Start-ups

Stanford University
Office of Technology Licensing
2016 Annual Report
Stanford is the center for start-ups.

Fiction, of course. But there are many people who think we are “Start-up Central!”

We admit—Silicon Valley is bursting with start-ups. The region is teeming with risk-taking entrepreneurs, savvy investors, experienced managers and eager service providers. Most of those new companies are totally unconnected to Stanford. Others are connected to Stanford through students, faculty or alumni who start companies without using Stanford intellectual property. Stanford’s Office of Technology Licensing (OTL) is only involved when the company’s Stanford connection includes intellectual property that is licensed from the University—a relatively small number of companies that nonetheless have made a big impact.

Stanford’s entrepreneurial spirit is in our DNA, dating back to the founders.

Governor Leland Stanford was a risk-taking entrepreneur who came out West during the Gold Rush and made his fortune. In 1884, Leland Stanford and his wife, Jane, decided to start a university in the memory of their son who died of typhoid fever when he was 15. They made some untraditional choices: the university would be coeducational in a time when most were all-male and it would be non-denominational when most were associated with a religious organization. They were also untraditionally practical. The University’s Founding Grant specifically stated that the object of their University would be “to qualify its students for personal success, and direct usefulness in life.”

Fast forward to the 1950s. Stanford Provost Frederick Terman encouraged his students such as David Hewlett, William Packard and the Varian brothers to form companies, which they did. Provost Terman also created the first university-owned industrial park, Stanford Research Park, which played a key role in creating Silicon Valley.

Many people can remember the early 1980s, when companies such as Sun Microsystems, Silicon Graphics, Cisco, MIPS and many more arose from work that began at Stanford. In the 1990s Google, Yahoo, VMware and others were all started by Stanford people or based on Stanford technology.

In this century, Stanford is more entrepreneurial than ever, from the President down to the undergraduate students. President Marc Tessier-Lavigne founded two start-ups and spent many years at a biotechnology company. Stanford’s former President John Hennessy took a leave of absence during his academic career to form a start-up. Other senior leaders at Stanford have worked very closely with both start-ups and well-established companies. If faculty can separate their academic responsibilities from their work with companies, then Stanford believes they can be both world-renowned academics and successful entrepreneurs.

It goes without saying that today students are often attracted to Stanford because of its entrepreneurial culture, from the courses taught, to the access to mentors, to
The networking organizations and clubs. One outgrowth of this entrepreneurial culture was StartX, which began in 2009 as a student-run program to find more ways to engage the alumni community with early-stage founders or students. Today, it is a thriving non-profit that has helped develop and grow over 450 companies.

Visitors from all over the country and the world come to Stanford to find the secret of Stanford’s entrepreneurial culture.

The secret, of course, is that there is no secret. It’s a mindset. It’s an approach. It’s the Stanford culture.

As many people have observed about Stanford, “it’s ok to experiment”—and to fail. It’s also ok to be successful, wildly successful.

Although the entrepreneurial spirit has always been at Stanford, many people may be surprised to know that the University had mixed feelings about the licensing of start-ups in the early years of OTL.

In the 1970s, there weren’t many start-ups. Furthermore, decisions about licensing to them were made on a case-by-case basis. As universities around the country began to develop policies and practices around licensing in the 1980s, interest in licensing began to grow. Stanford policy required that OTL grant only nonexclusive licenses to faculty-associated start-ups due to concerns about the potential conflict of interest associated with “going into business with faculty.” However, in 1994, following faculty debate and consensus, Stanford modified its patent policy and its conflict of interest policy. This cleared the path for OTL to grant exclusive licenses to faculty-associated start-ups and take equity, subject to appropriate conflict of interest review. Stanford has found that this policy strikes the right balance of protecting research integrity while enabling entrepreneurial activity. It has enabled OTL to license hundreds of start-up companies, while generating over $400M from equity to support research and teaching at the University. (For more information about Stanford policies and practices with respect to start-ups, see otl.stanford.edu/documents/OTLstartupguide.pdf.)

Since the 1990s, OTL has licensed many start-ups which were founded on intellectual property owned by Stanford under its patent, copyright and tangible research property policies (stanford.io/rph). Unlike many other technology transfer offices, OTL has never had the mandate to “create” new companies. Because of the Silicon Valley ecosystem and Stanford’s entrepreneurial culture, OTL has had the luxury of enabling them. OTL’s first license agreement to a start-up was in 1975 to Collagen Corporation, which eventually went public. Since then, OTL has licensed over 325 start-up companies, some of which were successful and many of which were not.

