

STANFORD

OFFICE OF TECHNOLOGY LICENSING
STANFORD UNIVERSITY
ANNUAL REPORT 2018

If you do things well,
do them better.
Be daring, be first, be different.

—Anita Roddick, businesswoman and human rights activist

FROM THE DIRECTOR

My first months at Stanford, getting to know the faculty, staff and research strengths, have been a truly amazing and humbling experience. Stanford's internationally renowned top-tier research, combined with its entrepreneurial spirit, has led to a wealth of innovative new technologies that make leading the technology transfer efforts at Stanford such an exciting and rewarding opportunity. Not wanting to rest on the OTL's well-earned laurels, I look forward to moving the office in a direction to better meet the needs of the increasingly complex research, technology development and commercialization relationships that are required to maintain Stanford's top tier status in innovation. We are transitioning some staff roles to increase the efficiency of the office, adding a new role focused on managing Stanford's increasing volume of complicated high-profile for- and non-profit research alliances, as well as expanding some of our research development and marketing activities, all to create an increasingly improved experience for Stanford researchers and our external stakeholders. With the many exciting new initiatives being implemented under Stanford's Long Range Plan, I am excited to lead OTL as it transitions to meet Stanford's evolving needs.



Karin H. Immergluck, PhD
Executive Director
Office of Technology Licensing (OTL)
Stanford University

This is a time of *transition* for the Office of Technology Licensing (OTL), with key changes in personnel, the need to support a growing number of large industry consortia, a move to the Redwood City campus and some new roles and organizational changes in our office. Through all these changes, we continue to maintain the central mission of OTL—*transitioning* Stanford technologies to industry in order to maximize their impact in society.

► **People:** With the retirement of our long-time Executive Director, Kathy Ku, we welcome a new leader to OTL, Dr. Karin Immergluck. Karin joins us from her prior role as the Executive Director of the Office of Technology Management at UCSF, bringing a wealth of experience managing another technology transfer organization, as well as deep insights into the life science aspect of OTL's work, which is becoming increasingly complex with the addition of large, multi-party research programs such as Takeda AIM. In addition, we are thrilled to be working under the guidance of our new Vice Provost and Dean of Research, Dr. Kathryn Ann "Kam" Moler who supports and enables our office to make a successful transition.

► **Location:** In addition to these internal office changes, our staff is preparing to move to Stanford's new Redwood City Campus. Along with the open space concept, there will be greatly increased opportunities for communication with offices that are closely related to OTL's mission, for example Office of Sponsored Research (OSR), Research Compliance Office (RCO), Office of Development (OOD) and Stanford Management Company (SMC).

► **Organization:** After many years of an internal structure in which our Licensing Associates have managed all aspects of large caseloads from "cradle to grave", the OTL has decided to move in a direction that is more consistent with other university technology transfer offices, i.e. a more centralized model for administrative functions. Our Licensing Associates will still be the primary interface to both inventors and licensees, but we envision other activities being centralized into groups to cover such areas as patent protection, drafting of certain agreements, marketing and business development. By hiring business development staff, we aim to accelerate the translation of research into products for the benefit of the public. This added capability will work to develop closer relationships with potential commercial partners and to keep them better informed of the specific innovations that are relevant to their businesses, with the dual goals of creating new industry-sponsored research opportunities for our faculty, as well as new markets for our licensable assets. Through such high-touch relationships, we think we can have a higher return on our marketing efforts.

Industry-supported research at Stanford is trending toward projects that are larger and more complex than in earlier years.

