Stanford Technology Brainstorm

THE NEWSLETTER OF STANFORD UNIVERSITY'S **OFFICE OF TECHNOLOGY LICENSING (OTL)**

VOLUME 12, NUMBER 3
Fall 2006

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IF = Inside Flap
OF = Outside Flap

Taking Stock of Equity

Stanford's OTL was founded 36 years ago and has been working with start-ups about as long. Stanford is surrounded by a host of fledgling companies, all striving to become the next Hewlett Packard, Genentech or Intel, along with a large infrastructure to support them - venture capital firms, seasoned executives, and law firms experienced with start-ups. Add innovative scientists and enthusiastic entrepreneurs from Stanford to the mix, and the possibility of creating groundbreaking products grows even larger. How the start-ups are established runs the gamut from eager doctoral students to well-connected professors to technology-savvy business people.

Stanford takes a hands-off approach to its start-ups, in part due to the plethora of local resources available to the new companies. If the founders need introductions to venture capitalists or law firms, OTL can provide these connections. But it does not go much further than providing a good license agreement for the technology that will form the basis of the company.

OTL understands that start-ups are accountable to other entities in their growth and development. Likewise, OTL has its constituents to consider, including inventors, administrators, and the U.S. government. The license agreement includes provisions that address and/or benefit these constituents. OTL's relationship with the company is key for all parties to succeed, and OTL's policies enable it to be fairly flexible, while maintaining Stanford's goals of research and education as the primary focus.

> "When negotiating the license agreement, equity, upfront, milestone, earned royalty and other cash payments are all a *balancing act.* Each negotiation with a company is unique and requires different considerations to promote that particular company and Stanford technology."

Beginning Negotiations

When negotiating with a start-up company, OTL often steps into their shoes. What does the start-up have? Where does it want to go? What does the start-up need to get there? If Stanford's technology can contribute to the company's potential success, and OTL believes the company can bring the technology to the marketplace, OTL will begin negotiating a license agreement. Since cash is normally scarce for start-ups, equity is one of the components OTL considers when formulating the structure of a deal.

Once a license is in negotiations, OTL will typically backload the cash terms of the agreement, putting a larger portion of the upfront due after financing. However, OTL does consider some amount of upfront payment essential. Cash poor start-ups still need to have the wherewithal to pull together some modest amount (usually around $5,000 to $25,000) to secure IP rights to ensure that the company is serious about the license. As with most academic institutions, OTL understands the need to wait until the company is getting value from the technology before the University can realize its value.

When negotiating the license agreement, equity, upfront, milestone, earned royalty and other cash payments are all a balancing act. Each negotiation with a company is unique and requires different considerations to promote that particular company and Stanford technology.

An important aspect of most licensing deals with universities is that the technologies are often very early stage. For biotechnology inventions, Stanford typically has early stage technologies available to license, with only in vitro data, or in conjunction with very little in vivo data. Therefore, a start-up company based on a licensed therapeutic compound must complete preclinical and clinical studies before a product is commercialized. In medical devices, technologies from

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STANFORD UNIVERSITY

STANFORD TECHNOLOGY *BRAINSTORM*

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Stanford Technology BRAINSTORM is published to provide information about OTL and general information of interest to the licensing community, both within and outside Stanford.

OTL's services are available to any Stanford faculty, students, or staff who invent technologies which may benefit the public or be of commercial value.

To learn about a specific technology or to disclose one of your own, contact us by any of the above means.

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Stanford are sometimes more advanced, but may have not been tested in animals or humans before they are licensed to industry. High technology inventions disclosed to OTL often span a wide range of development stages – from the theoretical to the product-ready, although most of the technologies are years away from implementation into a product.

Equity Considerations

Since the cash in a license is usually backloaded, OTL will often ask for equity in the start-up company. This is compensation for the risk OTL is taking, but it is also because OTL believes in the company. Although exact amounts of equity taken by Stanford vary, normally it will not acquire more than a 5% equity stake in a start-up and OTL will ordinarily maintain its equity percentage through Series A financing.

