

Start-Ups Across Health Care

iCardiac Technologies Inc.

A better cardiac rhythm for drug development

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Industry Segment: Drug Discovery Services

Business: Assessing cardiac risk in pharmaceutical development

Founded: February 2006

Founders: Jean-Philippe Couderc, PhD, CTO (University of Rochester Medical Center); Alexandra (Sasha) Latypova, EVP; J. Mikael Totterman; Alex Zapesochny, President & COO; Wojciech Zareba, MD, PhD, CMO (University of Rochester Medical Center)

Employees: 18

Financing to Date: \$4 million

Investors: Advantage Capital Partners; Stonehenge Capital Company; Trillium Group; New York State Common Retirement Fund; Pfizer Inc.; Angel investors

Board of Directors: J. Mikael Totterman; Alex Zapesochny; David E. Williams (MedPharma Partners); J. Montieth "Monty" Estes (Jaeckle Fleischmann Partners); Anik Bose (Lotus Management Consulting); José J. Coronas (Trillium Group); Timothy G. Cockshutt (Advantage Capital Partners); Brian S. Model, Board Advisor, (Stonehenge Capital Company)

Medical Advisor: Arthur J. Moss, MD (University of Rochester Medical Center)

Few issues are more nettlesome in drug development than the potential for a new drug to unleash rare but potentially lethal heart-rhythm irregularities. Several approved drugs have been pulled from the market after exposures were linked to sudden cardiac deaths; numerous drugs carry warnings because of possible links to arrhythmias; and many more potentially valuable compounds never made it that far because current unreliable cardiac safety measures warned they had the possibility of setting off arrhythmias. The industry has a glaring need for improved cardiac safety testing. **iCardiac Technologies Inc.** hopes to turn that need into a service business with its proprietary algorithms and advanced electrocardio-

gram biomarkers.

The pharmaceutical industry has long known it needs better ways to test for cardiac safety. The Food and Drug Administration has identified improved cardiac safety testing as a key to boosting productivity. A reliable way to assess cardiac safety could identify dangerous drugs long before events occur, help identify any segment of the population for whom a drug would not be safe, allow more drugs through to approval, and reduce costs for drug development and after-approval follow-up. Founded in 2006, iCardiac announced a major research alliance in January with **Pfizer Inc.**, confirming the value the industry perceives in what the young company hopes to achieve.

For three decades, electrocardiology researchers at the **University of Rochester Medical Center's** Heart Research Follow-up Program have studied the ventricular repolarization process of the heart. Much of that work has focused on arrhythmias known as torsades (for *torsades de pointes*, a French term for the "twisting peaks" pattern on an ECG that reveals the condition). Prior to a torsade showing up, an ECG may indicate the possibility of the condition developing through the abnormal prolongation of the QT interval, the fraction of a second between a heart's contraction and its recovery to beat again. The trouble is that when seen on an ECG, a prolonged QT interval is both hard to interpret—it fluctuates even in a healthy person throughout the day—and does not show at all in as many as 15% of those known to be genetically prone to torsades. Moreover, a lengthened QT interval that nonetheless falls short of the period known to be dangerous may or may not indicate a problem.

But any drug that impacts ion channels in the heart cells, and many do, can cause a prolonged QT interval, setting off alarm bells that can kill the development program—or the patient. Alexandra (Sasha) Latypova, EVP and co-founder of iCardiac, says, "The QT measurements presently in use are somewhat crude and risk squashing a good drug or letting through one that causes sudden cardiac death."

For instance, two former blockbuster agents, terfenadine (*Seldane*) and cisapride (*Propulsid*) were withdrawn after each was shown to induce torsades—with unresolved patient suits still dragging through the courts. And around 30 currently marketed drugs now carry warnings that patients should receive regular ECG testing; when evidence emerges of prolonged QT intervals, the patient must stop

taking the drug. The consequences of halting a prescription, though, may be even more dangerous: several prized antipsychotics carry just such warnings. Many other drugs, even OTC cough and cold medications, have also been tied to arrhythmias.

The FDA's deputy commissioner and CMO Janet Woodcock recently told the *Wall Street Journal* that sorting out the issues surrounding prolonged QT interval signal assessment would be "of inestimable value to everyone." The FDA's Critical Path Initiative specifically identified the need to improve cardiac safety testing as crucial to improving the industry's lagging productivity.

