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# Stanford's licensing and equity practices with biotechnology companies

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## Abstract

Stanford University's Office of Technology Licensing (OTL) has a long history of licensing technologies to biotechnology start-up companies. This paper presents (1) examples of how the OTL works with biotechnology start-ups to negotiate licence agreements for Stanford-owned intellectual property, taking into account a new company's scarce financial resources and needs but their large intellectual property appetite; and (2) an analysis of the rate of success of biotechnology companies emerging from Stanford based on information obtained from the equity records at Stanford's OTL. OTL started taking equity more often in start-up companies in the mid-1990s and generally takes equity as part of most exclusive licences to early-stage companies.

**Keywords:** technology transfer, start-up, biotechnology, equity

## 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 Systemix 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 it 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 the technology 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 these 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 shoes. What does the start-up have? Where does it want to go? What does the

**Option agreements are appropriate when a company is still evaluating a technology**

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.

**University technologies especially biotechnological inventions, are early stage**

Once a full licence with a start-up company is in negotiations, OTL will backload the licence 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 pull together some modest amount (US\$5,000–25,000) 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 value from the technology before Stanford can realise value.

**OTL considers equity as only partial compensation**

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 vitro* data, or very little *in vivo* data, available to license. 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 real 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 inventor is involved in the company, the conflict of interest review (discussed later) and potential for clinical trials at Stanford may both weigh 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

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**Equity liquidation occurs upon first possible liquidation event**

had to divest of its equity earlier because of a clinical trial being held at Stanford. Under OTL's licence 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 realised a good return on a few equity liquidations, there are many others where it could possibly have realised 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 valuing 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.<sup>1</sup>

**Partly due to economic conditions, OTL has recently renegotiated several licence agreements with companies**

### 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 maximisation of the equity return.

If an earned royalty rate that a company has already negotiated and finalised 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-associated start-ups as their development plans, 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.*<sup>2</sup> provide examples of earned royalty rates as well as other royalties received by universities in licensing deals. Under their analysis of deals from 1987 to 2003, earned royalties in such deals averaged between 3.9 and 5.1 per cent of net sales.<sup>2</sup>

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 licences – 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 creditable towards earned royalties, therefore meaning 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. The 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 inventors 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 arena 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 it 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.

**Conflict of interest reviews are required when an inventor is involved with a company licensing his/her invention**

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 handling the case writes a memo outlining the background of the technology and potential licence, 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,<sup>3</sup> 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 inventors of the licensed technology also receive a share of the equity.<sup>1</sup> Unlike some other universities, OTL requests that the start-up company issue the inventors' shares 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.

**Total number of Stanford-associated start-ups peaked between 1999 and 2001**

**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 1989. 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 '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 Bouchie that although university licensing continued increasing in the 2001-2003, the number of start-ups licensed decreased between 2001 and 2003.<sup>4</sup> 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 overall economy of the nation.

**Of the total number of companies Stanford has taken equity in through licences, slightly less than half are biotechnology/medical device companies**

