

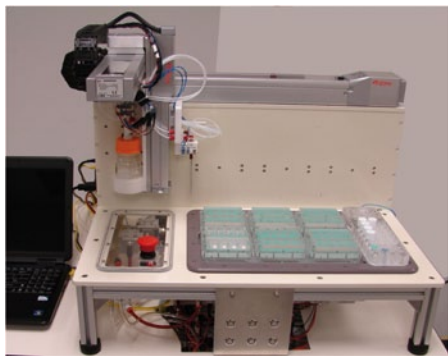
COMPANY VISION

Rheonix's novel CARD™ microfluidic technology provides an automated molecular diagnostic platform for human and veterinary in vitro diagnostics



Rheonix, Inc., a Ithaca, New York-based spin out of the microfluidic division of Kionix, Inc., has been created in Dec. 2008 and recently closed on a \$10M series A of funding.

The novel CARD™ (Chemistry And Reagent Device) microfluidic technology provides an automated diagnostic platform with applications in a broad spectrum of markets including human and veterinary in vitro diagnostics. In this interview of Greg Galvin, President & CEO, Kionix, we learn more about this technology and his thoughts about the coming years.



Rheonix CARD™ Workstation with 6 CARD™ placed on manifolds.

Yole Développement: Could you introduce Rheonix and its Microfluidics activities to our readers?

Greg Galvin: Rheonix Inc. is a medical device company focused on the in vitro diagnostic market, specifically the molecular diagnostic market. Rheonix began as a project within Kionix, Inc. in 2003 and was spun out as an independent company in December of 2008. Rheonix has built upon Kionix' deep engineering and manufacturing expertise. This know-how was leveraged against the multi-disciplinary skills of a core team of scientists made up of chemists, molecular biologists, physicists and software engineers to produce an unparalleled microfluidics diagnostic platform that is capable of processing on chip raw samples through endpoint detection without human intervention.

Rheonix introduced its platform to leading edge clinicians in a development partnership in 2008. A broad array of applications have been performed on raw clinical samples ranging from HPV and HIV detection to environmental pathogen detection (E. Coli and cryptosporidium parvum) to SNP analysis (warfarin dosing analysis). Thousands of tests have been conducted at multiple locations with a variety of operators and in each case the performance of the Rheonix CARD™ system is equal to or surpasses the appropriate gold standard.

YD: Can you elaborate on the technology and its applications?

GG: One of the primary benefits of the Rheonix CARD™ platform is the complete hands-free operation of molecular diagnosis across all of the potential applications from infectious disease detection to genotyping analysis. The CARD™

platform was designed to handle clinically relevant sample volumes, from microliters to milliliters, and a wide range of specimens. Once the raw sample is collected, it is added to the "sample reservoir" on the CARD™ and from this point on, the assay operations are conducted on CARD™ without any human intervention. For molecular diagnosis, on-CARD™ cell lysis, DNA extraction and purification, molecular amplification and multiplexed end-point detection using microarrays are performed. Unlike other platforms and equipment, Rheonix' CARD™ does not rely on highly sophisticated software to control and coordinate multiple complex and bulky workstations to complete these tasks. In fact, the disposable CARD™ and reagent cartridge are the only interchangeable components that require operator intervention. The design of the CARD™ platform is elegant in its simplicity and it has been designed so that there are no points of potential cross contamination of the tested sample(s).

Rheonix has been able to develop applications for its CARD™ platform in approximately 3 months. The team has already demonstrated with its' clinical partners the ability to deliver "sample in, results out" capabilities for the end-user, with sensitivity levels at least equivalent to gold standard. Rheonix is moving its CARD™ platform forward in 2010 as it prepares to bring a couple of molecular diagnostic applications through FDA registration process this coming year. In addition to the molecular diagnostic applications, the Rheonix team is working to partner with established businesses in the water testing, food safety and veterinary diagnosis markets for application development of its CARD™ platform.

YD: How does this technology differentiates from competition, and where does your key IP lies?

GG: The technology differentiators for the CARD™ platform are attributable to two primary features:

1. The ability to handle a vast array reagents, buffers and samples with broad spectrum of properties; and
2. The production of all functional components, including all on-CARD™ valves and pumps, as a by-product of Rheonix' proprietary solvent lamination fabrication process that is completed in ~15 seconds from an injection molded body and a thin film. Rheonix' CARD™ platform does not have discreet components that need to be integrated into a material or on a surface.

Scientists and technicians familiar with molecular test protocols understand that the reagents used for sample preparation are difficult to handle because they contain high concentrations of salt and/or are of high viscosity and/or are bubbly. Unless the on-CARD™ fluid manipulation components are capable of addressing a variety of reagent issues, the device is not functional in real world applications. A multitude of the microfluidic platforms developed in the past has been prone to these reagent handling difficulties. The CARD™ platform has both the large size fluidic channels and on-CARD™ diaphragm pumps driven by tremendous pneumatic force. The combination of these design features allows raw samples of hundreds of microliters to tens of milliliters and the requisite preparation reagents to pass through the fluidic network in a matter of seconds to minutes as opposed to other market platforms that only allow the passage of "clean" buffer after the template DNA is extracted.



Top and bottom views of the Rheonix HPV-CARD™

Rheonix' core intellectual property resides in the second differentiation factor - robust molecular diagnostic applications can be carried out on Rheonix' CARD™ products at a very low price point because the raw material costs, the costs of manufacturing and the development costs are minimal, which is necessary for wide spread use across a multitude of in-vitro diagnostic market applications. The Rheonix CARD™ is the only product made from two pieces of plastic; fabricated in seconds and delivers full molecular diagnostic functionality from raw sample to endpoint detection.