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► **Our Industrial Contracts Office** (ICO) is on the front-line working to support these new initiatives. One example is in the broad range of energy-related research being funded by ExxonMobil Research and Engineering Company. During FY2018, ICO entered into a five-year, \$20M strategic alliance agreement with ExxonMobil that is designed to support different types of research relationships at Stanford in the energy field, including sponsored research, a consortium, and industrial affiliates programs. The industrial affiliates programs support research led by a group of faculty in a general area of interest, for example, the Natural Gas Initiative, which brings together researchers from a range of disciplines at Stanford to generate knowledge needed to use natural gas to its greatest social, economic and environmental benefit. The sponsored research projects are typically a one-on-one arrangement, where a University principal investigator works with a technical manager at ExxonMobil, and heads a project defined by a specific statement of work. ExxonMobil and its affiliated companies are currently supporting and initiating a variety of sponsored research projects in energy in the Aero Astronautics,

Physics, Chemistry, Chemical Engineering, Energy Resources Engineering, Geophysics and Civil and Environmental Engineering Departments. The Strategic Energy Alliance Consortium will be funded by ExxonMobil, Bank of America, Total SA and Shell International Exploration and Production Inc. to support energy research projects proposed by Stanford faculty.

Another trend we are seeing in the life sciences is longer-term research agreements with companies, where principal investigators begin with preclinical research and later progress into clinical trials. In the past, these different phases of biomedical research have been separate and discrete, starting with an agreement for preclinical research. Then if one or more inventions resulted, the company would approach OTL at that time about a license before moving into clinical trials. Any resulting trial was handled under a separate agreement.

Now, companies and Stanford's School of Medicine are increasingly interested in forming longer-term, more comprehensive relationships where we have the opportunity to advance inventions beyond the laboratory and much further than in the past. In one example, the

gene and cell therapy company RocketPharma initiated a multi-year relationship spanning pre-clinical research and clinical trials, including the expansion of Stanford's cell and gene therapy manufacturing facility to provide materials for these and other clinical trials.

Companies also are seeking to work more collaboratively with Stanford researchers. The Stanford Alliance for Innovative Medicines (AIM) was created in partnership with Takeda Pharmaceutical Company Ltd. to accelerate the translation of research discoveries at Stanford into next-generation therapies of all modalities. AIM brings Stanford and Takeda scientists into close collaboration to share ideas, know-how, and technical acumen under Stanford ChEM-H. Stanford faculty projects selected to participate in the program will gain access to Takeda's drug development experience and to Takeda's research functionalities such as medicinal chemistry, high-throughput screening, scaled up protein production, monoclonal antibody discovery or engineering, pharmacokinetics, and profiling for safety and toxicity. Each project is co-led by the Stanford PI and a Takeda project leader.

During the past year, Stanford and Google LLC executed a master research agreement to explore the use of artificial intelligence (AI) solutions for healthcare. Google will fund and collaborate on a number of research projects at Stanford focused on improving clinical outcomes and the patient-provider experience in a cost-effective manner. The broad objectives are to improve the delivery of patient care, provide predictive models in the clinic, and improve clinical outcomes.

One project is assessing the feasibility of auto-generated physician notes. Another project is intended to assist clinicians with monitoring patient status. Both projects will develop AI-based tools to help clinicians gather, review, and understand relevant clinical information, with the goal of enabling timely and appropriate physician decisions.

Ensuring such systems are easily understood and trustworthy is an essential part of the goal. Google and Stanford researchers will work closely on these and future projects.

This past year, some of Stanford's licensed technologies saw their existing market share increase, while others launched as products for the first time or made significant progress in that direction.

► **edTPA**[®] is a performance-based, subject-specific assessment and support system used by teacher preparation programs throughout the United States to emphasize, measure and support the skills and knowledge that all teachers need from Day 1 in the classroom. Stanford University faculty and staff at the Stanford Center for Assessment, Learning, and Equity (SCALE) developed edTPA[®] and it was licensed to Pearson for implementation and distribution.

The SCALE team received substantive advice and feedback from teachers and teacher educators and drew from experience gained from over 25 years of developing performance-based assessments of teaching. This included National Board for Professional Teaching Standards (NBPTS), the Interstate Teacher Assessment and Support Consortium (InTASC) Standards portfolio, and the Performance Assessment for California Teachers. The design and review teams have included hundreds of university faculty, national subject-matter organization representatives (e.g., NCTM, NCTE, NSTA, etc.), and K-12 teachers.