One area of special concern for Stanford and most universities is conflict of interest (COI). If the inventor is involved in the company, the COI review and potential for clinical trials at Stanford may both weigh in as factors when assessing the likelihood of Stanford realizing value from the equity. Under Stanford policy, it cannot hold equity in companies conducting clinical trials at the University. Therefore, even though Stanford may have received equity in a company that eventually has an initial public offering (IPO), Stanford may have had to divest of its equity earlier due to a clinical trial being held at Stanford. OTL's license agreements must include provisions for companies to repurchase Stanford's equity for fair market value before the company begins any clinical trial at Stanford.

The current University policy is to cash out equity upon the first liquidation event, which is often at the IPO. Stanford is aware that it is not likely to receive the maximum value that the equity may eventually hold. Although Stanford has realized a good return on a few equity liquidations, there are many others where it could possibly have realized a greater financial gain if Stanford's policies towards liquidation were different. For these reasons, when equity is a component of negotiations, OTL makes it clear to the other party that it does not value it as greatly as others may.

When negotiating the amount of equity, often the biggest hurdle comes when OTL faces the venture capitalists (VCs) who will be funding the start-up. Their perception of the value of the equity is going to be based on a different perspective than Stanford's. OTL feels that the equity is partial compensation for the lower upfront cash payment, but OTL and VCs valuations can be vastly different.

> "...OTL must have a good relationship with the company to help enable it to create the products based on Stanford technologies. Many of the start-ups founded on Stanford technologies often return to Stanford for licenses to further technologies."

Once Stanford's equity is liquidated, OTL receives a portion of the funds, but the majority is applied to the OTL Research and Graduate Fellowship Fund, which benefits the Stanford community at large.

History and Return

OTL took equity in a company for the first time in 1970. However, for a period in the 1980s, Stanford's policies prohibited taking equity in faculty-associated companies. Therefore, OTL had very few equity acquisitions prior to 1989. The prohibition was lifted after many COI policies were implemented, resulting in an increased number of equity stakes in companies. As shown in the graph on page 4, these numbers grew throughout the 1990s and then started to drop in 2001. OTL believes that the number of start-ups it licenses, and therefore the number of companies it takes equity in, correlates with the ups and downs of the national economy.

In total, between 1989 and 2005, OTL has taken equity in 145 companies through licensing. Of those, 75 of the equity stakes were taken for biotechnology or medical device (biotech/MD) companies, compared to 70 in non-biotechology companies. A partial list of the names of companies OTL has taken equity in as at http://otl.stanford.edu/about/resources/equity.html.

Although OTL has taken equity in slightly more biotechnology companies, there have been fewer liquidation events than in the physical sciences/high technology. Additionally, the life sciences have a much lower average liquidation amount compared to the physical science companies. Not a single liquidation in the biotech/MD

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Start-Up Sampler

Meet a few new companies developing Stanford technology

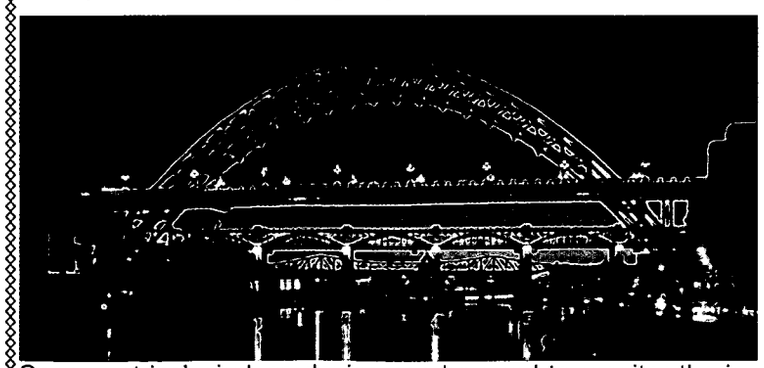
Sensametrics:"Health" of Structures

Wireless technology has changed our ability to monitor many different conditions, including human health. This approach can also be applied to monitoring the "health" of structures such as bridges, buildings, and plants - with the aim of identifying structural weakening before it can lead to tragic consequences like those that occurred at the De Gaulle Airport in Paris, the Alaskan Pipeline, the levees in New Orleans, and even the Big Dig in Boston.