In the big picture scheme of Silicon Valley, Stanford start-ups are only a drop in the bucket. And within OTL, start-up licenses are only a fraction of the licenses signed every year. For many years, only about 10% of new licenses per year were to start-up companies. However, in the last few years, OTL doubled the number of licenses to start-ups per year, and granted more “options to license” to hopeful entrepreneurs. This Annual Report is focused on that special group of start-ups who have licensed technology from Stanford. The information provided herein is based on licenses between FY 2007–2016.

The trend for the number of Stanford OTL start-ups is similar to the U.S. GDP which may indicate that OTL’s start-up activity reflects the overall economic health of the country and the entrepreneur’s ability to raise funding.
For the most part, the more early-stage investors (including friends and family, “angels” or venture capital funds) that are available, the more start-ups that spin out of Stanford. In some years, the investment community is more interested in investing in physical science start-ups (e.g., software, energy, self-driving cars) and other years, investors are interested in medical device, therapeutic or diagnostic companies. Investors are also interested in physical science inventions that are applied to biomedical applications, such as gene sequencing instruments, optogenetics hardware or consumer health monitoring apps.

Stanford has seven Schools: School of Medicine, School of Engineering, School of Humanities and Sciences, School of Earth, Energy & Environmental Sciences, Graduate School of Education, the School of Law and the Graduate School of Business. Stanford also has a tradition of several interdisciplinary programs through the Independent Laboratories, Centers and Institutes, which are an additional source of inventions. It is possible to separate start-ups by the School where the underlying technology originated, which indicates the type of inventions that form the basis of start-ups. The inventions from the School of Medicine and the School of Engineering are Stanford’s chief source of start-up technologies. Nonetheless, twenty-two percent of start-ups in the past 10 years involve Schools other than Medicine and Engineering.

Although the University is organized by Schools and Independent Laboratories, the innovation on campus is not constrained by those administrative boundaries. Stanford has been at the forefront of interdisciplinary research and education for many years, with the Clark Center becoming a focal point in 2003. As a result, OTL has seen a steady increase in interdisciplinary inventions because researchers from the different Schools are interacting on a daily basis.

In addition to the Schools of the inventors, the technology areas of Stanford start-ups can be viewed by the nature of the inventions with broad labels for Biological Science, Physical Science or Medical Device. Some inventions are easy to categorize — a cell therapy for cancer falls under Biological Science; a battery technology falls under Physical Science; and a catheter falls under Medical Device. Many of the technologies are not as clear cut — an instrument for cancer diagnostics; an organism engineered for biofuel production; or a wireless charging system for a pacemaker — all fall into an interdisciplinary gray zone that makes the criteria relatively loose. Over time, the number and variety of these interdisciplinary inventions has grown. Nonetheless, these labels provide another view of the range of innovations being developed by start-ups.
In the past ten years, the total number of start-ups licensed by OTL has grown. In that time, the School of Engineering has had more start-ups emanating from collaborations with other Schools than those based solely from Engineering. On the other hand, for the School of Medicine, the percentage of start-ups based on interdisciplinary research has decreased over time. In general, many of the interdisciplinary technologies are physical science inventions, often a platform that can be used for a life science application.
4C Air

4C Air, Inc. licensed a high efficiency air filter technology developed in Professor Yi Cui’s laboratory. The company is developing materials and solutions that could be used in both consumer products such as personal masks, indoor air purifiers or window screens, and in industry applications for clean rooms, hospitals, food processing equipment or exhaust systems. 4C Air’s products have higher efficiency and significantly lower air resistance than the products currently on the market.

Blueprint Genetics

Blueprint Genetics is changing diagnostics by providing accessible and actionable genetic testing for rare inherited diseases to all medical specialties. Based on an invention by Professor Hanlee Ji, Dr. Jason Buenrostro and Dr. Samuel Myllykangas, Blueprint has commercialized the OS-Seq technology to deliver fast, affordable and comprehensive genetic diagnostics services. Blueprint has built a genetic testing portfolio addressing >2,400 inherited disorders. They are growing quickly and, in just three years, they have processed close to 10,000 patient samples obtained from more than 500 physicians in 25 countries.

Ceribell

Based on an invention from Music Professor Chris Chafe and Neurology Professor Josef Parvizi, Ceribell is developing a wearable seizure detection device that offers the first instant EEG recording and interpretation. This device will enable patients suffering from recurrent seizures to detect the onset of a seizure. The company has proprietary hardware and software products to acquire and convert brain signals into sound, which will allow physicians to hear changes in brain activity and make instant diagnoses.