Aspiring teachers must prepare a portfolio of materials during their student teaching clinical experience. edTPA® requires aspiring teachers to demonstrate readiness to teach through lesson plans designed to support their students' strengths and needs; engage real students in ambitious learning; analyze whether their students are learning and adjust their instruction to demonstrate equitable instructional practices for all learners. Teacher candidates submit unedited video recordings of themselves at work in a real classroom as part of a portfolio that is scored by highly trained educators. edTPA® builds on decades of teacher performance assessment development and research regarding teaching skills and practices that improve student learning and currently measures 28 specific licensure fields/subject areas. edTPA® is used by more than 820 teacher preparation programs in 42 states and the District of Columbia as part of program completion or licensure requirements. Nineteen states throughout the USA have policies that include edTPA® to ensure their teachers are adequately prepared to enter the classroom. To date, more than 190,000 candidates have been officially scored by highly trained qualified educator scorers.

► **Spark Therapeutics** is a gene therapy company founded in 2013 based on technology and know-how from Children's Hospital of Philadelphia. With a focus on inherited orphan diseases, Spark was the first company to get an in vivo gene therapy for a genetic disease approved in the US with the approval of voretigene neparvovec (LUXTURNA®) for an inherited retinal disease.

Spark currently has an investigational gene therapy for hemophilia A, or factor VIII deficiency, entering Phase 3 clinical trials. The product candidate is SPK-8011, which contains a codon-optimized human factor VIII gene under the control of a liver-specific promoter. It is being studied as a potential one-time gene therapy for hemophilia A. SPK-8011 includes an engineered adeno-associated viral (AAV) vector that uses the AAV-LK03 capsid that came from the laboratory of Professor Mark Kay and was licensed from Stanford.

The Kay Lab engineered AAV-LK03 through a unique protocol of DNA shuffling and selection using a humanized murine model. This method facilitated the final selection of a vector that is capable of highly efficient functional transduction, leading to a high level of transgene expression and selective for human hepatocytes.

Preliminary data from the Phase 1/2 trial of investigational SPK-8011 shows the first 12 participants experienced notable reductions in bleeds and infusions. The earliest dosed 5 participants have shown persistent, stable factor VIII activity levels in this ongoing study.

► Food allergy is a chronic, life-threatening, accelerating, global epidemic now impacting 8-11% of the US population. The rate in children has doubled over the last generation and two out of three children who develop a food allergy didn't have a parent with the disease. These data points emphasize the dominant role that environmental factors, rather than genetic factors, are playing in the disease.

Fortunately, there is cause for hope, as researchers around the world have recently shown that food allergy is a preventable disease if certain environmental factors can be modified: most notably the infant diet. Dr. Kari Nadeau, the pediatrician, allergist, and biochemist who directs the Sean N. Parker Center for Allergy and Asthma Research at Stanford, is one of the world's foremost experts in the ways that dietary exposure to food proteins can modulate the immune system. In research conducted at Stanford,

she developed and patented a food-derived powdered ingredient to help reduce the likelihood that a child will develop a food allergy. This "foundational food blend" was designed to be added to a healthy child's daily diet beginning around the time of solid food introduction and continuing for a year or more so that the child's immune system can grow up accustomed to more than 90% of the foods that are associated with food allergies.

Dr. Nadeau partnered to form **Before Brands, Inc.** which licensed this IP estate from OTL. Since then, the company has raised \$48M in venture capital, multiple associated patents have issued, and as of late 2018, the company had released the SpoonfulOne™ line of infant nutritional products to help protect children from developing a food allergy. The products are being designed in healthy, delicious, family-friendly formats - mix-ins for baby food; puffs; biscuits and more - all to support long-term use starting in infancy and continuing through kindergarten, and beyond.

Already thousands of families have begun including SpoonfulOne in their children's diets to help protect them from developing a food allergy and the company is making significant investments to support health care provider outreach and education.

