USF continued from p. 153

non-confidential fliers that give a [technology] summary, we always ask faculty to review them to make sure we're saying the right things. I think [the portal will] help the faculty have confidence in our office because we're being transparent, and they know what's happening with their invention. They know we're making efforts to market their invention and find a company that will hopefully commercialize their invention."

The bottom line, she says, is more leads result in more licenses. "A lot of it is a matter of numbers," she says. "The more people you have the opportunity to reach out to, the better your chances are."

"I would agree exactly," says Golin. "Yes, we've always engaged with faculty researchers, but [now] they see who we're marketing to. They worked on fliers [prior to the online system's launch], but they did not know all that we have. They now are here in the marketing process, getting a better picture of what goes on and how we're trying to license and get their technologies out to the marketplace."

Contact Golin at lgolin@usf.edu; contact Tyrpak at 813-974-3732 or mtyrpak@usf.edu. ▶

Guest Commentary

NCATS breaks the mold: Case studies of unique tech transfer mechanisms

By: **Ami D. Gadhia, JD, LLM, CLP**
Senior Technology Transfer and Patenting Specialist

Rebecca A. Erwin-Cohen, PhD
Technology Patenting and Licensing Specialist

Krishna (Balki) Balakrishnan, PhD, MBA
Deputy Director

Lili M. Portilla, MPA
Director

Office of Strategic Alliances, National Center for Advancing Translational Sciences (NCATS), National Institutes of Health (NIH)

The National Institutes of Health (NIH) is a unique biomedical institution that is both a granting institution administered by our extramural program and a research enterprise fueled by our Division of Pre-Clinical Innovation (DPI). Very few institutions have both the funding to accomplish health initiatives through grants and contracts, as well as the internal scientific expertise to conduct original research themselves.

One of the 27 Institutes and Centers that form the NIH, the National Center for Advancing Translational Sciences (NCATS) presents an additional rarity in that 70% of the Center's work is inherently collaborative, joining NCATS employees with outside collaborators to carry out scientific work that neither party could do on its own. The collaborative culture at NCATS and the specialized granting mechanisms available within the NIH facilitate NCATS in its mission of advancing the medical translational science field in very broad, far-reaching strokes. For examples of far-reaching advances set in motion by NCATS, please see: https://ncats.nih.gov/research.

NCATS not only innovates in the scientific field, but also explores and practices innovation in technology transfer by establishing novel and creative ways of partnering to advance translational sciences and by using forward thinking grant mechanisms, which university TTOs and their faculty researchers can tap into.

Among the various funding mechanisms used by NIH, the Cooperative Agreement (CA) grant mechanism allows for remarkable flexibility in assembling diverse teams of scientists to define and advance newly emerging fields. In fact, since NCATS was launched as a separate Center within NIH in 2011, the CA mechanism has gained so much popularity within NCATS that approximately 50% of its active grant awards are CA grants. The CA grant stipulates in the Funding Opportunity Announcement (FOA) that a collaborative agreement be executed before the grant can be funded.

The agreement types by which these collaborations are carried out include an inter-institutional agreement (IIA), a research collaboration agreement (RCA), a cooperative research collaboration agreement (C-RCA), or a cooperative research and development agreement (CRADA).

An IIA is the agreement by which joint IP is managed. It allows one party to take the lead in

continued on page 155

NCATS continued from p. 154

patenting and licensing. The RCA, C-RCA, and CRADA are all collaborative agreements which require a research plan. A CRADA is most appropriate where a partner wants to provide funding to NCATS for collaborative work and where there is likely to be joint IP that the partner wants to license. An RCA or C-RCA are more appropriate where there is no funding by the partner. The C-RCA is a collaboration agreement that has CRADA-like properties but contains more streamlined language. The C-RCA facilitates faster negotiations amongst parties, thereby allowing the scientific work to begin sooner.

Of course, prior to entering a collaborative agreement the parties may need to exchange confidential information via a confidential disclosure agreement (CDA). If the parties want to outline their working relationship with broad goals to effectuate their understanding, then they may put in place a memorandum of understanding (MOU) or a Letter of Intent (LOI). And where clinical research may be conducted, then a clinical research agreement (CRA) is appropriate. Depending on the goals of the collaboration, any of these agreements can be used alone or in combination.

To help TTOs understand how they can work with NIH in ways they may not have considered, this article will discuss three case studies where wide-ranging partnerships -- including players from NCATS, industry, and academia -- have been successfully assembled and managed.

