Academic-industrial partnerships convey a cultural shift

Today, academic-industrial partnerships are part of an integrated development strategy for any of the world's top ten pharmaceutical companies and a growing number of academic institutions.

BY BARBARA NASTO

The long view on academic-industrial partnering trends reveals a cultural shift in the direction of openness and cooperation for both academic research institutes and the pharmaceutical industry. Conversations with experts from both camps point to two main factors driving a trend that dates back to the 1960s: the emergence of financial pressures on academic institutions and a better grasp on just how complex the biology of humans can be.

"What we have seen in the last eight years is a return of interest from the pharma companies in working directly with universities," described Lita Nelsen, who has worked in MIT's Technology Licensing Office since 1986. Along with other stalwarts such as the University of Oxford and, of course, the University of California, MIT consistently makes the list of the most active universities engaging in partnering deals with the pharmaceutical industry.

"The big thing pushing the scientists is the decline in the NIH funding," Nelsen stated. After increasing year on year from 1995 to 2002, appropriations for the US National Institutes of Health have been, in the relative sense, flat since 2003.

"In real dollar terms, it is cutting," explained Nelsen. "Other [granting] agencies are declining, and a lot of universities and research hospitals are feeling the pinch. Universities are vocal about making up the fall in funding."

Nelsen also thinks that a decline in investment over the decades for biotech companies led to "more interest in their [pharma companies'] doing work directly with the academics. New products coming from biotech were coming from academia, and new biotech companies were not getting formed when investors became skittish. These days almost all the [large pharma] companies have one form or another [of an] investor arm."

Spreading entrepreneurism

On the topic of entrepreneurism becoming more palatable to individual academic researchers, Nelsen said: "With a sufficient success and respectable success with the top academics, [it came to be] considered a way in which you get the results of your pure science into real people." This view is echoed by Ferran Prat's experience as vice president for Strategic Industry Ventures at the University of Texas' MD Anderson Cancer Center. Pratt's post was created two years ago. A former research chemist with a law degree, Prat is directly responsible for connecting researchers at the center with pharmaceutical companies.

"Most faculty got on board very quickly and saw there is a better way," said Prat, who described the appointment of Ronald DePinho, the fourth president of MD Anderson, as a turning point in the history of the University of Texas' cancer research center. An experienced entrepreneur (he co-founded Aveo Biotech), DePinho left a position as director of the Belfer Institute for Applied Cancer Science at the Dana-Farber Cancer Institute to assume the presidency.

"The shifting culture in the institution has been very surprising and very swift," Prat explained as he described a general willingness among the university's researchers to attend presentations and training sessions he provides on tech transfer. "It was agreed at a high level that we all wanted to to be part of strategic relationships that can change the standard of care," in contrast to "one-off projects that once required multiple levels of review just to obtain a few grams of the drug."

MD Anderson is a recent entry to the top-deals table for academic-industrial collaborations. Five of the top pharmaceutical companies signed deals with MD Anderson in 2014 (see *BioEntrepreneur* Data Page, March 2015[1]). Three—AstraZeneca, GlaxoSmithKline (GSK) and Pfizer—are participating in the Moon Shots Program, which is co-chaired by the leading cancer immunology scientist, Jim Allison.

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Allison published a landmark paper on immune-checkpoint inhibition and CTL-4 in 1996[2]. The research led to a greater understanding of how cancer could evade the immune system and eventually led to the development of Yervoy for the treatment of melanoma. MD Anderson's Moon Shots Program was devised to apply immune-checkpoint targeting to develop treatments for a range of cancer indications.

A native of Texas, Allison accepted the post in 2012 after a career that included appointments at Dana-Farber, the Ludwig Institute for Cancer Research, Memorial Sloan Kettering and the University of California, Berkeley. Two other leading clinical cancer researchers, Patrick Hwu and Padmanee Sharma, are the other Moon Shots chairpersons. Sharma and Allison recently founded the biotech startup Jounce Therapeutics.