YD: Rheonix developed two products for different markets; A portable POC device and a laboratory workstation for higher throughput multiplexed analyses. These two markets require a different approach. How do you deal with that?

GG: Although these markets appear to differ in their requirements, Rheonix' underlying technology is similar across both market platforms. As described above, once fabricated, the Rheonix CARD™ becomes fully functional as a result of the control provided by the applied pneumatic forces that result

in diaphragm actuation. For the POC applications, Rheonix designs and fabricates the CARD™ with the necessary reagent reservoirs on-CARD™ in a closed system, which, with the exception of sample introduction, allows for hands-free operation. For the laboratory environment where higher throughput is necessary and desired, Rheonix developed a simple liquid handler workstation to transfer process and reaction reagents from a reagent cartridge to multiple CARDS™ on a single platform, which can then be run in parallel. This approach allows Rheonix to address both markets while keeping our technology development effort manageable.

YD: How do you see these markets evolve in the coming years?

GG: Nucleic acid-based testing is growing by double digits year over year for a multitude of good reasons. There is clinically relevant data emerging from the research community daily. As the healthcare industry continues to sag under economic pressure, tests that identify disease states before the show or very early have shown to result in less costly treatments and as such the investment in this research has continued to grow

aggressively. However, there remains a large gap between the research science and the clinical applications. Today, the FDA has approved ~19 bacterial/fungal tests, ~14 viral tests and ~18 human tests (there are multiple products/test). This represents only a handful of the potential tests and many promising molecular diagnosis areas are yet to be addressed such as early disease detection, the prognosis of disease evolution and personalized medicine that predicts a patient's response to specific therapies. The future market potential is enormous if the challenges of cost and time can be addressed. The molecular diagnostic test is typically a tedious process that requires stringent control and highly trained personnel. The introduction of the Rheonix CARD™ platform can result in the widespread commercialization of rapid, user-friendly, inexpensive and high-informative molecular diagnostic tests and the enablement of a new wave of molecular diagnostic applications.

**Frédéric Breussin, Project Manager,
Microfluidics, Yole Développement**



**Dr. Gregory J. Galvin
President and CEO, Kionix**

Dr. Galvin founded Kionix in 1993 to commercialize a novel micromechanical technology pioneered by researchers at Cornell University. From 1993 to 2000, Kionix grew from its two founders to over 40 employees and developed products in inertial sensors, microfluidics, data storage, micro-relays, and micro-optics. Late in

2000, Kionix was acquired for its optical switching technology by Calient Networks of San Jose, CA and renamed Calient Optical Components. Just prior to the acquisition, a new company was spun out to the then Kionix shareholders to pursue inertial sensor, microfluidics, and data storage markets. This company regained the Kionix name post acquisition. From the acquisition until June 2002, Dr. Galvin served as President and CEO of Calient Optical Components and on the boards of both Calient Networks and the new Kionix. In July

2002, he returned full time to Kionix as President and CEO and advanced the Company to its 2009 acquisition as a wholly-owned subsidiary by Rohm Co., Ltd. of Japan. In addition to continuing service as Kionix's President and CEO, Dr. Galvin also serves as Chairman of Rheonix, Inc., a corporate entity established in December 2008 to commercialize a unique polymer chip microfluidic technology developed by Kionix scientists.

MARKET FOCUS

Emerging markets for microfluidic applications in life Sciences and in-vitro diagnostics

Microfluidics Industry, on route to a mature market?

Yole Développement releases its new report, Emerging Market of Microfluidic Applications (EMMA) dedicated to the microfluidics applications in the diagnostic and life Sciences fields. Microfluidics has entered the Life Sciences market as a key technology to provide solution to the market requirements in terms of analysis automation, reduced analysis cost by lowering sample volume and reagents used faster analysis ... In 2014, the market of microfluidic devices will exceed \$3 billion, according to Yole Développement. Drug discovery remains the first microfluidics market, and will continue to grow significantly as well. This is particularly true for the technologies enabling multiplexing. However, the largest growth is expected in the field of Point of Care diagnostics. Microtechnologies or Microsystems technologies are considered today as a mainstream miniaturization and parallelization approaches for Life Science applications. Indeed, microsystems skills, associated materials and processes are often of great value to achieving new steps towards automation,

portability, lower response time, parallel processing of samples (Multiplexing) ...

Alliances, mergers and acquisitions allowed the organization of the Microfluidic market

The microfluidics supply chain is now structured, in particular in Europe and USA where 70% of the active players in the field of microfluidics are companies, with the other 30 % being university groups and Contract Research Organizations (CRO).

This market structuring goes together with a significant number of mergers and acquisitions. As one example, Siemens has acquired three major diagnostic companies, DPC, Bayer Diagnostics and Dade Behring and consequently has become one of the top 3 diagnostics companies. Amic, setup in 1998 as a microfluidics Fab, refocused its business in 2003 and positioned itself as a diagnostics company, has been recently acquired by Johnson & Johnson to be integrated into Ortho-Clinical Diagnostics.

The microfluidic market is still changing today. For example, some products are moving from re-search applications to the clinical diagnostics and point of care fields. This trend is limited due to:

- The relative high manufacturing costs of many microfluidic devices
- The fact that significant hurdles remain in the technology itself and its fusion into the healthcare system.

However, the microfluidic market organization really started and ensures now a profitable market for several key players. With 2009 EMMA release, Yole Développement provides to the players, keys to understanding the current and future microfluidics market. The company presents its analysis (key players, key products) and its data for the period 2009-2014. Moreover this report contains a special chapter focused on analysis of the last three years.

For more information about this report, please contact David Jourdan (jourdan@yole.fr)