The first involves an internal Research & Development project, an academic research partner, and its start-up company. IIA, patents, and licenses are featured in that case study. The second case study is a partnership between an academic center, the NCATS Extramural Program, and the NCATS Intramural program and it utilized a Cooperative Grant Mechanism and the C-RCA. The third and final case study is a program that includes an academic center, the NCATS Extramural Program, and industry. This last case study utilized various technology transfer agreements including the CDA, MOU, and CRA.

Case Study 1

• **Academic + Start-up + NCATS Intramural.** Collaborations, a spin-off company, and a creative approach to funding have helped NCATS navigate its new blood-cell cancer drug through the dreaded preclinical "Valley of Death." NCATS and the Cincinnati Children's Hospital Medical Center, a top-ranked pediatric medical center and research institution, collaborated to develop small molecules for treating myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML). AML and MDS are blood cell cancers that urgently need improved treatments. Collectively, more than 30,000 new cases of MDS and AML are diagnosed in the U.S. each year. The median survival time for MDS is only 2.5 years after diagnosis, and the five-year survival rate for AML is only 27%.

Interleukin-1 receptor-associated kinase (IRAK) and FLT3 kinase enzymes play key roles in driving the progression of AML and MDS. Small-molecule inhibitors of FLT3 have shown initial promise in treating AML. However, FLT3 inhibitors have not led to long-lasting remission, since FLT3 inhibition results in increased compensatory signaling through IRAK1/4. The new treatment co-developed by NCATS and Cincinnati Children's will have potential to provide long-term benefits for MDS and AML by inhibiting both IRAK and FLT3.

NCATS Office of Strategic Alliances (OSA) worked closely with Cincinnati Children's Innovation Ventures to explore pathways to support technology development through the late preclinical development phase (*i.e.*, "Valley of Death"). This phase of product development often fails because it is significantly more expensive than early-stage discovery; it involves lengthy process development, scale-up, and toxicology testing; and it is less likely to receive federal funding.

NCATS entered into an IIA that allowed Cincinnati Children's Innovation Ventures to take the lead in filing patent applications, marketing, and exclusively licensing their joint intellectual property (IP) for the new IRAK/FLT3 inhibitors. The Innovation Ventures team filed and secured patents for the composition of matter and the methods of use for the inhibitors, and they also recruited an experienced entrepreneur-in-residence (EIR) to manage the project operation, coordinate product development by NCATS and Cincinnati Children's investigators, and build the business case for company creation.

The experienced entrepreneur worked with Cincinnati Children's Innovation Ventures for fifteen months prior to company launch. As a result, unlike many university-formed start-ups, it could obtain significant institutional funding upon formation.

continued on page 156

NCATS continued from p. 155

Innovation Ventures then partnered with CincyTech, a Cincinnati-based seed stage venture capital fund, to facilitate funding for the new company, Kurome Therapeutics, whose mission is dedicated specifically to the preclinical and clinical development of the novel IRAK/FLT3 inhibitors. In February 2020, Kurome closed on a $4M seed round led by CincyTech and including several outside investors. The EIR became Kurome's CEO. In April 2021, Kurome closed a $15M Series A round led by an international VC focused on the life sciences sector and an international hedge fund.

NCATS and Innovation Ventures worked together to enable Cincinnati Children's to enter into an exclusive license with Kurome for the IP involved. Cincinnati Children's, Kurome Therapeutics, and NCATS also entered into a cooperative research and development agreement (CRADA), providing Kurome with options to license future IP relevant to the inhibitors. The investment and collaboration under the CRADA have facilitated rapid progression from lead identification (prior to company formation) through lead optimization to development candidate selection in 2.5 years. This type of speed is typically seen only in large pharma/biotech operations, not in a small start-up, and certainly not in most academic institutions. This unique three-way collaboration is a productive and effective model for accelerating translational drug development at both the scientific and commercial levels.

The exclusive license agreement and the CRADA provide Kurome Therapeutics with a sustainable IP portfolio. Since Kurome was founded, it has used the proceeds from its capital raises to fund ongoing preclinical developments by the investigators at NCATS and Cincinnati Children's, dramatically accelerating the drug development. Significant progress has already been made, as a development candidate has been identified, process development initiated, and new patent applications have been filed.

Case Study 2

• **3-D Tissue Bioprinting Program.** The 3-D Tissue Bioprinting Program is a collection of partnerships between various academic centers, the NCATS Extramural Program, and the NCATS Division of Pre-clinical Innovation (DPI). This program was established due to a critical need that exists for cell-based laboratory tests and animal models used during drug discovery that currently are not always predictive of results of the therapeutic in humans. New *in vitro* assays are needed that can better predict effectiveness and toxicity in humans, a challenge that could be assisted by the emerging field of 3-D bioprinting of living tissues.

