

DIAGNOSTICS

Xagenic Inc.

*Detecting nucleic acids
with electrochemical sensors*

If the \$Cdn35.5 million Xagenic Inc. has raised since its founding in May 2010 were not sufficient evidence of its investors' determination to succeed, their choice of president and CEO confirms big ambitions. Few individuals in the world have as much experience commercializing point-of-care diagnostic tests as Timothy I. Still. He was hired in October 2014 to help Xagenic commercialize a diagnostic testing method based on electrochemical sensing methodology.

Still had already worked for Bio-Rad Laboratories and Roche Diagnostics by the time he became VP of sales and marketing at Cholestech, a pioneer of POC testing that operated on the "razor/razor blade" business model. The five-minute *Cholestech LDX* test of cholesterol, triglycerides, and blood glucose launched in 1991 and has been promoted for decades to consumers as well as clinicians. It is, for instance, consistently featured in "healthy lifestyle" segments on TV programs like the *Today* show and *The Dr. Oz Show*.

Cholestech was acquired by Alere Inc. (formerly Inverness Medical) in the spring of 2007 for just over \$326 million. By then, Still had been working for several years as EVP and eventually chief commercial officer of Hemosense. Alere acquired it, too, just months after buying Cholestech. Hemosense developed, manufactured, and commercialized a blood coagulation diagnostic test. The handheld device that processes testing strips became a success after obtaining a CLIA waiver declaring its readouts equivalent to those of tests run in reference laboratories.

After Cholestech and Hemosense, Still went on to become president and CEO of Accumetrics Inc. Its *VerifyNow* testing platform helps physicians determine which anti-platelet drug to prescribe, at what dosage. The test reportedly helped boost sales of Eli Lilly & Co.'s anti-clot-

ting drug *Effient* (prasugrel), by showing that the leading drug *Plavix* (clopidogrel), co-marketed by Bristol Myers-Squibb Co. and Sanofi, was less than fully efficient in one-third of patients taking it. Accumetrics was acquired in 2013, under terms more typical of a merger, by hemostasis management specialist ITC Nexus Holding Company. Together they became *Accriva Diagnostics*.

Clearly, Xagenic's investors are hoping that Still will be able to work his magic with this start-up's chip-based electrochemical sensing technology. Exit by acquisition could be a possibility, as that is the path most frequently traveled by diagnostics companies and Still has engineered such deals before, calling them the best way to expand use of product lines. But Xagenic could conceivably be one of the rare breed that becomes a powerhouse itself. Still believes the company's technology platform represents "a multi-billion-dollar opportunity."

"As a witness to the medical diagnostics industry for the past 25 years, I've seen that as better methodologies are developed, it usually makes sense to bring them out of the research lab, into the clinical lab and eventually to point-of-care," Still says. He adds that, "whenever a physician can test a patient within a 15- to 30-minute window, drug prescriptions [for that ailment] go up." While Xagenic perceives good commercial opportunity for POC testing for common infections such as influenza and Streptococcus, Still notes that "many of those already have suitable lateral-flow tests that can be done at point-of-care, so we have initially focused on more of a technical challenge."

Company co-founder Shana Kelley, now serving as chief technology officer at Xagenic, is an expert in electrochemical sensing who invented the core assay technology in her lab at the University

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Contact: Timothy I. Still, CEO

Business: Chip-based rapid diagnostics

Founded: May 2010

Founders: Shana Kelley, PhD, CTO;
Edward Sargent, PhD

Employees: 40

Financing To Date: \$Cdn35.5 million

Investors: Domain Associates; CTI Life Sciences Fund; Ontario Capital Growth Corp.; Qiagen; BDC Capital

Board Of Directors: Erik Holmlin, PhD (BioNano Genomics); Shana Kelley; Dion Madsen (BDC Venture Capital); Timothy I. Still; Shermaine Tilley, PhD (CTI Life Sciences); Jesse Treu (Domain Associates)

of Toronto. Her co-founder and husband, Edward Sargent, is also employed by the university. An electrical engineer specializing in fabrication, he devised the physical format for electrochemical sensing. Kelley says the start-up believes the chip-based tests can be cost-effectively manufactured in volume.