Translating complementarity

"Pharmaceutical companies have a shared interest with academic centers," commented Robert Urban, Head of Johnson and Johnson Innovation Center in Boston. Nelsen elaborated on distinctions that serve to maintain their complementarity. "Long-range research is trying to understand the fundamentals; companies are product and project orientated. One is supposed to be driven by pushing the frontiers of knowledge. Who would have thought studying eye color in fruit flies could spark a genetic revolution?"

Other changes in recent decades include a loss of naiveté with respect to just how complex the so-called big questions are: "First we had the human genome, and we thought we had it knocked [on the head]," noted Nelson. "Now there is the epigenome. We certainly don't have it knocked. And it's not one gene, one protein. I think we are just beginning to learn how hard they [the big questions] are."

"The big ideas need to come from the science," opined Susan Galbraith, AstraZeneca's vice president of oncology and head of the Oncology Innovative Medicine unit, while discussing academic partnerships in the context of fueling the company's cancer pipeline. "You cannot have a monopoly on all the good ideas. We look at the total number of people working in the space, and it is their ideas that need to prompt the next wave. Our internal resources compose a small fraction of the effort."

Galbraith went on to state that access to patients, better preclinical models and proximity to AstraZeneca's Boston-based research center motivated the company to collaborate with Dana-Farber on the development of AZD9291. A lung cancer therapy, AZD9291 targets the T790M mutation that mediates drug resistance to anti–epidermal-growth-factor receptor (EGFR)–tyrosine kinase inhibitors. When resistance to the targeted therapies emerged in lung cancer patients, an academic research group at Harvard was among those that set out to determine the mechanism[3]. AZD9291 is currently in phase 1/2 trials to treat EGFR-positive lung cancer patients.

MIT. Lita Nelsen has served in MIT's licensing office since 1986.

"I think it is important to take a dual approach based on what you know and maintain a more open view. I think you need that duality," emphasized Galbraith, who went on to describe AstraZeneca's collaboration with the Medical Research Council (MRC). The MRC is an organization that provides research grants to academics in the UK.

Last year AstraZeneca agreed to create a high-throughput drug screening facility and provide MRC researchers with access to the facility and to their therapeutic compound library. "They screen the library for the targets they choose, over two million molecules. We may be interested [in taking their findings further], but they [the scientists] are not solely restricted [to dealing with AstraZeneca. The benefit is that] it enables a scientific exchange of information."

AstraZeneca's relocation to Cambridge, UK also promises to entrench ties with the University of Cambridge's biomedical research community, which includes the MRC Cancer Unit, Cancer Research UK's Cambridge Institute and Addenbrooke's Hospital. The site of AstraZeneca's new global research and development center and corporate headquarters (currently under construction) is shared by Cancer Research UK's Cambridge Institute. Up to 60 AstraZeneca scientists will be working in the Institute for three years while their laboratories are being built.

"They are being helpful in making room for us in the Cambridge Institute," said Galbraith. "Our scientists and theirs will be side by side working with cancer biology. The agreement is cooperative and nonspecific. The exchange of ideas promises to be mutually beneficial." She added, "We have conducted multiple clinical trial investigations and collaborated with Cancer Research UK on a number of clinical and preclinical oncology projects. We are simply building onto those existing collaborations."

A high level of flexibility is also apparent in the approach taken by Johnson & Johnson, the company that ranked second in BioCentury's academic partnering deals tally for 2014[1]. "Johnson & Johnson enters without preconceived notions," described Urban, "The question we ask is, 'How we might work to get to the same objective?' It could mean sponsored research, a collaborative exchange or an exchange of materials with a laboratory."

"Unique insights are wonderfully present in academia," according to Urban, who explained that the remit for relationships with academia goes beyond pharmaceuticals and also channels into the company's consumer and med tech divisions.

"Every disease can benefit from a better understanding, and some areas need these collaborations more than others. Neuroscience has a long way to go and is particularly deeply dependent on the relationship between academia and industry. The microbiome is another one." Both neuroscience and the microbiome are strategic research areas for Johnson & Johnson Innovation.