DiGisight Technologies

DiGisight Technologies, Inc., is a digital health company developing a mobile ophthalmic camera, Paxos Scope. The camera is designed so health care professionals can quickly capture images of the eye and retina at the point of care with their mobile device. Invented by a team of Stanford scientists led by Dr. Robert Chang, Paxos Scope has a secure image sharing and messaging feature to communicate with colleagues and coordinate care in real-time.

Epinomics

If the genome is the hardware of our bodies, then the epigenome may be considered the software component, since it regulates which genes are turned on and off. The epigenome may hold the key to personalized medicine because it dynamically responds to the environment and reflects an individual’s state of health at any given moment. In 2012, Professors William Greenleaf and Howard Chang and their colleagues at Stanford University invented “ATAC-seq” (Assay for Transposase-Accessible Chromatin with high throughput sequencing), a breakthrough technology that can decode the epigenome. Licensed to Epinomics, the ATAC-seq and analytics platform can be used for discovering biomarkers that can be used in clinical research and advancing immuno-oncology applications.

Globavir

Globavir Biosciences, Inc. is a private biotechnology company that is developing multiple technologies licensed from Stanford. Professor Benjamin Pinsky and Dr. Jesse Waggoner invented a molecular diagnostic platform useful for detecting and differentiating Dengue virus infection in humans. This technology became the basis for Globavir’s PanGlob® and Denglob® diagnostic products. Globavir has received CE IVD regulatory approval for distribution and use in Europe and India. The company has also partnered PanGlob® with Bio-Rad as part of a multiplex test that will be launched globally in 2017.

Globavir also licensed GBV006 from Stanford. GBV006 is a combination of two FDA-approved drugs for the treatment of certain viral infections, most notably Dengue and Ebola virus. Invented by Professor Shint Einav and her colleagues, Globavir is currently working with potential partners to start Phase Ib/IIa clinical trials in South East Asia in 2017 with the FDA and EMEA. Globavir emerged from the Stanford-StartX accelerator program, and has completed three rounds of private financing.

Heisen Research

Heisen Research, LLC is developing a revolutionary method to validate and verify computer systems and chips based on error detection inventions from Professors Deming Chen’s and Subhasish Mitra’s laboratories. The technology reduces bug trace length by 1 million times, enabling a process that is ultimately 100 times faster and much more cost effective than the current state-of-the-art techniques used in industry. This detection system could provide a range of companies — from automotive manufacturers to semiconductor design houses — with a faster validation process that makes development more efficient and frees up engineering staff to take on even more complex projects.

iRhythm Technologies

As a specialist in heart rhythm problems, Dr. Uday Kumar always thought there had to be a better way to monitor patients suspected of having abnormal heart rhythms when they were outside of the clinic, going about their usual activities. Traditionally, patients were given a large cassette player-sized device which they attached to their bodies via electrodes in order to capture and record their heart rhythm throughout the day and night.

When he was a fellow in the Stanford Biodiognostic Program in 2005-06, Kumar (now a Consulting Associate Professor of Bioengineering) set his sights on finding a more cost-effective, user-friendly solution. He founded iRhythm Technologies, Inc. in 2006 to develop and commercialize his invention, which was the basis for the ZIO Patch®. The ZIO Patch® extended continuous ambulatory cardiac monitoring system has now been used by more than 500,000 patients. It is one of dozens of devices to emerge from the Biodiognostic Program’s innovation process, which has become the international model for inventing new medical technologies. Based on the company’s continued growth and adoption across the U.S., iRhythm Technologies, Inc. went public in October 2016.
FY 2016 YEAR IN REVIEW

Stanford received $94.22M in gross royalty revenue from 779 technologies, with royalties ranging from $10.05 to $62,000,000. 7/779 inventions generated $1M or more in royalties, while 731 inventions brought in <$100,000 in royalties each. Cumulatively, this long-tail creates a steady royalty base for Stanford.

We filed 289 patents. We signed 141 license agreements. Of one hundred forty one licenses signed, 54 were nonexclusive, 48 were exclusive, and 39 were option agreements.

Royalty distribution: Stanford’s royalty-sharing policy provides for the distribution of cash net royalties (gross royalties less 15% for OTL’s administrative expenses, minus direct expenses) to inventors, their departments and their schools. In addition, the University assesses an infrastructure charge on the department and school shares of royalty income. Inventors received personal income of $24 M. Departments received $21 M and Schools received $20.8 M. OTL also shared $840,000 with other institutions based on arrangements for handling joint inventions on behalf of other organizations, or under agreements with the Howard Hughes Medical Institute, the Department of Veterans Affairs (VA), and the National Institutes of Health (NIH).

