



Corporate Backgrounder

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diaDexus, Inc.

Overview

diaDexus is a privately held biotechnology company focused on the discovery, development, and commercialization of novel, patent-protected diagnostic products with high clinical value. The company's first product, the PLAC[®] test, is a simple blood test that measures levels of a new risk factor for coronary heart disease and stroke—lipoprotein-associated phospholipase A₂ (Lp-PLA₂), a cardiovascular-specific inflammatory marker implicated in the formation of vulnerable, rupture-prone plaque. The PLAC test is cleared for marketing by the U.S. Food and Drug Administration (FDA) as an aid in determining risk for coronary heart disease and ischemic stroke associated with atherosclerosis.

In addition to developing and marketing the PLAC test, diaDexus is developing a pipeline of promising, patentable cancer diagnostics tests, the most advanced of which is being evaluated for use in the early detection of ovarian cancer. The company also has initiated a nucleic acid diagnostics program focused on developing tests to aid in the prognosis and staging of breast, colorectal, and other cancers.

diaDexus was formed in 1997 as a joint venture by SmithKline Beecham and Incyte Genomics.

Cardiovascular Disease & the PLAC Test

The PLAC test for Lp-PLA₂ addresses a significant unmet clinical need by identifying people at high risk for heart attack and stroke who currently are not identified by traditional risk factors.

Elevated Lp-PLA₂ places patients into a higher risk category to drive more aggressive preventive treatment programs. Cardiovascular disease is the single leading cause of death in the United States, with nearly 500,000 coronary heart disease (CHD) deaths annually and almost 158,000 deaths from stroke. Cardiovascular disease also exacts a high economic toll—experts estimate 2006 direct and indirect costs of \$142.5 billion for CHD and \$57.9 billion for stroke.

Approximately 50 percent of all coronary events strike people with low-to-moderate cholesterol levels, and about 20 percent occur in individuals with none of the four major risk factors (high cholesterol, high blood pressure, smoking, or diabetes), illustrating the need for additional methods to improve diagnosis and treatment. Stroke risk, in particular, is difficult to assess, and until the PLAC test, there was no FDA-approved blood test to help ascertain the risk of stroke.

The PLAC test is being used by a growing number of physicians in a variety of medical specialties, including cardiologists, internists, family practitioners, endocrinologists, and stroke neurologists. The market for the test includes almost half of U.S. adults age 40–75 who fall into the intermediate-risk category for cardiovascular disease and are potential candidates for secondary risk stratification. This group represents about 45 million people in the United States.

Numerous large epidemiological studies have shown Lp-PLA₂ to have clinical value in the assessment of CHD and stroke risk. People with elevated Lp-PLA₂ have a twofold greater risk of suffering a heart attack or stroke than those with low Lp-PLA₂, even after adjusting for traditional risk factors. For patients with the highest Lp-PLA₂ levels along with high blood pressure, stroke risk increases sixfold.

Lp-PLA₂ is an enzyme that associates in the blood primarily with low-density lipoprotein (LDL, the “bad” cholesterol). Lp-PLA₂ is carried to the walls of coronary arteries by LDL, where the enzyme can activate an inflammatory response, making plaque more prone to rupture. As a result, Lp-PLA₂ serves as a specific indicator of vascular inflammation. Patients identified as being at high risk for CHD or stroke based on elevated Lp-PLA₂ levels may benefit from more aggressive treatment programs, such as lifestyle modification or therapeutic intervention,

including statins and daily aspirin. In addition, GlaxoSmithKline is developing small molecule inhibitors that directly target Lp-PLA₂ as potential anti-atherosclerotic treatments.