The 3-D Tissue Bioprinting Program's goal is the development of "disease-relevant tissue models" that more closely mimic human tissues and reduce the predictability gap. The Bioprinting Program utilizes an NIH Cooperative Grant mechanism to solve a problem that required both the NCATS intramural scientists' expertise on a platform technology, and the academic collaborators' knowledge/expertise about the disease model. The cooperative grant mechanism stipulated the need for a collaboration agreement between NCATS and the academic collaborator.

The NCATS Office of Strategic Alliances (OSA) advised the NCATS Program Officers on language to be included in the cooperative grant FOA to ensure that technology transfer and IP provisions would be agreed upon before the grant work could begin. A common C-RCA template was used with all the grantees/collaborators to enable execution of the agreements in a timely fashion and to work within their granting/budgeting constraints.

The academic center, grant program officer, and NCATS DPI all played unique roles in the collaboration. The NCATS DPI scientists provided expertise for 3-D bioprinting, assay development, and high throughput drug screening. The academic center investigators provided appropriate cell resources, disease-specific expertise, and model validation, while the NCATS DPI scientists performed drug screening on bioprinted materials.

One recent example from this program includes a collaboration with the University of Texas Medical Branch and the Texas A&M Engineering Experiment Station. The collaboration centers around the issue of spontaneous preterm birth (PTB), which is a significant contributor to neonatal mortalities and morbidities. Challenges in testing drug transport, metabolic changes, and teratogenicity have hindered PTB drug development. Current *in vitro* cell culture models and animal models have several limitations, prompting the development of several tissue chip models to help overcome limitations; however, they lacked high-throughput screening (HTS) capabilities.

The researchers submitted a proposal to the NCATS Tissue Bioprinting Program to develop a

continued on page 157

NCATS continued from p. 156

high-throughput 3-D bioprinted tissue chip to be used for HTS of large drug libraries. A research plan covering this scientific collaboration was included in the C-RCA that was executed between all three parties. Results would be shared so that the knowledge derived from different improvements are available to the community. The fetal-maternal interface Organ-on-Chips can be used to screen for environmental toxins and provide a novel tool to understand the earliest impact and effect of various drugs on the developing fetus. These innovative tools will be critical to public health efforts to reduce adverse pregnancy outcomes.

Over the years, this program has spawned new collaborations with pharma and biotech companies to enable benchmarking and establish translational capacity for these 3D-printed tissues.

Case Study 3

• **New Therapeutic Uses Program.** Therapeutic development of new drugs is a costly, time-consuming enterprise; thus, repurposing an existing therapeutic candidate for a new disease indication could be extremely worthwhile. NCATS designed its New Therapeutic Uses (NTU) Program for existing molecules. The NTU Program focused on matching academic researchers with pharmaceutical assets to help them test ideas for new therapeutic uses.

Over the years, pharma partners have included: AstraZeneca, AbbVie, Bristol Meyers Squibb, Lilly, Glaxo Smith Kline, Janssen, Mereo BioPharma, Pfizer, and Sanofi. The assets selected for the NTU Program had undergone at least some clinical studies and had an acceptable safety profile that allowed further clinical investigation for other therapeutic uses. The program supported studies through Phase II clinical trials, and each investigator filed an investigator-sponsored Investigational New Drug application (IND) with the FDA to conduct the proposed clinical trials. While this program is sunsetting, its architecture as well as the agreements used are informative for future programs.

From a technology transfer perspective, the NTU Program was set up for success because it provided a clear IP roadmap. Participating pharma company partners retained ownership of their compounds. The academic medical center (AMC) partners owned any IP they discovered through the research project with the right to publish the results of their work. The pharma company collaborator had the first option to license the academic research partners' new IP arising out of the research.

The program also incorporated innovative template agreements, for each company, that were designed to streamline the process and reduce prolonged negotiations. These template agreements included: an MOU between NCATS and a pharmaceutical company; a confidential disclosure agreement (CDA) between an AMC and a pharma company; and a collaborative research agreement between an AMC and a pharma company. The collaborative research agreement became a useful template to many AMCs who were not a part of this NTU program simply as model agreement for their pharma collaborations. The agreement templates were downloaded more than 700 times.