Lex Machina
Professor Mark Lemley established the Intellectual Property Litigation Clearinghouse, (IPLC) at the Stanford Law School to examine intellectual property litigation. At the IPLC, he led the development of a system that could be used to analyze legal historical performance, to compute corresponding correlations between statistical variables and to calculate ongoing legal trends based on legal documents. In 2010, the IPLC spun out into a start-up, Lex Machina, Inc. and the tools created at Stanford were licensed to the company. Lex Machina further developed those technologies and was acquired by LexisNexis in 2015.

Zenflow
In 2014, a Stanford Biodesign fellowship team created a novel minimally invasive treatment for the symptoms of benign prostatic hyperplasia (BPH or enlarged prostate). Excited by the prospect of developing a solution that could help hundreds of millions of men worldwide, inventors Nick Damiano and Shreya Mehta completed their fellowships and founded a company called Zenflow, Inc. The invention, licensed from Stanford, became the basis for the company’s primary product called the Spring System. In early 2016, Zenflow began first-in-human clinical trials for this device in Europe and New Zealand.

ProbiusDx
ProbiusDx, Inc. is developing a broad-spectrum, “embedded” point-of-care diagnostic solution based on an electronic sensing platform developed by Professors Roger Howe and Boris Murmann along with Chaitanya Gupta and Ross Walker. This portable device can analyze multiple target proteins in real time, enabling doctors to rapidly deliver appropriate therapy to patients in need of critical care within clinical settings. The company has plans to introduce the technology for blood-draw quality checks and for a broad screening panel in the emergency care setting before working toward a wider range of personalized diagnostics applications.

Selten Pharma
In 2011, Professor Edda Speikerkotter and a team of Stanford researchers discovered that low doses of the drug FK506 activates a signaling pathway which is implicated in pulmonary arterial hypertension (PAH). PAH is a rare disease with a mean life expectancy of 2 to 5 years from the time of diagnosis if untreated. Patients diagnosed with PAH (mostly young women) have a poor prognosis, a compromised quality of life and no current treatment options to prevent the disease from progressing. Shortly after the clinical trials of FK506 for PAH began, Selten Pharma, LLC licensed the technology from Stanford. Selten developed a new, convenient formulation and then devised a second-generation compound. Selten Pharma was recently acquired by Vivus, Inc. to further the commercialization of FK506 for this indication.

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We take a financial risk each time we decide to file for a patent. In this period of tremendous change in the intellectual property landscape as court cases determine new patent law, we must weigh the likelihood of licensing a technology versus the expense of patenting or litigation. We are being more selective in our filings now than in the past because the U.S. Patent Office is requiring more data to support the invention and issuing fewer broad patents. The patent landscape is not favorable to patentees these days.

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OTL is facing its first big revenue challenge in almost 20 years now that our biggest royalty-producing patent has expired. In those 20 years, the number of invention disclosures has increased from 200 to over 450 a year and OTL has grown from a staff of 20 to 44 as our active caseload has almost tripled and interest in intellectual property has heightened. It is clear that Stanford faculty are interested in both publishing their research results and filing patents on their promising discoveries. Students are also much more sophisticated in their understanding of and interest in patents and commercialization. The challenge is that the trend in patent law and court cases has been to weaken patent law, making it much more difficult to defend inventions. Professors are more willing to seek patents or, at a minimum, to make patents much more vulnerable to challenge. Thus, the likelihood of another big revenue winner is much more uncertain.

Nonetheless, the University understands the importance of supporting innovation and technology transfer and is committed to ensuring that OTL has the resources to serve the Stanford community.

OTL is always thinking about how to improve its operations to be as efficient and effective as possible. To help with this goal, OTL has worked with different Graduate School of Business Alumni Consulting Teams (ACT) several times in the past to get an outside perspective on OTL. This year, the very strong ACT team of David Pritchard, Sam Pai and Deborah Byron provided us with excellent suggestions on how to move forward in this uncertain time. We continue to work with them and OTL staff to implement their recommendations.

WHAT’S NEW

CHALLENGES OF THE FUTURE

As discussed earlier in this Annual Report, universities are increasingly asked to examine their role in facilitating technology development and maturation, entrepreneurial activity and start-up formation. In 2013, with former President Hennessy’s financial support, the Stanford Innovation Program (SIP) started as an experiment to use University funding to further develop unlicensed inventions to become more licensable. Because the funds are not for “research” but for “development”, the projects must have strong endorsement by OTL and active faculty involvement. They require milestone-driven benchmarks and quarterly in-person reporting. Now in its third year, SIP has funded 17 projects, with 7 of them to date resulting in a likely or actual license. Although SIP is not intended to help create start-ups, the likely licensees of SIP projects are often Stanford start-ups who are willing to take the risk on these early stage projects.