All structures undergo changes over time. Actively tracking those changes can be useful for scheduling preventative maintenance or to prepare for a structural failure. Additionally, it is important to measure the integrity of structures after catastrophic events such as earthquakes, hurricanes, or blasts. Sensametrics, a Palo Alto company founded in 2002, is developing a wireless monitoring device to monitor structural health. The product is based on a wireless network of sensors developed at Stanford. These sensors send information to a base station that processes the data and forwards the analysis to a central location.

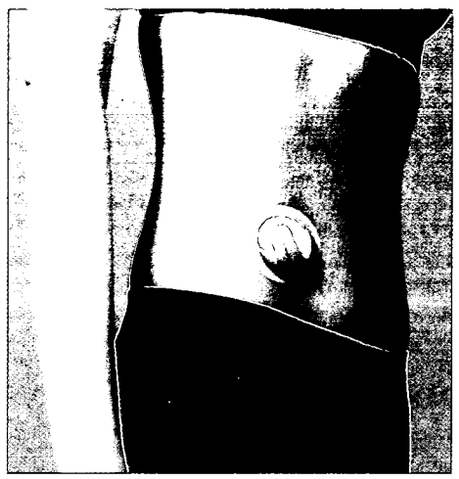
The National Institute of Standards and Technology recognized the utility of the Sensametrics product in 2004 when it awarded the company a $2 million Advanced Technology Program Grant to further develop the invention. Sensametrics is now looking for additional funding to help propel the company forward.

Sensametrics is planning to install their monitoring device on a bridge in California within one year. This will provide information for optimizing the product and a platform to validate the technology. Sensametrics believes they will have a product ready for commercial use in a year and within five years they hope to be a major provider for structure monitoring throughout the United States. Ultimately, as our buildings and national infrastructure age, this technology could help save money and lives by helping to prevent structural failures.



Sensametrics' wireless device can be used to monitor the integrity of all types of structures, including bridges.

StrataGent Delivers



Above is an artist's rendering of the Stratagent patch device positioned to deliver its drug payload.

What is tinier than a matchbox and can be programmed to deliver specified doses of any drug across the skin as fast as an injection but without pain?

The answer is StrataGent Life Sciences, Inc.'s new patch device that can be worn for days at a time to painlessly deliver drugs. Based on pulsed liquid microjet technology invented at Stanford, the device creates small, high-speed jets of liquid that penetrate the outer layer of the skin and precisely deposit drugs into the epidermis (the top layer of skin), enabling rapid absorption by the body, while avoiding the pain receptors that lie below in the dermis. This means that the device delivers drugs as effectively as an injection, but without needles.

The original microjet developed at Stanford required a desktop box that was the size of a DVD player. StrataGent has been working hard for over two years to miniaturize it into a wearable, light, discreet patch. They have also been working on features like the ability to program the patch to deliver drugs according to different schedules. Depending on the disease, large doses can be given intermittently, or small amounts of drug can be given continually. Patient controlled on-demand dosing and sensor driven dosing are also possible.

StrataGent Life Sciences, based in the San Jose BioCenter, is the recipient of an Advanced Technology Program award, a competitive award granted by the federal government, which has funded much of its technology development and testing. Extensive animal testing has demonstrated that the device successfully delivers its drug payload systemically, including injectable macromolecules (such as peptides or proteins), with onset comparable to a standard injection, and without skin irritation.

The next step for the company is to initiate clinical trials. The company plans to use the device to deliver generic or in-licensed drugs, or to partner and co-develop therapies with drug companies. They already have their first partner, a leading Japanese pharmaceutical company, that is funding new studies. StrataGent is currently looking for funding to conduct its first clinical studies.

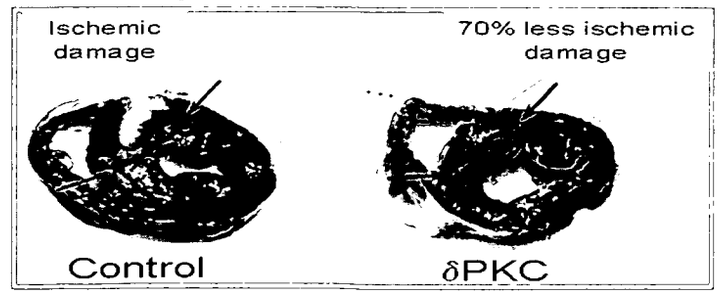
KAI Pharmaceuticals: No Nonsense

"No" is something that KAI Pharmaceuticals' founders (Daria Mochly-Rosen and Leon Chen) heard more times than they could count three years ago while they were raising the initial funding for the company. In fact, they discovered that potential investors were not shy about telling these entrepreneurs exactly what they hated and loved about KAI's technology – a portfolio of drug candidates with applications for treating cardiovascular disease, stroke, pain, and drug addiction. But KAI's founders were undeterred. They were determined to see these drugs, which had already shown promising results in pig hearts, start down the path to becoming human therapies.