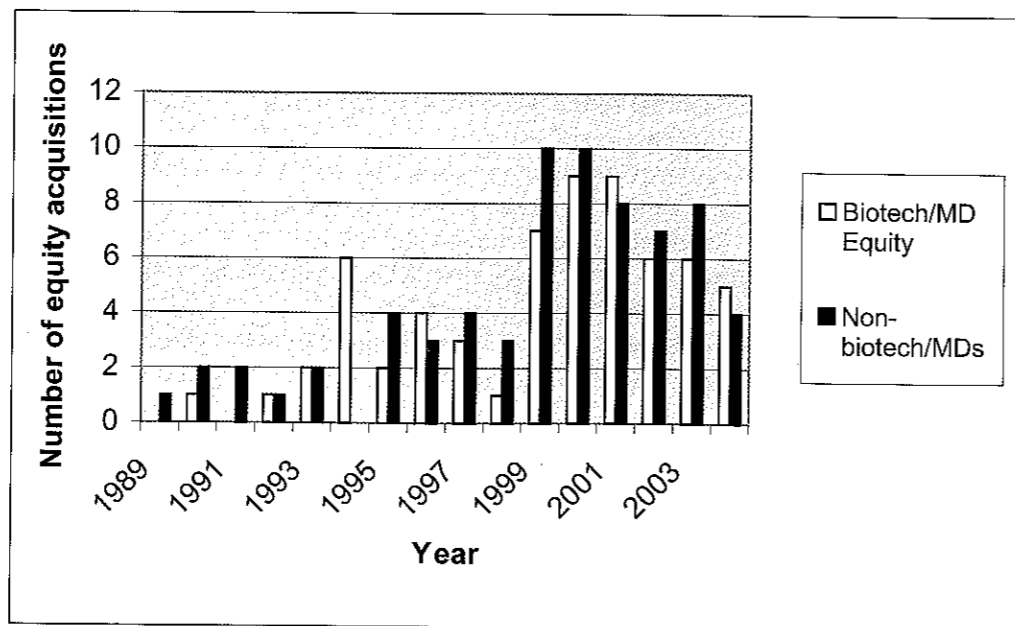
In total, Stanford's OTL has taken equity through licensing in 132 companies between 1989 and 2004. Of those, 63 of the equity stakes were taken for biotechnology or medical device (biotech/MD) companies, compared with

69 for non-biotechnology or medical device companies. Most of these non-biotechnology inventions were from the School of Engineering.

Of the 63 equity stakes taken in biotech/MD companies, OTL has cashed out of 18 (see Table 1). The average number of years from acquisition to liquidation is 5.4, but the range is between 1 and 10. Stanford's OTL first took equity in a medical company in the early 1970s, but the majority of equity-bearing deals have been negotiated since 1999.

Despite the slightly larger number of companies in which OTL has taken equity in the non-biotechnology areas, there have been fewer liquidation events than in the life sciences. At the same time, the life sciences have a much lower average liquidation amount compared with the physical science companies. Not a single liquidation in the biotech/MD sector has generated over US\$1m for OTL. Also, it is noteworthy to compare equity liquidations to OTL cash income. The total of all equity liquidations (US\$22.8m) is significantly less than OTL's cumulative cash income of over US\$500m (as of 31st August, 2004). OTL does not rely on equity liquidations for its budget and income projections.

The medians for biotech/MD and



**Figure 1:** Biotechnology and medical device equity acquisitions v. non-biotechnology and non-medical device equity acquisitions per year since 1989

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

	Number of companies with liquidation events	Total monies from liquidated equity (US\$)	Average liquidation amount (US\$)	Median (US\$)
Biotechnology/medical device	18	1,946,835	108,157	21,308
Non-biotechnology/medical device	14	20,888,249*	1,492,017	240,173
All technologies		22,835,084	713,596	

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

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

non-biotech/MD are significantly different from the averages, and, as can be guessed, 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 amounts 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 larger 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.<sup>5</sup>

**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 minima,

**Stanford does not seek maximisation of its equity revenue**

earned royalties and sublicensing payments. All inventors, including the inventor-founders of the company, received a portion of the equity from the licence agreement. As with many companies, the start-up renegotiated 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 six 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.

**The goal is to have products developed that benefit mankind**

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 companies 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.

### Acknowledgments

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### Paul Goldsmith

is a co-founder of DanioLabs. He is a practising clinical neurologist with a PhD in retinal degeneration. A graduate of both Cambridge and Oxford Universities, he has overall responsibility for the company's scientific, drug development and clinical strategy.

### Derek Jones

was Commercial Director at BioWisdom, and also Head of Business Collaboration at Chiroscience. At Chiroscience he was responsible for the licensing and the ongoing partnership management of several key programmes. A medicinal chemist by training, he has had operational and commercial responsibilities in start-up organisations, in addition to an MBA from Cambridge University. He is COO of DanioLabs.

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# How DanioLabs has evolved its relationship with the CIMR

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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 knit 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. Three players 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 each party wants from such an agreement: the scientist often wants his/her work to be acknowledged as world-beating, to generate scientific publications and kudos; the TTO, wanting to ensure that some of the value is returned to the university; while for the company, the need is 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 surprising amenable to disease modelling in larvae form as they are tiny, transparent vertebrates that have