Xagenic calls its testing methodology Amplified Redox Assay (*AuRA*) detection. The system utilizes chip-based arrays of microelectrodes to test samples for the presence of telltale nucleic acid strands. Kelley says that the electrochemical sensors in glucose meters developed decades ago inspired her and others to investigate the possibility of detecting other analytes in a similar way. "It took a while to understand how to move past this limited application," she declares, explaining, "Nucleic acids floating in solution are big and move slowly. We figured out a way to bring a 3D sensor to them. The trick is having a large surface area to interact with the molecules."

Because Xagenic's methodology is chip-based, Kelley points out that it should be simple to "multiplex," or run multiple tests on a single chip. "We can put 20 sensors or 100 on a chip and our

cost doesn't change," she explains, "so as we grow [the menu of test offerings] we should be able to reap more [profit] margin." The format allows the company to run controls in parallel with the diagnostic test it is developing.

Disposable chip-based cartridges contain all the necessary assay reagents, and no sample extraction or preparation is needed to run the test. Unlike many molecular diagnostic tests, Xagenic's platform does not rely on PCR, the polymerase chain reaction, which uses enzymes to create many, many copies of nucleic acid sequences that become easier to detect en masse. Nor does AuRA use optical detection components to get a readout. Because there are no biological reagents in the cartridges, they can be shipped and stored without refrigeration, simplifying use for physicians' offices. The system was deliberately designed so that a person with no training can use it, Kelley says: "The user interface is very specific, very simple. It's what customers in physicians' offices want to see."

Xagenic expects its initial offering to be a 20-minute diagnostic for chlamydia and gonorrhea (CT and NG). The company is planning to take this product into clinical testing in 2015, and to launch it commercially in 2016. The key technical hurdle is the same as for all POC tests: proving that

the data this still experimental system generates are equivalent to CT/NG tests carried out in clinical laboratories.

Attaining equivalence to lab testing in a POC format is no easy matter. Maintaining that quality in batch after batch of product can be hard too. Alere Inc. is experiencing that challenge now. The *INRatio2 PT/INR Monitoring System (Professional Use)* it acquired with Hemosense was subject to a Class I recall in April 2014. This is the FDA's most serious type of recall, imposed in situations in which there is a reasonable probability that use of a product will cause serious adverse health consequences or death.

The recall was imposed after some patients' clinical condition deteriorated, and it was learned that the Alere test strip used by professionals to make a quantitative determination of internal normalized ratio (INR), and so assess the effect of warfarin on clotting time, had shown a therapeutic or near-therapeutic INR result. Re-testing performed by a central laboratory showed a significantly higher INR beyond therapeutic range. The test strip Alere markets for consumers to use at home was not recalled.

If all goes well with the testing and launch of Xagenic's POC test for CT/NG, the company expects to develop other diagnostic tests for its chip-based platform.

Still says Xagenic sees "women's health" as a promising area, and the firm has previously said it views herpes simplex virus 1 and 2 as promising for POC testing, along with trichomoniasis, HCV, and upper respiratory infections. Still notes that Xagenic's cartridge has been designed to accommodate a variety of specimen types, cell types, and targets, because the start-up hopes to be able to expand its menu of tests without major modifications to the platform.

Some 25 million tests for CT/NG are run each year in the US alone, Still points out, and the EU is also a large market. If and when Xagenic wins marketing approval for its POC test, Still predicts it will be quickly adopted. "Most physicians won't take a lot of convincing," he asserts, "because our test will have an attractive reimbursement profile, will be easy to run, and will let them quickly go from sample to answer."

To date, Xagenic has raised \$Cdn35.5 million from investors including Domain Associates, CTI Life Sciences Fund, Ontario Capital Growth Corp., Qiagen, and BDC Capital. **SU**

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- Deborah Erickson