SBIR·STTR America's Seed Fund

U.S. DEPARTMENT OF ENERGY | SBIR/STTR Programs Office

CLINICAL MICRO SENSORS

The story of many successful high-tech startups begins with an SBIR (or STTR) grant and evolves on a commercialization path that varies from company to company. Documenting this path is usually challenging because the SBIR grant occurs at the company's earliest stages of development, being often the only means for the company to carry out critical R&D leading to a prototype. Once the startup graduates from the seed fund stage, communication with funding Government agencies lessens and the full picture of the company's evolution and outcomes over a period of many years cannot be always reconstructed. In the case of Clinical Micro Sensors we were fortunate to get in touch with the company's former Chief Scientist, Dr. Stephen O'Connor.

FACTS

PHASE III SUCCESS
After a DOE SBIR Phase II award, Clinical Micro Sensors obtained venture capital investments, leading to an acquisition and subsequent creation of GenMark Diagnostics, a publicly traded company.

IMPACT
A unique molecular diagnostic system invented at Caltech was developed with support from DOE SBIR and is currently sold in hospitals and clinical laboratories worldwide.

DOE PROGRAM
Biological and Environmental Research (BER)

WWW.GENMARKDX.COM

Since his role with Clinical Micro Sensors Dr. O'Connor has led 16 technology startups in various high-tech sectors, including diagnostics, drug discovery, and water treatment. Dr. O'Connor gave us an account of the entire commercialization timeline for Clinical Micro Sensors (CMS for short), from the time the company was founded in 1995 as a spin-off of the California Institute of Technology (Caltech), initially operating out of a garage, to the present days. Today Clinical Micro Sensors operates as GenMark Diagnostic, a publicly traded company (NASDAQ: GNMK).

Everything started with a novel technology invented by Dr. Jon Faiz Kayyem at Caltech in 1993, which combined DNA strands and microelectronics to realize the first electronic sensor for DNA detection. At the time Clinical Micro Sensors was founded, industry and academia had just started realizing the importance of expanding medical diagnostics based on DNA for identifying both infectious and genetic diseases. A novel idea emerged that employed the immobilization of single stranded DNA (capture probe) on a surface. Detection of a target DNA sample from a patient could then be achieved by hybridization with the probe, and consequent measurement of the resulting electrochemical response.

The team led by Dr. Kayyem at CMS was able to transform this novel idea in a promising electronic sensor technology for DNA, offering unprecedented opportunities for faster and cost-effective genetic screening and detection. CMS technology employs small gold electrodes with preassembled DNA capture probes, which are deposited onto a circuit board chip equipped with a microfluidic chamber. A solution containing a target DNA complex from a patient is then pumped into the microfluidic chip, reacting with the capture probe DNA. Bonding of the complementary target DNA to the probe DNA changes the electronic properties of the complex attached to the electrode, yielding a current/voltage response that unequivocally identifies the patient DNA molecule. CMS innovative device is based on three technological breakthroughs achieved by Dr. Kayyem's team involving: 1) the bonding and assembly of DNA strands to gold electrodes, 2) the proper preparation of the patient DNA sample, and 3) the electronic engineering needed to apply voltage to the electrodes and measure the resulting signal with high sensitivity.

A significant advantage of CMS technology is that it can be easily multiplexed, allowing for simultaneous detection of several DNA strands at once. For example, if a patient wants to find the cause of a respiratory infection, the CMS device can analyze the patient's DNA for influenza, pneumonia, and any other condition resulting in a respiratory infection in a single pass. The DNA "eSensor" microchips developed by CMS are sold today by GenMark Diagnostics and regularly employed in today's healthcare industry. "It's a great feeling" says Dr. O'Connor "when I see a hospital of healthcare facility using the product we developed and helped commercialize years ago".

The commercialization path pursued by CMS can be considered a textbook example for its linearity and effectiveness, offering inspiration to any startup entrepreneur in high tech. CMS received its first round of seed funds in 1995 shortly after the company was founded through a DOE Phase I SBIR followed by a Phase II award. The Phase I brought a stamp of approval that helped secure some Venture Capital (VC) investments. More substantial VC funds came after the Phase II. A couple of years later, CMS received two additional Federal grants, one from the Defense Advanced Research Projects Agency (DARPA), and a subsequent one from the Department of Commerce through the Advanced Technology Program (ATP).

Having raised private capital during multiple entrepreneurial efforts, Dr. O'Connor is familiar with many types of investors and their due diligence process. He recognizes that an SBIR or STTR grant is a great seal of approval for investors due to at least three reasons. Most importantly, an SBIR/STTR grant provides outside technical validation through a competitive scientific peer review. Federal grants are also viewed favorably as a form of non-diluted financing which brings leverage to investors. Finally, DOE, like other Federal agencies with

SBIR/STTR programs, selects projects based on a professional evaluation of their commercialization potential in addition to their technical merit, which offers more assurance to an investor.

However, an SBIR grant alone will not yield a private investment unless other factors are present. Besides a positive evaluation of the market size, having a good team with a sound scientific background and some business experience is a key factor, especially when it comes to communicate technical aspects to a business audience. The presence of intellectual property is also important, especially for companies developing hardware and devices in general. In the case of CMS, the company had not generated any product sales at the time it received VC capital. Sales came only several years later, which is often the case for companies developing drugs or medical diagnostics, for which FDA approval is required.

According to Dr. O'Connor, because the number and type of investors grew in recent years, being located in California or the Boston area is no longer an essential factor for raising private capital. "When it comes to target the right investor" explains Dr. O'Connor, "it is helpful to know that VCs prefer teams that include an entrepreneur with previous commercialization experience. If this is not the case, Angel investors are a preferable choice." Alternatively, there are many foundations that provide financial support for technologies that are closely tied to a specific cause, whether this is finding a cure for cancer or an environmental cause. Because the number of high-tech entrepreneurs has also increased in recent years as compared to the 90s, convincing investors remains challenging, and any startup needs to be prepared to pitch its proposition to multiple investors before closing a deal. Nevertheless, Dr. O'Connor is of the opinion that if a company has a good idea and a good team, private investors can be found in any technical field.

In the year 2000, CMS was acquired for $320M by the Life Science Division of Motorola, which had been until then a strategic partner of CMS. The acquisition was critical for moving the DNA eSensor technology to the final stage and finally launching a product. Later on, when Motorola management made the decision to exit the bioarray research market as part of its restructuring, the former CMS went through a few changes in strategy and leadership, briefly operating as Osmetech and soon after as GenMark Diagnostics. Dr. Kayyem became actively involved again in 2009, returning as an investor and then as CEO. Dr. Kayyem currently serves as strategic advisor to GenMark management and board. Sales of products and revenues resulting from the eSensor technology developed by CMS begun with GenMark, a reminder that many great commercialization successes we see in the market today required many years of development and great commitment from all the stakeholders involved to mature.

Written By Claudia Cantoni, Commercialization Program Manager, DOE SBIR/STTR, July 2019.