Dr. Ashley Dombkowski, CEO of Before Brands said: "There is a quote engraved into the Museum of Science and Industry in Chicago that reads, 'Science discerns the laws of nature. Industry applies them to the needs of man.' I can think of no better way to describe the work we've done to exploit Dr. Nadeau's outstanding academic research to help a new generation of children avoid the pain and suffering of such a devastating condition."

► **CareDx** is a diagnostics company that provides noninvasive tests for the organ transplant market. Among the variety of products that they offer for the transplant market is AlloSure, for kidney transplants. Allosure is the first non-invasive test that assesses the health of the transplanted organ by directly measuring injury to the organ. This ability to determine active rejection allows better management of kidney transplant patients.

AlloSure is based on cell-free DNA (cfDNA) technology developed in Professor Stephen Quake's lab here at Stanford. The company acquired the technology in 2014 and has run multiple clinical trials to demonstrate the value of measuring donor-derived cfDNA with AlloSure in kidney transplant patients. The data from the trials also supported CareDx's application for Medicare reimbursement, which the company received in October, 2017.

► **Butterfly Network** is successfully developing a micro-electromechanical system (MEMS) and complementary metal oxide semiconductor (CMOS). The MEMS component of this technology is embodied as capacitive micromachined ultrasound transducers (CMUTs) which was developed in the laboratory of Stanford's Pierre Khuri-Yakub. CMUTs are a type of ultrasonic transducer which aims to replace conventional piezoelectric transducers. CMUTs are micromachined and integrate with silicon, enabling them to utilize efficient semiconductor processing techniques. CMUTs have a broad range of possible applications including medical imaging, gas, chemical, and biological sensors, and cargo scanning for security applications.

Butterfly Network, founded by Dr. Jonathan Rothberg, is focused on democratizing healthcare by making medical imaging more broadly accessible to everyone around the world. They are currently bringing their Butterfly iQ ultrasound-on-a-chip system into the market. Butterfly has verified and validated its device and subsequently attained FDA clearance for 13 indications, which is more than any single ultrasound probe previously marketed.

The Butterfly iQ is a low cost, portable ultrasound scanner with the ability to integrate with a smartphone. Its MEMS technology has a high acoustic bandwidth which allows for many applications when coupled with high-precision integrated analog and digital circuitry, reducing the need for a large cart and bulky accompanying hardware. This is a breakthrough in enabling a portable ultrasound device. Additionally, it has lowered the cost by 10 to 100 times.

► OTL-LICENSING

In FY2018, Stanford received \$40.96M in gross royalty revenue from 813 technologies, with royalties ranging from \$11 dollars to \$11.1M dollars. Fifty-three (53) of the 813 inventions generated \$100,000 or more in royalties. Seven inventions received \$1M or more. As you can see, we have a long tail of inventions that bring in less than \$100,000 in royalties but this long tail is the steady royalty base for Stanford.

We evaluated 560 new invention disclosures and signed 150 new licenses. Seventy-six (76) of the licenses were nonexclusive, 41 were exclusive and 33 were option agreements. Twenty-eight (28) of the 150 agreements were with Stanford start-ups and 24 of them involved equity.

► 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. OTL distributed personal income totaling \$9.549M to 900 inventors. Stanford departments received \$8.458M and schools received \$7.613M after the University assessed an infrastructure charge on their shares of royalty income.

Stanford also paid 26 other organizations \$1.057M for jointly-owned technologies for which Stanford has licensing responsibility.

► EXPENSES

Filing and maintaining patents is an expensive proposition and we spent \$11.606M in legal expenses with more than 58% of legal expenses eventually reimbursed by licensees or royalty payments. Our operating budget for the year (excluding patent expenses) was \$7.309M.

► EQUITY

As of August 31, 2018, Stanford held equity in 184 companies as a result of a license agreement. For institutional conflict-of-interest reasons and insider trading concerns, the Stanford Management Company sells our public equities as soon as Stanford is allowed to liquidate rather than holding equity to maximize return.

