Study Finds Corus CAD to Be More Accurate in Excluding the Diagnosis of Obstructive Coronary Artery Disease in Women than Standard Diagnostic Methods

- Additional Data Underscore the Value of Corus CAD in Improving Primary Care Providers' (PCP) Precision at Excluding the Diagnosis of Obstructive Coronary Artery Disease in Female Patients Early in the Diagnostic Pathway -

- Both Studies Presented at Women's Health 2013: 21st Annual Congress -

PALO ALTO, Calif. – March 25, 2013 – CardioDx, Inc., a pioneer in the field of cardiovascular genomic diagnostics, today announced data demonstrating that Corus® CAD, the only clinically validated gene expression test for the assessment of obstructive coronary artery disease (CAD), has higher diagnostic accuracy than commonly used risk assessment modalities including symptom evaluation and myocardial perfusion imaging (MPI) in women. The sex-specific analysis of the PREDICT (Personalized Risk Evaluation and Diagnosis in the Coronary Tree) Trial was presented during a poster session at the Women's Health 2013: 21st Annual Congress, which took place in Washington D.C. from March 22nd - 24th.

There is a growing body of clinical evidence confirming that standard diagnostic approaches used to evaluate patients for obstructive CAD lead to many unnecessary noninvasive and invasive procedures such as MPI, stress echocardiogram, computed tomography angiography and coronary angiography, especially in women[1]. According to the results of the PREDICT Trial, MPI was not a significant predictor of obstructive CAD in women. This may be due to the presence of breast and fatty tissue in women, which leads to a higher rate of false-positive diagnoses[2] and, consequently, a higher rate of unnecessary referrals for additional invasive testing. The study also found that chest pain and other clinical factors are not reliable predictors of obstructive CAD in women. The traditional chest pain symptom classification as defined by Diamond and Forrester is helpful in diagnosing men, but does not correspond to presence of obstructive CAD in women. Furthermore, women with obstructive CAD tend to present with atypical, nonspecific symptoms such as shortness of breath, fatigue, and abdominal pain. Only the Corus CAD score and dyslipidemia were associated with the findings of obstructive CAD in women.

"Since the symptoms of coronary disease in women are not as well defined as in men, clinicians cannot use the same assessment criteria in women as they do in men," said Alexandra Lansky, MD, Associate Professor of Medicine and Director of the Cardiovascular Research Center, Yale University School of Medicine, the senior author of the study and one of the PREDICT co-investigators. "Women have more angina and less obstructive coronary artery disease compared to age-matched men and are significantly over-referred to invasive coronary angiography, as current noninvasive diagnostic approaches have limitations in women. Women need tests that are both specific to their biology and can reliably assess the origin of their symptoms. Corus CAD is the only sex-specific test for evaluating obstructive CAD and represents a paradigm shift in how clinicians may diagnose heart disease in women, who account for half of the U.S. population."

The PREDICT cohorts analyzed included 1,160 stable non-diabetic men and women referred for cardiac catheterization with typical and atypical symptoms suggestive of obstructive CAD or who were asymptomatic with a high risk of CAD: a substudy of 492 women was included in this sex-specific

analysis. Of the women referred to invasive coronary angiography with abnormal MPI results (N=295), only 22 percent had obstructive CAD upon invasive coronary angiography. The study showed that Corus CAD results were more accurate than MPI and were significantly associated with the extent and severity of obstructive CAD. Corus CAD was a significant classifier of obstructive CAD in the overall population ($p<0.001$) and in the male ($p=0.001$) and female ($p<0.001$) subgroups separately, whereas MPI was not found to be an independent indicator of obstructive CAD. Each 10-point increase in the Corus CAD score was associated with a twofold increase in the likelihood of obstructive CAD in men, and a 3.4-fold increase in the likelihood of obstructive CAD in women. The results demonstrate the improved ability of Corus CAD to safely exclude obstructive CAD as a diagnosis, particularly in women.

