Stanford’s licensing and equity practices with biotechnology companies

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INTRODUCTION

Stanford’s Office of Technology Licensing (OTL) was founded 36 years ago and has been working with start-ups just about as long. Situated in Silicon Valley, Stanford is surrounded by large existing companies, venture capital firms, experienced executives and a host of fledgling companies, all striving to become the next Hewlett-Packard, Genentech or Intel. Add innovative scientists and enthusiastic entrepreneurs from Stanford to the mix, and the possibilities for creating ground-breaking products grow even larger.

Two early examples of Stanford-associated biotechnology start-ups are Syenex and T Cell Sciences. In the past few years, Stanford-associated start-ups included Kai Pharmaceuticals, Bayhill Therapeutics and Cellerant. How the start-ups are first established runs the gamut—from eager doctoral students to well-connected professors to local businesspeople looking for the next great idea.

Stanford takes a fairly hands-off approach on its start-ups, which is able to do in part because of the plethora of local resources available to the new companies. If the founders need introductions to venture capitalists, OTL can provide these connections, but does not go much further in helping the company other than providing a good licence agreement for their intellectual property on which they want to base the company. OTL understands that start-ups have many other entities to account to in their growth and development process. OTL also has constituents to consider, including inventors, administrators and the US Government, and the licence agreement includes provisions for policies and general practices that address and/or benefit those constituents. OTL’s relationship with the company is key for all parties to succeed, and OTL’s practices and policies enable it to be fairly flexible, although Stanford’s goals of research and education are primary factors. These goals may also be enhanced by the opportunities working with industry may provide.

BEGINNING NEGOTIATIONS

When negotiating with a start-up company, OTL often steps into their show. 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 negotiate a licence agreement. Equity is one of the components OTL considers when formulating the structure of a deal with a start-up company.

When licensing a Stanford-owned technology, OTL is willing to consider an option agreement with a start-up, which would not necessarily entail equity. If the company decides to exercise the option, then equity would normally be a part of the consideration. Companies, including start-ups, sometimes ask to negotiate the financial terms of the licence and include them in an option agreement. If this is the case, OTL prefers to go straight to the licence and skip executing an option agreement as the purpose of the option is to give the company some time to evaluate the technology and make business decisions based on that evaluation.

With a full licence with a start-up company in negotiations, OTL will back licence the asset for as far as the cash terms are considered, putting a larger portion of the upfront due after financing, but OTL considers some amount of upfront cash essential. Cash poor start-ups still need to have the wherewithal to push together some modest amount ($US5,000–25,000) to secure intellectual property (IP) rights to ensure that the company is serious about the licence option. As with most universities, OTL understands the need to wait until the company is getting some value from the technology before Stanford can realise value.

An important aspect to remember about most licensing deals with universities is that the technologies are often very early stage. For biotechnology inventions, Stanford usually only has early-stage technologies with only in silico data, or very little in vivo data, available to licence. Therefore, a start-up company based on potential therapeutic licensed from a university still must often get through preclinical and clinical studies before a product is commercialised. In medical devices, the technologies from Stanford are sometimes more advanced and may have already been tested in animals or even in humans when they are licensed to industry.

EQUITY CONSIDERATIONS

Since the licence will be backloaded, OTL will also ask for equity in the company in order to be compensated for the risk it is taking, but also because OTL believes in the company. Stanford has the potential of significant gain if the company does well. The equity component is an unknown value to Stanford or, in most cases, a zero or very small value. The statistics presented later in this paper show a comparison on return on equity for biotechnology versus all of OTL’s other technologies. Although exact amounts of equity taken by Stanford are not discussed here, Stanford will normally not take more than a 5 per cent equity stake in a start-up. OTL will ordinarily maintain its equity percentage through Series A financing.

When negotiating the amount of equity, 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 from Stanford’s. OTL feels that the equity is partial compensation for the lower upfront cash payment, but OTL and the VCs’ valuations can be vastly different. If the investor is involved in the company, the conflict of interest review (if discussed) and potential for clinical trials at Stanford may be weighed in as factors in assessing potential likelihood of Stanford realising value from the equity.

In the case of clinical trials, under Stanford policy, Stanford cannot hold any equity in companies conducting clinical trials at Stanford. 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 because of a clinical trial being held at Stanford. Under OTL's licensing agreements, companies must agree to repurchase Stanford's equity in the company for fair market value before the company begins any clinical trial at Stanford.