This year, we received equity from 24 companies. Twenty-eight (28) of our start-up licenses were defined as a "start-up based primarily on Stanford technology." We also received \$1.099M in liquidated equity from 10 companies.

\$40.96M
IN GROSS ROYALTY REVENUE FROM
813
TECHNOLOGIES

\$2.52M
IN LIQUIDATED EQUITY FROM 15 COMPANIES

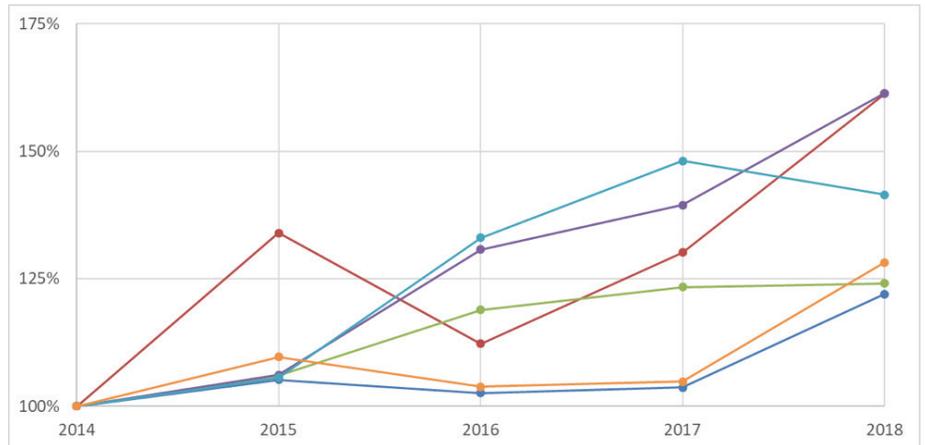
► **NEW DISCLOSURES**

In FY2018, we received 560 new technology disclosures. One of the most challenging responsibilities for OTL is to decide whether or not to spend University funds on filing patents. Many inventions do not need to have a patent in order to license the technology.

► **STANFORD TRADEMARK ENFORCEMENT FUND AND PATENT EXPENSES**

The Stanford Trademark Enforcement Fund (STEF) was established to support the costs associated with the protection of the Stanford name and associated logos and trademarks. In addition, some of the funding is used to provide support to OTL. Stanford charges 6% of the department and school royalties to fund STEF.

The following figure shows trends for OTL-Licensing over 5 years, with the ratio of change relative to 2014.



- New dockets
- New dockets with industry sponsor, foundation, CIRM, BioHub, PICI, HHMI, VA
- Number of technologies producing income
- Number of active companies in which OTL has equity
- Number of new licenses
- Number of inventors receiving distributions

560
NEW TECHNOLOGY
DISCLOSURES

150
NEW LICENSE
AGREEMENTS



76
NON-EXCLUSIVE
41
EXCLUSIVE
33
OPTION AGREEMENTS

28
AGREEMENTS WERE WITH
STANFORD STARTUPS

► INDUSTRIAL CONTRACTS OFFICE

The Industrial Contracts Office (ICO) is a group within OTL that specializes in research agreements with industry. In FY2018, ICO finalized a total of 189 new industry sponsored research agreements (SRAs) where companies fund and sometimes collaborate on research projects at Stanford and 214 amendments to existing SRAs. The School of Medicine accounted for over half of these agreements with 99 new industry-funded research agreements. The Department of Medicine was home to the largest number of industry research agreements, with 73 new SRAs. The Radiology Department in the School of Medicine accounted for 34 SRAs; Pathology had 22 new and amended SRAs; Pediatrics had 13 new and amended SRAs.

The School of Engineering accounted for about a third of the total SRAs, with 57 new industry-funded sponsored research agreements and 58 amendments to existing SRAs. The Electrical Engineering Department was home to the largest number of new Engineering industry research agreements, with 17 SRAs; Computer Science accounted for 12 SRAs; Mechanical Engineering had 9 new SRAs; and Aeronautics and Astronautics accounted for 6 new SRAs.