Separately, a poster confirming the clinical utility of Corus CAD in the primary care setting to accurately exclude the diagnosis of obstructive CAD in stable, symptomatic female patients was also presented at the Women's Health Congress. The poster titled, "The Use of a Personalized Gene Expression Test to Improve Decision Making in the Evaluation of Women with Symptoms of Suspected Obstructive Coronary Artery Disease" represents a substudy that included 141 women of a 317 total patient population in this sex-specific analysis led by Michael Conlin, MD, Johns Creek Primary Care. Results showed that Corus CAD scores could reliably separate female patients into elevated risk (score ≥15) and low risk (score ≤15) groups, allowing primary care physicians to more accurately triage patients. Use of Corus CAD led to a reduction in referrals to cardiologists of 77 percent in the low-scoring female patient group ($p<0.001$).

"With test overutilization contributing to the approximately $5 billion in annual cardiac-related diagnostic costs in this population, primary care providers are concerned with accountable care now more than ever," said Dr. Conlin. "As the symptoms in women are harder to diagnose, they are often referred to additional and more invasive testing that ultimately produces low yields of obstructive CAD. Therefore, we welcome sex-specific tools like Corus CAD to help us more effectively identify the right patients who need further noninvasive and invasive cardiac workup."

Among the 141 women studied, 73 percent had low Corus CAD scores. PCPs referred 12 percent of patients with low scores and 48 percent with non-low scores to cardiology. Of the patients with low scores who underwent additional testing, none were found to have clinically significant obstructive CAD. The average follow-up duration was 163 days, and no patients experienced a major adverse event during this time.

About Obstructive Coronary Artery Disease

Coronary artery disease is a very common heart condition in the United States. One in five 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 Corus CAD

With a simple blood draw, Corus CAD can safely, accurately and conveniently help primary care clinicians and cardiologists assess whether or not a stable non-diabetic patient's symptoms are due to obstructive coronary artery disease, enabling many patients to avoid unnecessary invasive procedures and exposure to imaging-related radiation risks or imaging agent intolerance. The test has been clinically validated in multiple independent patient cohorts, including two prospective, multicenter U.S. studies,

PREDICT and COMPASS. Additionally, a retrospective, multicenter chart review study and the prospective IMPACT trial at Vanderbilt University demonstrated that Corus CAD use yields statistically significant and clinically relevant changes in patient management decisions in both primary care and cardiology settings. Corus CAD has been used commercially by clinicians in more than 35,000 patients and is a covered benefit for more than 40 million Medicare enrollees in the U.S.

Corus CAD has also 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 Ten Medical Breakthroughs. CardioDx was recently honored as one of *FierceMedicalDevices*' "Fierce 15" most promising privately held medical device and diagnostic companies.

The Corus CAD test is intended for use in non-diabetic stable patients who present with typical or atypical symptoms suggestive of CAD, with no known history of CAD, no prior myocardial infarction (MI) or revascularization procedure, and who are not currently taking steroids, immunosuppressive agents or chemotherapeutic agents.

About CardioDx

CardioDx, Inc., a pioneer in the field of cardiovascular genomic diagnostics, is committed to developing clinically validated tests that empower clinicians to better tailor care to each individual patient. Strategically focused on coronary artery disease, cardiac arrhythmia and heart failure, CardioDx is poised to expand patient access and improve healthcare quality and efficiency through the commercialization of genomic technologies. For more information, please visit www.cardiodx.com.

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[1] Kwok Y, Kim C, Grady D, et al. Meta-Analysis of Exercise Testing to Detect Coronary Artery Disease in Women. *Am J Cardiol* 1999;83: 660-6.
[2] Fleischmann KE, Hunink MGM, Kuntz KM, et al. Exercise Echocardiography or Exercise SPECT imaging? A Meta-Analysis of Diagnostic Test Performance. *JAMA* 1998;280:913-20.
[3] Lloyd-Jones D, Adams R, Carnethon M, et al. Heart Disease and Stroke Statistics--2009 Update: A Report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. 2009;119:480–486.