The PLAC test is a sandwich enzyme-linked immunosorbent assay (ELISA), a biochemical technique used by clinical labs to detect and quantify the presence of an antibody or antigen in a sample. diaDexus has entered into non-exclusive license and supply agreements for the PLAC test with a number of clinical reference and academic laboratories, several of which include co-marketing agreements. The company's lab partners include:

- LabCorp
- Quest Diagnostics, Incorporated
- Mayo Medical Laboratories
- ARUP Laboratories
- Berkeley HeartLab

Epidemiologic Research

Since its inception, diaDexus has had a robust and ongoing epidemiology program in partnership with leading academic centers, resulting in numerous published studies showing the role of Lp-PLA₂ in the development of cardiovascular disease and the value of the PLAC test in clinical practice. Key studies include:

- An analysis from the West of Scotland Coronary Prevention Study (WOSCOPS), a five-year trial of 6,595 men with elevated cholesterol and no history of heart attack, showed that Lp-PLA₂ was the most powerful predictor of cardiovascular events, among four candidate biomarkers. Patients with the highest levels of Lp-PLA₂ had twice the risk of an event compared with patients with the lowest levels, even after adjusting for traditional risk factors and the other biomarkers.
- The Atherosclerosis Risk in Communities (ARIC) coronary heart disease study demonstrated that in individuals with normal LDL, Lp-PLA₂ levels were associated with heart disease, independent of traditional risk factors and C-reactive protein.
- The ARIC study also found that Lp-PLA₂ levels predicted future ischemic stroke, even after adjustment for traditional risk factors, body mass index, and C-reactive protein.

Individuals with elevated Lp-PLA₂ levels were twice as likely to experience a stroke as individuals with lower levels of the enzyme.

- Findings from another recent study verified the role of Lp-PLA₂ in the formation and progression of unstable arterial plaque. Rupture of unstable arterial plaque is the most common cause of heart attack and stroke.

Cancer Diagnostics

Cancer is the second leading cause of death in the United States and the industrialized world. The American Cancer Society (ACS) estimates that more than 500,000 people die of cancer annually in the U.S. Tragically, many cancers are detected too late, when the cancer has spread, reducing effective surgical and therapeutic options. The ACS reports that earlier treatment of most cancers could lead to five-year survival rates exceeding 90 percent. To achieve such survival rates, new diagnostics that detect early stage cancer are clearly needed.

diaDexus owns or has exclusively licensed patents or patent applications covering hundreds of novel molecular targets associated with cancer. The company is developing simple blood tests to detect early stage cancer in otherwise healthy individuals. Multiple cancer diagnostic products are in preclinical or clinical development, and the company has begun discussions with the FDA about the regulatory path for a blood-based test to detect ovarian cancer in the estimated 3 million women in the United States considered to be at high risk of developing the disease.

In addition, diaDexus' molecular diagnostics program leverages genomic and nucleic acid technological expertise, with the goal of improving the prognosis and staging of breast, colorectal, and other cancers. For example, half of all breast cancer diagnoses are classified as low risk based on traditional prognostic factors. However, after treatment, up to 15 percent of these patients will experience a recurrence within 10 years. As a result, there is a clinical need for tests to identify patients at higher risk for recurrence who would benefit from chemotherapy. Alternatively, such a test could help avoid unnecessary treatment in patients predicted to have good outcomes.

Senior Management & Clinical Collaborators

Patrick Plewman, diaDexus' president and chief executive officer, has been with the company since its inception and previously was with SmithKline Beecham. Plewman heads a senior management team with significant expertise in the fields of biotechnology, diagnostics, pharmaceuticals, medical devices, molecular diagnostics, and biotechnology patent law, among others. In particular, the company's executive vice president of diagnostics and chief medical officer bring extensive experience in diagnostic research, biotechnology, and advanced diagnostic blood and lipid testing.

diaDexus also works closely with a panel of experts in the scientific and medical community who advise the company about the clinical need and role of its technologies in clinical practice. Chief among these clinical collaborators is Christie M. Ballantyne, M.D., director of the Center for Cardiovascular Disease Prevention at Baylor College of Medicine and the Methodist DeBakey Heart Center in Houston. Ballantyne is a renowned expert in the prevention of atherosclerotic vascular disease and is director of the core laboratory for the ARIC clinical study.

Board of Directors

In addition to Patrick Plewman, the diaDexus board of directors includes:

- Louis C. Bock, managing director, Bank of America Venture Partners
- Michael Goller, associate, Baker Brothers Advisors, LLC
- John Keller, Ph.D., executive vice president and chief business officer, Incyte Corporation
- Kelvin Neu, M.D., associate, Baker Brothers Advisors, LLC

diaDexus is headquartered in South San Francisco, Calif. The company employs 70 people. For more information, visit www.diaDexus.com or www.plactest.com.

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