ICO also advises other University offices on intellectual property terms for research agreements, including nonprofit foundation grants. We helped other offices negotiate 330 agreements in FY2018, up from 280 agreements in FY 2017.

Industrial Affiliates Programs

ICO handles Industrial Affiliates Program approvals, renewals and related agreements. During the year, 65 Affiliates Programs brought in a total of \$44.8M, up from a total of \$36.3M in fiscal 2017. SystemX in the School of Engineering continued to be the largest program, with \$4.6M in funding.

Six new Affiliates Programs were approved in the past fiscal year, four of which were in the School of Engineering:

- AI Safety;
- AHA Agile Hardware Affiliates Program;
- Nanoscale Prototyping Lab;
- Distributed Trust Initiative;

one in the School of Earth Sciences:

- SUPRI-Tides;

and one under the Dean of Research:

- Population Health Sciences.

189

NEW INDUSTRY-SPONSORED RESEARCH AGREEMENTS

637

NEW MTAs

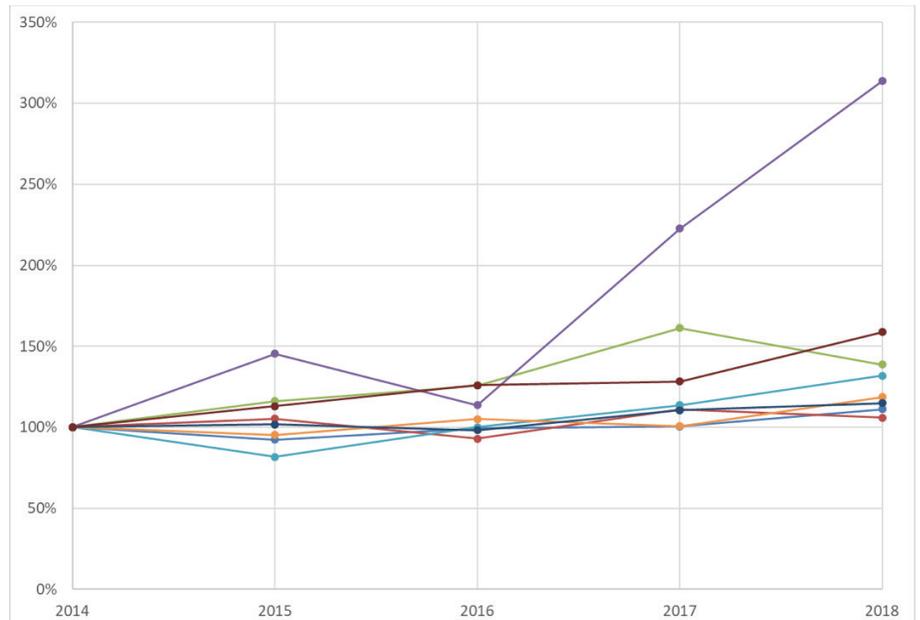
65

AFFILIATES PROGRAMS BROUGHT IN

\$44.8M

All in all, ICO finalized 1,238 new agreements in FY2018. This includes 637 new Material Transfer Agreements (MTAs); 67 Human Tissue Transfer Agreements; 43 Unfunded Collaborations; 69 Data Transfer Agreements; 29 Equipment Loans and a variety of other research-related agreements with companies.

The following figure shows trends for ICO over 5 years, with the ratio of change relative to 2014.



- New SRAs
- New Collaboration Agreements
- New Equipment Agreements
- Total Agreements
- New MTAs
- New Data Agreements
- Other Agreements Supported (OSR, etc.)
- Affiliates Programs Total Funding

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NEW AFFILIATE PROGRAMS WERE APPROVED

ICO FINALIZED
1,238
NEW AGREEMENTS

69

DATA TRANSFER AGREEMENTS



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