The current policy is to cash out the equity upon first possible liquidation event, which is often at the IPO, or as soon after as is legally possible as a sale may be delayed to certain restrictions on the equity. Therefore, and excuse the pun, OTL does not hold much stock in publicly held equity. Stanford is aware that it will probably not receive the maximum benefit the equity may 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 a different liquidation strategy had been employed. This is one of the important points OTL makes in its negotiations when equity is a component so the other party knows that OTL is not relying on or valorizing it as greatly as others may.

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. This fund benefits graduate students, research and the Stanford community at large.

**EARNED ROYALTIES, ANNUAL MINIMA AND MILESTONE PAYMENTS**

OTL also fully expects and negotiates for earned royalties based on the net sales of products sold by the company. OTL has generally taken the stance that start-ups should pay a higher earned royalty rate than a large company if the start-up paid little cash upfront. Start-ups find this difficult to swallow, though, because they and the VCs are worried that a larger earned royalty rate could make them uncompetitive. Instead they argue that our equity should make up the difference. However:

- OTL's earned royalty rates are quite low in general, both for start-ups and large companies;
- start-ups often return to OTL and ask to renegotiate earned royalty rates, an option OTL would not have with the company if the rate were too low;
- equity is very risky;
- Stanford's liquidation policy (sell upon first liquidation event) does not allow for maximization of the equity return.

If an earned royalty rate that a company has already negotiated and finalized with Stanford in its licence agreement is causing financial issues for the company, OTL works with the company to find a solution. Since 2001, OTL has renegotiated numerous licence agreements with Stanford-associate start-ups as their development and financial expectations and other factors have all been affected by the change in the investing environment and the general economy. Although Stanford does not publish the earned royalty rates it asks of companies, Edwards et al. provide examples of earned royalty rates as well as other royalties received by universities in licensing deals from 1987 to 2003. Earned royalties in such deals averaged between 3.9 and 5.1 per cent of net sales.

Especially in biotechnology, it often takes a long time, if ever, for a licensed company to pay an earned royalty to a university. Therefore OTL also typically requests two other types of payments in its licence agreements, annual minima and milestone payments. The annual minimum is an amount that is due each year from the licensing company. In part it is seen as an indication of diligence (companies usually will not pay for technologies they are not developing into products), but it is also normally credited towards earned royalties, therefore maximizing the "minimum" amount due each year from product sales.

**The combination of payments made under a licence agreement are a balancing act**

Milestone payments are very common in start-up licences as well since the start-ups are often cash-poor in their first years of life. The milestone payments can be due at certain dates (eg five years after signing) or when certain achievements are reached, such as a certain amount of financing, development of a prototype, initiation of stages of clinical trials or issuance of a patent. For milestone payments need to fit the technology and the company's development plan and should mirror some of the developmental diligence milestones that are also included in the agreement. The milestone payments reflect that as the value of the technology increases, Stanford shares in the benefit, especially in the case of a start-up company that did not have the resources earlier to compensate Stanford for the licence.

Equity, upfront, 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.

**INVENTOR ROLES AND CONFLICTS**

At Stanford, the relationship between faculty and other inventors with industry is an important connection. It is not uncommon for the inventor to be their own industry contact, in a sense, by involvement in a start-up. The technical expertise of the inventor is prized in the development of their own invention, if it can be paired with the proper business acumen. OTL's history of working with Stanford inventors and inventions and how equity factors into its licences in the biotechnology area illustrate the necessity to be flexible in finding value in early-stage technology in exchange for allowing a group of entrepreneurial individuals the opportunity to get a developed and disseminated to those that can benefit from it. Part of the financial value can then be brought back to the university to further its mission of research and education.

If a faculty member is going to be involved in a start-up company that is licensing the faculty's invention, a conflict of interest review is required. Under conflict of interest review at Stanford, the OTL associate handles the conflict of interest memo outlining the background of the technology and potential license, the other contacts with companies and their responses, the justification for choosing the inventor-associated company as the partner, and an outline of the general licensing deal. This memo, along with a memo from the faculty member associated with the company, is reviewed by two Deans well versed in Stanford policies. In order to proceed with a licence agreement to the start-up, the Deans must provide approval of the licence, often after discussing the company, licence and faculty's research with both OTL and the faculty member. The approval includes a memo to the faculty member outlining the procedures he or she must follow in order to ensure there is no conflict between his or her ongoing primary appointment at Stanford and his relationship with the licensing company.