After all, it was the "no's" that led them to forming a new company in the first place. Basic research over ten years in Mochly-Rosen's lab at Stanford had resulted in the discovery of a series of molecules that work by selectively targeting a family of proteins called Protein Kinase C (PKC). Originally, OTL and Mochly-Rosen hoped to license the technology to an existing company for drug development. However, these companies had tried and failed to make PKC-targeting drugs in the past. They could not be convinced that the novel set of drug candidates from Stanford were able to zero-in on individual PKC family members and avoid the unwanted side effects that caused problems with previous drug candidates.

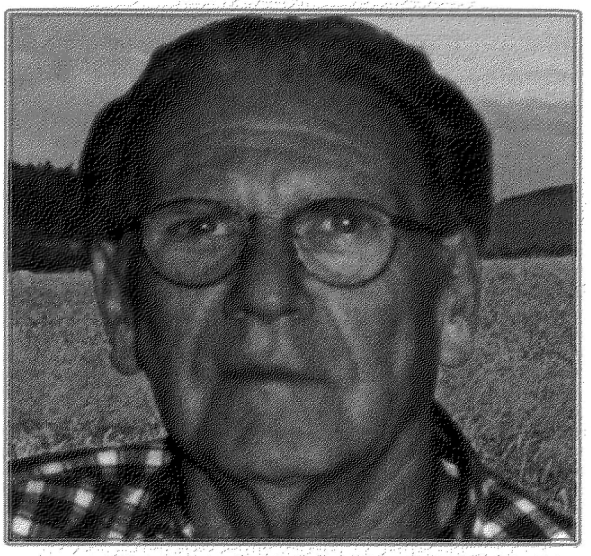
At this point it became apparent to Mochly-Rosen and Chen that the best chance for commercializing the technology was through a new venture. So they reluctantly became entrepreneurs. KAI (which is an acronym for Kinase Activators and Inhibitors) eventually found investors who said yes. With that initial round of financing, the founders accomplished their objective of getting a lead product (DELTAMI) into patients in a clinical trial. Mochly-Rosen credits OTL for its role in making this goal a reality by ensuring that Stanford had the intellectual property protection necessary to provide incentive for undertaking such a costly endeavor.

In the past year KAI Pharmaceuticals completed a Phase IIA drug trial for DELTAMI to treat reperfusion injury after heart attacks. It also closed on its second round of funding (for $35 million) and formed an alliance with a large pharmaceutical company. In addition, there are more candidates in the pipeline. The company is planning to begin clinical trials on its second drug candidate by the end of the year. Now KAI does not hear "no" quite so often.



The Elevator Pitch: To demonstrate the effectiveness of the KAI technology, the company's founders would show the above pictures to potential investors. They illustrate that, following a heart attack, a pig's heart treated with a PKC-targeting drug (right) has 70% less injury than the untreated heart on the left.

In Memoriam - Floyd Grolle



In April of this year, the Office of Technology Licensing (OTL) lost a dear friend, Floyd Grolle. Floyd spent 17 of his 25 Stanford years at OTL, leaving behind a remarkable legacy and lasting impression to those who had the good fortune to work with him. Floyd joined OTL in 1982, and in addition to many other functions, he held the position of Manager of License Administration for Stanford and UC's Recombinant DNA Cloning Technology until his retirement in 1999. Floyd's amazing DNA notes and records are still referred to at OTL today.

Floyd grew up on his family's farm in Perrysburg, Ohio before he went on to obtain many degrees, including a Master's in Pharmaceutical Chemistry, a Master's in Market Research and a Ph.D. in Marketing Management Pharmacy from the University of Michigan. Floyd worked in an executive role at many companies, including Upjohn, Becton Dickinson, G.D. Searle, and SRI International before joining Stanford. While his diverse education and experience were impressive, Floyd's personality and manner are most memorable to those who knew him.