An example of an NTU creative collaborative structure is a partnership between NCATS, the University of Alabama-Birmingham (UAB), and AstraZeneca. This project involved Alpha-1 antitrypsin deficiency (AATD), which is the most common genetic cause of chronic obstructive pulmonary disease and emphysema. Individuals with AATD have extremely low plasma and lung levels of AAT, a protein that helps lung tissue remain elastic and flexible. Current treatments for AATD are invasive, expensive, and do not permanently slow the development of lung damage.

UAB scientists later partnered with NCATS and Mereo BioPharma to create a multidisciplinary team to study the safety, tolerability, and effectiveness of AZD9668 as an improved, noninvasive treatment for patients with AATD. (Note that AstraZeneca out licensed the drug to Mereo BioPharma.)

From the technology transfer perspective, the partnership between industry, academia, and a government extramural program represents the trifecta of cooperative collaboration. The impact of these innovative partnerships is evident in the outcome: Mereo BioPharma recently reported results from their Phase II trial indicating both a high degree of efficacy and safety of the drug in a trial of 99 patients with severe AATD-related lung disease.

In summary, NCATS tailors its research programs to meet the institutional mission "to get more treatments to more patients more quickly" using a team-based approach. As such, the Center may partner with other government agencies, academia, industry, and nonprofit patient organizations.

continued on page 158

NCATS continued from p. 157

No single organization can succeed alone as effectively as when they synergize their efforts with other organizations with complementary capabilities. These three case studies illustrate that point. Each case study utilized various technology transfer mechanisms including the new cooperative research collaboration agreement (C-RCA). The mechanisms allowed for collaboration and public-private-partnerships to commence promptly, thereby accelerating scientific work. This acceleration through successful partnerships has resulted in numerous publications, clinical trials, and tangible treatments to benefit people with unmet health needs. ▶

TTO uses targeted webinars to educate faculty innovators

Although no one would argue that the world is a better place due to the COVID-19 pandemic, there have been a few unexpected positives, particularly in new ways of communicating necessitated by lack of in-person meetings. In many cases these changes, implemented out of necessity, have been adopted into regular practice even as the world has veered back toward normalcy. The University of Kentucky (UK) Office of Technology Commercialization's (OTC) continuation of an educational outreach program they started when they were unable to hold in-person learning opportunities for their faculty is a perfect case in point.

"COVID hit, I realized that we couldn't go see people in person," says **Jacqueline (Jacqui) J. Greene**, director of marketing and communications for UK Innovate at the University of Kentucky. "So, we began doing the monthly webinars. They've been very successful, so we continue to do them even though we still do some in-person faculty education."

Green welcomes any effective means of communication with faculty inventors, and the regular webinars have certainly fit the bill. "For us, success is providing an avenue to educate faculty on our work and those things they need to know to protect their innovations," she comments. "We need to be making a difference with our faculty and helping them learn something new."

The webinar topics generally cover subjects that are beneficial for any faculty member on campus who is interested in commercialization. Topics so far have included:

- "How Can the Commercialization Team Help You," which introduced the webinar series as well as the entire commercialization team, who discussed how they work with faculty.
- "New Innovation Disclosure Process," with presenter Matt Upton, senior associate director of intellectual property development, giving step-by-step instructions for faculty using the OTC's new electronic innovation disclosure form.
- "Death of the LLC," with Eric Hartman, senior associate director of commercialization, who discussed how the OTC can help start-ups decide on the best corporate structure and advise them on how to interpret the advice the get from their accountant or attorney.
- "Everything You Need to Know About Agreements 2022," scheduled for broadcast in October, in which the agreements team will discuss which contracts innovators need and when they need them.

There are a few ways in which they come up with topics. Sometimes, when there is something new, like the new disclosure process, it was obvious that they should hold a webinar to walk people through the system. Other times, they realize that there are certain topics, like agreements, that they talk about frequently but that new faculty may not know much about.

"These topics typically come from OTC's staff who speak with many faculty, who let them know the areas where they'd like to learn more," says Greene. "There are new faculty or people who haven't been to one of our webinars, and we want to make sure they understand things like Material Transfer Agreements, Non-Disclosures Agreements, and Data Use Agreements. It's important for faculty to know that process, and that they need it to protect their materials and the research that they're doing."

Greene also picks up potential topics while attending IP, commercialization, and contract team meetings. "I hear a lot of the conversations they are having that may spark an idea. We start seeing patterns," she notes. "For example, LLC used to be the thing. But now it's not the primary [structure] that we would recommend for a start-up. And so, we thought it was important to do a webinar so that we could get

continued on page 159