One of the issues often addressed in the conflict of interest review is the faculty's involvement with the company. Under Stanford's policy for consulting, faculty may spend 13 days per quarter working with outside entities, although they are not allowed to have a line management role at the companies. Many faculty members take advantage of the ability to work with companies in order to expand their knowledge of research and development taking place in industry. When Stanford receives equity through a licence agreement, the inventor of the licensed technology also receive a share of the equity. Unlike some other universities, OTL requests that the start-up company issue the inventor's stock directly to the inventors once the licence is signed. The inventors have control over their equity and can liquidate it at their option. Therefore they are not subject to Stanford equity liquidation policy.
MEASURING (EQUITY) SUCCESS

In order to examine the success of Stanford-associated biotechnology start-ups, the authors pulled the existing equity data from the OTL database. The first company Stanford’s OTL took equity in was in 1970, but there were only a few equity acquisitions prior to 1980. For a period in the 1980s, Stanford’s policies prohibited taking equity in a faculty-associated company based on a concern that it would be in its business with its faculty. Once this prohibition was lifted, equity stakes in companies increased throughout the 1990s, then started dropping in 2001, as exemplified in Figure 1. This correlates with findings from Bouche that although university licensing continued increasing in the 2001–2005, the number of start-ups licensed decreased between 2001 and 2003. Of the total number of companies Stanford has taken equity in through licences, slightly less than half are biotechnology/medical device companies.

Only a few of the biotechnology companies in which Stanford has taken equity in have failed, however few currently have products available for sale.

![Figure 1: Biotechnology and medical device equity acquisitions v. non-biotechnology and non-medical device equity acquisitions per year since 1989](image)

**Table 1: A comparison between Stanford’s biotechnology/medical device and physical sciences equity liquidation events**

<table>
<thead>
<tr>
<th>Number of companies with liquidation events</th>
<th>Total monies from liquidated equity (US$)</th>
<th>Average liquidation amount (US$)</th>
<th>Median liquidation amount (US$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biotechnology/medical device</td>
<td>18</td>
<td>1,944,635</td>
<td>106,157</td>
</tr>
<tr>
<td>Non-biotechnology/medical device</td>
<td>14</td>
<td>20,888,249*</td>
<td>1,492,017</td>
</tr>
<tr>
<td>All technologies</td>
<td>22</td>
<td>22,833,884</td>
<td>732,956</td>
</tr>
</tbody>
</table>

*Google equity liquidation not included as it was unknown as of 28th April, 2005.

non-biotech/MD are significantly different from the average, and, as can be gauged, are due to some liquidations that are orders of magnitude larger than the median amounts. The median for all companies would be quite lower if the number of failed companies was also included in the statistics.

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

- less equity is taken due to higher cash upfronts or other future payments;
- companies have an IPO or another liquidation event at an earlier stage in their product development;
- if the company initiates clinical trials at Stanford, Stanford must liquidate its equity before the trials begin to avoid conflicts of interest;
- in the physical sciences, there have been a couple of very ‘big hits’, whereas in biotech/MD there have been none thus far.

None of these reasons have been verified yet by in-depth analysis.

Notably, of the 63 biotech/MD companies that Stanford has taken an equity stake in, only 6 (10 per cent) thus far have failed (are no longer existing and never had a liquidation event). Considering that 18 of the 63 (28.6 per cent) have had liquidation events, it is very pleasing that so many companies have made it to later and later stages of their business. However, OTL’s main mission is to have companies develop products that are beneficial to the public. Few of the Stanford-associated biotech/MD start-ups that OTL has equity in have actually sold product based on the technologies licensed from Stanford, in part due to the long research, development and approval processes associated with many of the technologies since, as mentioned previously, the technologies licensed from a university are often at a very early stage in development when the company takes them on.

More than 60 per cent of the biotech/MD companies Stanford’s OTL has taken equity in so far still exist, but have not yet had a liquidation event. A partial list of the names of companies OTL has taken equity in is given at the university website.

**SHORT CASE STUDY**

One somewhat typical biotechnology company in which Stanford took equity began when a couple of the inventors decided to start a company after no other companies expressed an interest in licensing and developing the technology. In this particular case, the start-up first took an option to the technology, which was subsequently converted to a full exclusive licence. Since the inventors starting the company had left Stanford, a conflict of interest review was not necessary.