NEW RESEARCH PROGRAMS

Technology Development

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Copyright is an intellectual property right that is often misunderstood, particularly in the context of commercialization. In order to provide our researchers with information and guidance about copyright licensing issues, we developed a "Creator’s Guide to Commercializing Copyrighted Work" which is available in hard copy and on the web (stanford.io/copyrightguide). We hope this will be a valuable resource for creators as they develop software and other copyrighted works which may be distributed or commercialized.

China

OTL continues to explore how best to work with Chinese companies, particularly in markets that are unique to China. We understand that relationships and trust are important to successful collaborations and have made regular visits to China and Hong Kong to build that foundation. China is a market that cannot be ignored and, as their intellectual property system matures, Chinese patents may become important for licensing. For most universities, this is still uncharted territory but we believe it is important to develop good, long-term relationships in China as the opportunity arises.

Changing of the Guard

OTL has only had two Directors in 47 years, which is remarkable in itself. After 25 years of leading OTL and 10 years managing technologies in the office before that, our Executive Director Katharine Ku has announced her plans to retire. Stanford has engaged a search firm to find OTL’s third director and a search committee will be appointed by Vice Provost and Dean of Research Ann Arvin. Ku will continue to head the office until the new Executive Director takes the helm.

Keeping the Engine Running

In our ongoing effort to provide efficient service to Stanford inventors, we are very pleased to have updated our Standard Operating Procedures (SOPs) and the information on our new and improved internal wiki. We have also been continuously improving our robust and complex relational database and recently incorporated an intuitive web-based interface. Our database is the repository of all information for our inventions and we use it every day for everything. If the whole office staff suddenly disappeared, someone could recreate OTL by relying on the wiki, our database and our website!

Industrial Contracts Office

New Industry Sponsored Research Agreements

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<th>In FY 2016, Ico Finalized</th>
<th>The school of medicine accounted for just over half of these SRAs, with</th>
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New Industry Sponsored Research Agreements (SRAs), Where Companies Fund and Sometimes Collaborate on Research Projects in Stanford Laboratories.

Material Transfer Agreements

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Another

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<th>Agreements Cover Stanford Investigators Sending Out Biospecimens for Research Purposes.</th>
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Other ICO Agreements Included More Than

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<th>Amendments to Existing Sponsored Research Agreements, Plus New Collaborations, Data Sharing, Equipment Loans, Non-Disclosure and other Research-Related Agreements.</th>
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During the year, ICO finalized a multi-year agreement for the “Baseline Study” with Baseline Study LLC, a company being formed by Alphabet’s Verily Life Sciences LLC. The Baseline Study is a multi-cohort, long term, observational, epidemiological study to collect human data and samples for scientific and medical research. The goal is to understand human health and the transition to disease. Stanford and Duke University are participating. Professor Sam Gambhir (Radiology) is leading the work at Stanford.

Oncology professor Hanlee Ji received funding from Aduro Biotech, Inc. Dr. Ji’s laboratory will use clinical genomics to identify immunogenic neoantigens in colorectal cancer in order to develop a precision vaccine for colorectal cancer.

Johnson and Johnson Vision Care, Inc. signed a master research agreement and funded three projects in Professor Gerry Fuller’s laboratory (Chemical Engineering). The goal of these projects is to better understand the nature of tear film across contact lenses and the cornea.

Stanford has had a long and productive relationship with Siemens Medical Solutions, including two master research agreements and many research projects. In the past fiscal year, ICO put in place another master research agreement with Siemens – this time with their Corporate Technology Group. The projects funded under this master research agreement include:

- “Generation of Real-time Optimization-based Controllers on the Siemens Design Building Automation System” and “Optimal Controller Tuning Method for Power System Oscillation Damping” for Professor Stephen Boyd (Electrical Engineering) to develop more efficient optimization of systems.

- “Application of Reinforcement Learning to Self-Organizing Manufacturing Systems” for Professor Tsachy Weissman (Electrical Engineering) to develop an algorithm to reduce costs and boost productivity in self-organized manufacturing systems.

- “Optimal Operation of Water Supply Network via Distributed Optimization and Convex Relaxation” for Professor Yinyu Ye (Management Science and Engineering) to improve efficiency of water supply networks.

IN MEMORIAM
Sergey Marechek
Bernard A. Shoor