Some parallel aspects of AstraZeneca's and Johnson & Johnson's academic engagement strategies, such as having academic and industrial research scientists work side by side, are now widely used by the industry. "We have a team of drug developers working alongside academics in search of models that are robust and relevant to biomarkers at Dana Farber," Urban noted.

Number 3?

In 2014, the BCIQ database indicated Johnson & Johnson had the second highest number of deals with academic institutions, 3 deals behind AstraZeneca's 18. GSK was listed as the third most active company (in total number of deals), with 13 deals taking place that year. In a discussion about the third-place ranking, Malcolm Skingle, director of academic liaison at GSK, expressed surprise that GSK was not first.

To be fair, deals data is not the only measure of the pharmaceutical industry's interaction with academia. Skingle points to a survey conducted by the British Pharmaceutical Industry Association that tracked, among other parameters, the number of post-doctoral positions sponsored by the pharmaceutical industry. "GSK blows the others away relative to post-doc grants," Skingle emphasized.

Reiterating Nelsen's view on increased interest in working with academia, Skingle added: "It [Interest in working with academia] certainly has grown; we [the pharma industry] do not have a monopoly on all ideas and we are never going to be able to do all the science. Consortia are a good option for when you cannot find the science on our own. The human genome forced some great science."

On the topic of what universities gain from industrial collaborations, Skingle asserted, "Universities want to work with us because they see the value of our science. It is a true intellectual collaboration pushing the frontiers of science forward." He continued: "The company has better tools to validate their work and can test hypotheses with better molecules."

Skingle noted that some GSK collaborations "teach academics drug discovery. We have unique discovery partnerships with two to three academic groups where we co-project-manage early development milestones. The academics can eventually go out on their own or with competitors."

Among GSK's many academic-engagement programs is their Discovery Fast-Track Challenge. The program is an open call to scientists in Europe, Canada and the United States who may wish to participate. Members of the academic research community are invited to submit details about the biological targets or pathways they are researching and provide the scientific rationale on how their research could be applied directly to future drug development. GSK announced a challenge for the third time in March 2015.

GSK will select up to 12 proposals, and the scientists who submitted them will have the opportunity to collaborate with two relevant teams at GSK: the Discovery Partnerships with Academia (or DPAc) team and the Molecular Discovery Research team. The challenge bears a resemblance to open innovation initiatives that have become popular with pharmaceutical companies. "We cultivate a range [of academic relations] through our Open Innovation website," explained Galbraith. The website (http://openinnovation.astrazeneca.com/) outlines offerings along the entire drug development chain from broad access to compounds for clinical and preclinical research, and also offers an open invitation to share drug target ideas directed to succinct objectives, such as a direct challenge to develop clinically relevant models for diffuse large B cell lymphoma. Meanwhile, Johnson & Johnson Innovation's Idea Portal (http://www.jnjinnovation.com/partner-with-us) extends an open invitation to patented ideas that align with the company's business priorities.

Providing infrastructure for promising translational science is another strategy implemented by large pharmaceutical companies seeking to optimize the translation of research to application. In an effort to stimulate new ways of thinking about how research is carried out, GSK created the Tres Cantos Open Lab Foundation, a nonprofit in Madrid that provides lab space to external scientists and academics who are working on neglected diseases.

"Consider just how much we [the industry] do for diseases of the developing world just because it is the right thing to do," Skingle challenged. To

put some numbers to the Tres Cantos Foundation endeavor, GSK donated £5 million in January 2010 to set up an independent charity. In 2012, the company doubled the funding (£10 million) in the hope that the amount (with other donations) could sustain the flow of around ten early-stage drug discovery projects to be maintained at the open lab. Currently the foundation employs 100 scientist with a range of experience in chemistry, biology, biochemistry, toxicology, assay development, and *in vivo*, *in vitro* and high-throughput screening. The Campus has partnerships with other nonprofit groups focused on neglected diseases, including the Medicines for Malaria Venture (MMV), the Global Alliance for TB Drug Development (GATB), the Drugs for Neglected Disease Initiative (DNDi) and the Wellcome Trust. GSK invites proposals from research bodies that believe the foundation's collaborative atmosphere can help to advance their research.