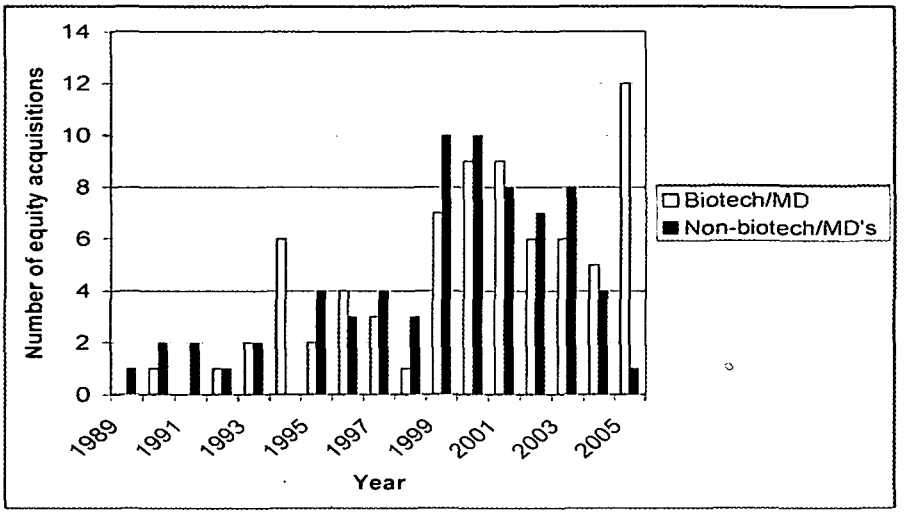
Known for what Kathy Ku, Director of OTL, terms as "Floyd-isms," Floyd could be heard saying "Today is another day to excel" on most days. He always came to work with a wonderful sense of humor and was completely dedicated to the good of the office. Kathy remembers Floyd finding someone he knew whenever he traveled and labeled him the personification of someone with six degrees of separation from everyone else.

Floyd's custom carpentry and craftwork live on at the OTL office. Sally Hines, Administrative Services Manager, remembers that if you mentioned something you needed one day, it would magically appear on your desk the next. From the quilted baby blanket Floyd knitted for Kathy's daughter to Christmas reindeer, wine corkers, children's rockers, and silk scarves – all are part of a beautiful collection of Floyd's works of art that have a presence in the OTL office today.

Floyd will be dearly missed by OTL, but he has left many memories that will not be soon forgotten.

Stanford Equity Acquisitions 1989 - 2005

This graph shows the total number of Biotechnology and Medical Device equity acquisitions vs. Non-biotechnology and non-medical device (usually high technology) equity acquisitions per year since 1989. OTL believes the number of companies it takes equity in correlates with the ups and downs of the national economy.



Equity... **continued from page 2**

sector has generated over $1 million for OTL, whereas five liquidations in the high technology sector have generated over $1 million.

Some possible reasons why the average liquidation amounts are lower in biotechnology/medical devices include:

- Less equity is taken in biotech/MD companies due to higher cash upfronts or other future payments
- Biotech/MD companies have an IPO or another liquidation event at an earlier stage in their product development
- If a company initiates clinical trials at Stanford, Stanford must liquidate its equity before the trials begin to avoid conflicts of interest
- In the physical sciences/high tech, there have been a few very "big hits," whereas in biotech/MD there have been none thus far

New company formation is a gamble, as is each technology licensed and any path chosen to develop that technology. Likewise, taking equity is a risk, and one that OTL does not rely on for its income and budget projections. For Stanford, equity is one of the license term components it considers, but it does not depend on equity alone for its revenue streams. Although Stanford does not seek maximization of its equity value, it considers a liquidation event a success since the liquidation event represents another party's belief in the company and its technologies.

OTL relies on licensed companies to develop and eventually sell products. In order for this to happen, OTL must have a good relationship with the company to help enable it to create the products based on Stanford technologies. One indication of the strength of the relationships is that many of the start-ups founded on Stanford technologies often return to Stanford for licenses to further technologies.

This article is adapted from an article by Kirsten Leute, published in the *Journal of Commercial Biotechnology*, 2005; Vol II, No. 4:318-324.

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