene expression into a single score (1-40 scale) corresponding to the likelihood of obstructive coronary artery disease (CAD).* Findings from the substudy were presented at the 65th American College of Cardiology Annual Scientific Meeting, on April 3, 2016, in Chicago, IL.

In this study, the PROMISE Trial investigators asked if a blood-based, age- and sex-adjusted, gene expression score (ASGES or Corus CAD), previously validated for the detection of obstructive CAD, was also predictive of CAD events. The primary analysis showed that cardiovascular event rates, as defined by the composite rate of death, myocardial infarction (MI), hospitalization for unstable angina, or revascularization, were associated with the Corus CAD test in a score-dependent manner: Patients with higher Corus CAD test scores (>15, n=1312 patients) had higher event rates that were statistically different from patients with lower Corus CAD test scores (1-15, n=1058 patients) (odds ratio of 2.6, p<0.001). Additionally, the results from the substudy found that at 25-month median follow-up, the clinical event rates for patients with low Corus CAD scores (≤ 15), were low and no different from negative or normal noninvasive test results using either cardiac stress testing or coronary CT-angiography (CTA) (3.2% vs. 2.6%, p=0.29). This relationship between Corus CAD test scores and event rates remained significant after adjusting for common clinical risk factors using the Framingham Risk Score (FRS) and provided independent and incremental information beyond noninvasive test results (stress testing or CTA). Lastly, the increased risk of clinical events seen with higher Corus CAD scores were largely driven by an increased rate of revascularization procedures in this group, thus reaffirming that the likelihood of obstructive CAD (defined as >70% stenosis by CTA) increases with Corus CAD scores.

The study utilized 2,370 non-diabetic patients from the PROMISE trial biobank repository. Almost half of the patients in the substudy were randomized to the 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 increased obstructive CAD likelihood (OR 2.5, p < 0.001). Findings from the PROMISE Trial provide independent confirmation of the association between the Corus CAD test scores and the presence and extent of coronary artery disease in patients and the likelihood of obstructive CAD.

"Findings from this PROMISE substudy demonstrate the opportunity to use a simple blood test in the initial evaluation of symptomatic patients with suspected CAD to help clinicians determine next steps and make clinical decisions," said Deepak Voora, M.D. Assistant Professor of Medicine, Duke Center for Applied Genomics & Precision Medicine. "The lower likelihood of not only CAD but risk of

revascularization procedures seen in patients with low scores suggests that the score, in conjunction with a physician's clinical assessment, could provide additional information to help physicians efficiently and effectively rule out clinically significant obstructive CAD in the outpatient setting."

"We are very excited to see that the results from the large genomic substudy from the NIH-funded PROMISE Trial independently corroborate findings from our earlier Corus CAD clinical studies on the clinical validity of the test in the evaluation of obstructive CAD. In addition, while we have seen that in previous studies that patients with low Corus CAD test scores have a very low likelihood of major cardiac events within a one-year follow up period, it is very reassuring that the PROMISE substudy results confirm and extend this finding with greater than two years of follow-up seen here," said Mark Monane, M.D., FACP, Chief Medical Officer of CardioDx. "Lastly, we note the finding that clinical outcomes among the patients with the low scores on the Corus CAD blood test (approximately 45% of the study patients) were no different from patients with normal cardiac stress testing or CT-angiography. Taken together, these three results highlight the characteristics of the Corus CAD test to safely and accurately help clinicians risk stratify symptomatic patients, so that patients can potentially avoid additional cardiac testing and procedures that may be potentially unnecessary."

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.[1] 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).[2]

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.[3,4] 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.[5] To date, over 150,000 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.

For media inquiries, please contact Glenn Silver of Lazar Partners, +1-212-871-8485, gsilver@lazarpartners.com.

* Obstructive CAD is defined as at least one atherosclerotic plaque causing ≥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).

References

[1] 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 – 2015 Update: A Report from the American Heart Association. *Circulation*. 2015;131(4):e29-e322.

[2] 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.

[3] 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.

[4] 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.