More recently, GSK announced another innovative infrastructure partnership with the University of North Carolina at Chapel Hill (UNC) that will focus on discovering a cure for AIDS. The two agreed to establish an HIV Care Centre on the university's campus and create a jointly owned company, Qura, to handle the business side of the partnership, including intellectual property, commercialization, manufacturing and governance. GSK will invest $4 million per year for five years to fund the initial HIV Care Center research plan, and a small research team from GSK will move to Chapel Hill to be colocated with UNC researchers. Like the Tres Cantos Foundation, the HIV Cure Center and Qura Therapeutics are meant to serve as catalysts for engaging additional partners and funding from organizations and governments that share in the interest of eradicating HIV.

Johnson and Johnson innovation's J-LABS is another example of incubation space provided to start-ups by a pharmaceutical company. "There is a point when you move away," Urban explained. "J-LABS underwrites the costs and organizes for an efficient transfer [of assets]." Starting a company at J-LABS comes with no strings attached. Established in San Diego, San Francisco and Boston, JLABs is undergoing expansion to include locations in South San Francisco and Houston).

References

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BOX 1: CONSORTIA AND BIG QUESTIONS

Founded in 2008, the Quebec Consortium for Drug Discovery (CQDM) is a manifestation of the idea that no one lab or one company possesses all the resources necessary to address complex interrogations associated with drug development. Motivated by the changing pharmaceutical landscape which had undergone a great deal of consolidation in Quebec and Toronto, Canada's federal government was keen to support translational research. Based at Université Laval, CQDM's funding program solely promotes the development of new technologies that will enhance and accelerate drug discovery. Remarkably, nine of the major pharmaceutical companies have joined the non-profit's pre-competitve research consortium.

"At the time, there was a strong presence of industry in Quebec," CQDM President and CEO Diane Gosselin explained. "Merck Pfizer and Astra Zeneca were very active and willing to work together. The difficulty in developing new molecules for drug development was apparent. And, we all thought we should see if we can work together to solve these problems."

CQDM applies an open innovation, collaborative R&D model to stimulate pre-competitive research coordinating grant competitions for early stage biotech, and academic and public institutions in Canada. Pfizer, Merck and Astra Zeneca are founding members. Boehringer Ingelheim, Janssen, GSK, Novartis, Lilly and Sanofi are now also members taking part in the funding programs coordinated by CQDM.

When asked about how CQDM manages to avoid conflicts of interests for the 9 companies, Gosselin explained, "We spend time on how we can improve the process [of drug development] and leverage funding tools to support research projects that will have an impact. At the end of the project, the scientists can use the tool for research purposes and companies have a fully paid off tool they can use to accelerate their own research."

To date, CQDM has established 7 programs, organized 22 competitions and delegated $645 million in funding. The programs take drug development to the multidisciplinary edges of science. For example, the EXPLORE program provides funds for early concept validation of computational tools and other novel approaches to drug development.

High throughput biosensors developed by Michel Bouvier of Université de Montréal are an example of successful technology that has been spun out from academic research. Designed to identify cellular events associated with drug therapies, the multiplexed biosensors marked a stark improvement over single function assays used for screening drug candidates interacting with G-protein coupled receptors. Pfizer liked the results so much they decided to invest 700 thousand to develop a customized platform with Bouvier. The original platform was also licensed to Domain Therapeutics, a French based company developing QCPR-targeted therapies.

"When I first presented the idea to academics, I had the feeling people would throw tomatoes. It met with skepticism and people raised the question: what is in it for me?," Gosselin described. What happened next implicates the catalyst for change described by Nelsen. "We identified some strong projects and publicized how they created benefit for the academic culture. Every researcher wants to have an impact."

Quebec City. The scenic city is home to Université Laval and the CQDM.