As part of the consideration of the exclusive licence, Stanford received some shares of stock in the company, but the licence also contains an upfront payment, milestone payments, annual minimum,
earned royalties and sublicensing payments. All investors, including the inventor-founders of the company, received a portion of the equity from the licence agreement. As with many companies, the start-up reneged with Stanford some pieces of their licence owing to certain situations that arose. The company had their IPO and, after the lock-up period was over, Stanford sold its equity as soon as possible, per the equity liquidation policy noted earlier in the paper. Although the company does not have a product out yet, the company is still in existence, developing the licensed technology and working hard to get out a product that will benefit people.

**WHAT DOES ALL OF THIS MEAN?**
For Stanford, equity is one of the licence term components it considers, but it does not depend on equity alone for its revenue streams. Other universities have very different philosophies and policies. Since 1999, only six (less than 10 per cent) of the biotech/MD companies Stanford has taken equity have folded, whereas 28 per cent have had liquidation events. Considering the majority of biotech/MD companies Stanford has equity in are less than 10 years old and the average date between acquisition and liquidation is 5.4 years, Stanford will probably have many more successes in its current biotech/MD equity holdings. This may include a 'big hit' such as the larger returns Stanford has seen on the physical sciences side. Although Stanford does not seek maximisation of its equity revenue, it considers a liquidation event a success since the liquidation event represents other parties' belief in the company and its technologies.

Start-ups are a gamble, as is a technology that is licensed and any path chosen to develop that technology. Equity is a risk as well, and one that Stanford's OTL does not rely on. What does OTL rely on? The company it licenses developing and eventually selling 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. Many of the start-ups founded on Stanford technologies often return to Stanford for licences to further technologies.

**Acknowledgements**
Many thanks to Mary Watanabe and Katherine Kuo of Stanford's Office of Technology Licensing for their advice and encouragement.

**References**
5. URL: http://otl.stanford.edu/about/resources/equity.html

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**How DanioLabs has evolved its relationship with the CIMR**

Paul Goldsmith

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Abstract

The commonest interaction of industry with academia is as the passive recipient of intellectual property: A much deeper and productive interaction is possible with the creation of closely linked collaborations. Here the barriers to achieving this and how they may be overcome are explored.

**INTRODUCTION**

The majority of universities encourage the formation of spin-out companies. These spring forth from some, at least when the funding environment allows. One would therefore expect a close relationship to exist between emerging companies and universities, and by implication, academic scientists within the university. After the initial spin-out, further technology assets may need to be acquired and licensed from the university by the company. This relationship is often managed through the Technology Transfer Office (TTO).

One of the more complex relationships to manage between the spin-out company and the university is the one that involves any long-term collaborative agreement. These projects need to be aligned to ensure that any such collaboration is successful: the academic scientist, the TTO and the company, each likely to have a different view on the nature of the relationship and its measure of success. It is therefore not surprising that these relationships, if not carefully crafted and managed, can be fraught with difficulty. Consider for example what such parties want from such an agreement: the scientist often wants his/her work to be acknowledged as world-leading, to generate scientific publications and kudos; the TTO, wanting to ensure that some of the value is returned to the university; while the company, the need to own and protect any intellectual property, and ultimately to increase value to their shareholders.

The UK Government is keen to encourage productive technology transfer relationships through schemes such as the LINK and KTP (Knowledge Transfer Partnerships), but the dynamics still exist between the 'competing' parties. Key to a successful relationship, like all relationships, is the give and take in negotiations, a clear understanding of outcome, and an open and honest dialogue through the complete process, from initial discussions to completion of the last experiment and subsequent licensing agreements.

**COMPANY BACKGROUND**

DanioLabs is a therapeutics company that was founded in 2002 as a spin-out of the Department of Anatomy, University of Cambridge, following the completion of one of the founder's PhD. The university is an investor, and with previous representation on the Board, has always had a strong link with the company. The other initial investor was the Wellcome Trust, which was keen to encourage and facilitate interaction with universities in general.

A key part of DanioLabs’ approach to drug discovery and development is the use of zebrafish to identify in vivo activities through the creation of validated disease models. Zebrafish are surprisingly amenable to disease modelling in larval form as they are tiny, transparent vertebrates that have