Rochester scientists' studies of long QT syndrome (LQTS), the genetic predisposition to arrhythmias, resulted in an important longitudinal ECG database. The investigators discovered that certain biomarkers related to the morphology of the T wave—a period on the ECG corresponding to the brief interval between the heartbeats—were highly predictive of ion channel abnormalities. Rochester colleagues Jean-Philippe Couderc, now holding a dual position as an assistant professor of medicine at the University of Rochester and iCardiac's CTO, and Wojciech Zareba, the director of the Heart Research Follow-Up Program at the University of Rochester and the company's CMO, and others drew on the database to develop predictive algorithms that were licensed along with the biomarkers to form the technology platform for iCardiac. The company is now making this technology platform available to the pharmaceutical industry clients who are desiring more robust and cost-effective cardiac safety testing for their drugs in early development. Latypova says, "Our pilot data indicate that we can potentially predict who will develop dangerous reaction to drugs and who can safely take them."

Although the FDA requires their use in pharmaceutical testing, current QT measurements provide ambiguous answers at best. Most pharmaceutical

firms give a nod to the test and only look at the numbers seriously as more patients take their drug. According to Latypova, the iCardiac tools can be applied fruitfully much earlier in development. "In some cases we can reduce the study population by up to 67%."

Pfizer is one of many companies pursuing better ways to test for cardiac safety. In January, Pfizer and iCardiac entered into a multi-year research alliance to further development of iCardiac's platform and advanced ECG markers for use in the safety testing of in-development and on-market drugs. The deal includes a cross-licensing arrangement by which iCardiac will receive rights to ECG analysis technologies developed within Pfizer.

Under the terms of the agreement, iCardiac and Pfizer will collaborate on a research program composed of a series of studies, including retrospective and prospective ECG data analyses. iCardiac will receive an equity investment and technology license payment, plus research and development funding over the term of the alliance.

The deal does not restrict iCardiac from commercializing results of the alliance for building out its technology platform and any new biomarkers for future application in cardiac safety clinical trials and technologies. "Pfizer recognizes this is a problem for the entire industry," says Alex Zapesochny, president & COO of iCardiac. "They're pushing the industry forward."

Zapesochny had been general counsel and director of business development for Lenel Systems International, a developer and global supplier of high-end software, products, and services for the security industry. The company was sold in 2005 to United Technologies Corp. for \$440 million. Latypova was previously a senior executive together with CEO J. Mikael Totterman at VirtualScopics Inc., a developer of image-based biomarkers for improving pharmaceutical development.

Latypova, Zapesochny, and Totterman considered how best to structure a biomarker service business.

They identified **eResearch Technology Inc.**, which focuses on cardiac safety for the industry and has around \$100 million in annual revenue, as a comparable business model. Additionally, the industry is already familiar with the FDA's E14 guidance on cardiac safety testing. "ECG is already broadly used," says Zapesochny, "and there is existing guidance. It's not as big a leap as proteomic or genomic biomarkers. A thorough QT study today costs about \$1 million per drug. It's not new magic funds that need to be found in the industry."

Eventually, the iCardiac testing platform could be used to segment populations both during clinical trials and once a drug goes to market. Says Latypova: "We can envision drugs being co-prescribed with our ECG test. Physicians could use it to determine whether to prescribe a drug or not or whether to alter the dose for safety reasons." Such co-development programs would likely move away from the service model to a royalty arrangement.

In addition to the undisclosed equity investment and research alliance support from Pfizer, iCardiac has closed on a \$4-million VC round. Totterman says the company "raised more money than anticipated," and should reach breakeven without needing more financing. However, he says, "We may want additional capital to pursue other commercialization opportunities."

The Pfizer cardiac safety alliance program is enough by itself to keep the current 18-person software and laboratory staff busy. However, Totterman says they are looking to add several dozen people over the next couple of years. The company has been in discussions with other pharmaceutical companies and expects to enter into further deals. A medical device developer has also approached them about using their software in cardiac defibrillators and other devices. Totterman says, "We anticipate considerable growth."

—Marc Wortman